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DOUTORADO EM ODONTOLOGIA

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**CONSUMO DE BEBIDAS RICAS EM AÇÚCARES DE ADIÇÃO: INVESTIGANDO
AS REDES DE INTERAÇÕES DAS DOENÇAS CRÔNICAS NÃO TRANSMISSÍVEIS
BUCAIS E SISTÊMICAS NOS CICLOS DA VIDA**

SÃO LUÍS

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Tese apresentada ao Programa de Pós- Graduação em Odontologia da Universidade Federal do Maranhão como requisito parcial à obtenção do título de Doutor em Odontologia.

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Silas Alves Costa

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COSTA, Silas Alves. **Consumo de bebidas ricas em açúcares de adição: investigando as redes de interações das doenças crônicas não transmissíveis bucais e sistêmicas nos ciclos da vida**, 2025, Tese (Doutorado em Odontologia) – Programa de Pós-graduação em Odontologia, Universidade Federal do Maranhão, São Luís, 345p.

RESUMO

A abordagem de redes complexas desponta como uma ferramenta promissora para explorar a intrincada teia de interações entre os fatores de risco das doenças crônicas não transmissíveis (DCNTs) bucais e sistêmicas. Essa perspectiva permite compreender como essas conexões se organizam e se transformam ao longo do curso da vida, desde os primeiros anos até a idade adulta, além de identificar alvos estratégicos para o desenvolvimento de políticas públicas e intervenções que contribuam para a redução da carga dessas doenças. Esta tese é composta por sete capítulos. Os dois primeiros capítulos apresentam uma abordagem inicial sobre a relação entre a periodontite e fatores de risco comportamentais e metabólicos, com ênfase no consumo de bebidas ricas em açúcares de adição, principal fonte de calorias discricionárias na dieta ocidental. Os três capítulos seguintes aprofundam a investigação por meio da aplicação da análise de redes complexas, com o objetivo de explorar as inter-relações entre doenças bucais e sistêmicas, bem como seus fatores de risco comuns, em distintas fases do ciclo vital. O sexto capítulo amplia o escopo da tese ao examinar a disseminação global do consumo de bebidas ricas em açúcares de adição e projetar seu impacto até o ano de 2050. Por fim, o capítulo final dedica-se à tradução do conhecimento gerado neste doutorado para a sociedade, por meio da elaboração de um livro digital voltado a cirurgiões-dentistas, que aborda de forma inédita a Teoria das Origens do Desenvolvimento da Saúde e da Doença (DOHaD) aplicada à Odontologia. No CAPÍTULO 1, levantamos a hipótese de que a prevalência de periodontite no Brasil tem aumentando nas últimas três décadas, acompanhada por um maior consumo das bebidas ricas em açúcares de adição, e que resultou no artigo original **“Behavioral and metabolic risk factors associated with periodontitis in Brazil, 1990-2019: a multidimensional analysis for the Global Burden of Disease Study 2019”**, publicado na revista *Clinical Oral Investigations* (Fator de Impacto 3.1, DOI: 10.1007/s00784-023-05384-6). Este estudo teve como objetivo analisar a relação entre periodontite e os fatores de risco comportamentais e metabólicos comuns às DCNTs em adultos brasileiros ao longo de três décadas. Para isso, foram utilizados dados do estudo *Global Burden of Disease Study 2019*. A análise foi conduzida por meio da regressão de Prais-Winsten, a fim de identificar tendências nas séries temporais, e da regressão de efeitos fixos, para investigar as associações entre as

variáveis. Os resultados indicaram que, desde 2005, a prevalência de periodontite tem aumentado no Brasil, mesmo diante da redução do tabagismo. Além disso, a doença periodontal mostrou-se associada ao consumo de bebidas ricas em açúcares de adição, ao sobrepeso/obesidade, à dislipidemia e à hiperglicemia. Esses achados oferecem uma nova perspectiva sobre a inter-relação entre periodontite e DCNTs, destacando a relevância de estratégias preventivas centradas em fatores comportamentais e metabólicos. Este estudo também marcou o início do contato com os Programas de Pós-graduação em Odontologia (PPGO-UFMA), Ciências da Saúde (PPGCS-UFMA) e Ciências da Computação (PPGCC-UFMA) no âmbito do Programa de Desenvolvimento da Pós-Graduação na Amazônia Legal (PDPG Amazônia Legal-CAPES), pelo qual recebo minha bolsa de doutorado. Além disso, este estudo foi decisivo para o início da minha parceria com um pesquisador da *Duke-NUS Medical School Medical School*, em Singapura, que posteriormente se tornaria meu coorientador. Após a publicação do primeiro artigo, tive a oportunidade de realizar um estágio de doutorado sanduíche na instituição, com apoio financeiro do Programa Nacional de Cooperação Acadêmica na Amazônia (PROCAD Amazônia-CAPES). Durante esse período, aprofundi meus conhecimentos analíticos e avancei na compreensão das inter-relações entre fatores comportamentais e metabólicos na periodontite. O produto desse estágio corresponde ao CAPÍTULO 2 desta tese, que foi o artigo original intitulado **“Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study”**, que foi publicado no *Journal of Clinical Periodontology* (Fator de Impacto 6.8, DOI: 10.1111/jcpe.13961). Este estudo investigou a relação entre o consumo de bebidas ricas em açúcares de adição e a periodontite, utilizando dados da *National Health and Nutrition Examination Survey (NHANES III)*, envolvendo adultos americanos com idades entre 30 e 50 anos. O consumo das bebidas foi associado a periodontite quando os indivíduos consumiram ≥ 5 , ≥ 7 e ≥ 14 vezes por semana. Os resultados contribuem para o entendimento dos fatores que influenciam a saúde bucal e ressaltam a importância de intervenções direcionadas à prevenção do consumo excessivo dessas bebidas. Esses achados nos motivaram a aprofundar a compreensão das interconexões entre as DCNTs bucais e sistêmicas, uma vez que o consumo de açúcar parece ser um ponto comum a todas elas. Essa perspectiva nos levou a formular a terceira hipótese deste estudo: as DCNTs estariam interligadas desde os primeiros anos de vida, com sua complexidade crescendo à medida que novos órgãos e sistemas são afetados com o avançar da idade. Para compreender melhor a dinâmica dessas doenças e suas inter-relações, buscamos uma colaboração estreita com o Instituto de Ciências Matemáticas e de Computação (ICMC/USP), o que possibilitou a aplicação de abordagens analíticas avançadas em redes

complexas. O CAPÍTULO 3 desta tese é baseado no artigo original intitulado **“Caries Is the Hub of a Complex Network of Chronic Diseases across the Life Decades”**, que foi publicado no *Journal of Dental Research* (Fator de Impacto 5.9, DOI: 10.1177/00220345251317487). Este estudo explorou as interconexões das DCNTs em todas as fases da vida, usando uma análise de rede complexa para desvendar caminhos que podem dar suporte para estratégias de intervenção aprimoradas, melhorando o gerenciamento das DCNTs desde a infância até a velhice. A pesquisa utilizou dados dos ciclos de 2011-2012 e 2013-2014 da *National Health and Nutrition Examination Survey (NHANES)*, que incluíram indicadores de riscos metabólicos, diabetes, câncer, doenças cardiovasculares, autoimunes, respiratórias, mentais e bucais. Desde os primeiros anos de vida, a cárie esteve intimamente ligada ao sobrepeso/obesidade e a asma, e à medida que a idade avançava, novas doenças se conectavam, aumentando a complexidade da rede. A depressão teve um papel essencial na vida adulta, enquanto, na velhice, episódios de esquecimento e confusão mental passaram a ter maior importância. A centralidade do diabetes, doenças cardiovasculares e câncer aumentou com a idade, atingindo seu pico na faixa etária de 60 anos ou mais, sendo o diabetes a condição mais proeminente. Os resultados indicaram que todas as faixas etárias apresentaram altos coeficientes de agrupamento entre as DCNTs, evidenciando a interdependência entre as doenças. A cárie dentária permaneceu como o elemento central (hub) ao longo das décadas, com outras condições de saúde orbitando ao seu redor. O estudo representou um avanço significativo na aplicação de redes complexas como ferramenta analítica, proporcionando uma visão mais clara e dinâmica das relações entre as doenças, sendo um direcionamento mais preciso das intervenções para reduzir a carga das DCNTs na população. Os resultados obtidos no capítulo anterior, mapeando as interconexões entre as DCNTs ao longo da vida, incentivaram uma investigação mais aprofundada, não apenas sobre as doenças em si, mas também sobre seus determinantes sociais, além dos fatores de risco comportamentais e metabólicos em adolescentes brasileiros. A adolescência é um período sensível do desenvolvimento, em que padrões que moldam o desenvolvimento das DCNTs podem ser identificados, permitindo intervenções com maior impacto preventivo. Assim, o CAPÍTULO 4 resultou no artigo original intitulado **“High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the Complex Network of Non-Communicable Diseases in Adolescents”**, publicado na *Diabetology & Metabolic Syndrome* (Fator de Impacto 3.9, DOI: 10.1186/s13098-024-01469-8). Este estudo utilizou dados do Consórcio de Coortes RPS da cidade de São Luís, no seguimento dos adolescentes de 18 a 19 anos (n=2.515). A partir de uma análise de redes complexas, investigamos como variáveis socioeconômicas,

comportamentais e metabólicas, incluindo renda, dieta, qualidade do sono, índice TyG (indicador de resistência insulínica), e condições crônicas como depressão, asma, cárie e periodontite, interagem e moldam a dinâmica das DCNTs nessa faixa etária. Para caracterizar a rede, utilizamos métricas como grau, intermediação, valor de autovetor, transitividade local, entropia de Shannon e coeficientes de agrupamento. Os resultados destacaram três hubs principais na rede geral: dieta rica em açúcares livres, resistência à insulina e baixa classe socioeconômica. Entre os meninos, baixa ingestão de fibras e alta razão triglicérides/HDL destacaram-se como marcadores de risco cardiometabólico. Já entre as meninas, comportamento sedentário e sono inadequado estiveram fortemente associados a desfechos metabólicos e psicológicos. Em ambos os sexos, a cárie dentária reafirmou o papel central da saúde bucal na interação com condições sistêmicas. Estes achados reforçam a adolescência como um período estratégico para intervenções integradas que abordem os elementos centrais identificados. A compreensão da adolescência como uma janela de oportunidade para a prevenção das DCNTs ampliou a nossa perspectiva sobre a importância de investigar fases mais precoces do ciclo de vida. Nesse sentido, o CAPÍTULO 5 aprofunda a investigação das raízes transgeracionais das DCNTs, explorando exposições durante a gestação e nos primeiros anos de vida, com o artigo **“Decoding the Complexity of Health-Related Factors Connections around the First Thousand Days of Life: Network Analysis”**. O manuscrito será submetido à revista científica *Pediatrics* (Fator de Impacto 6.4). Este estudo utilizou dados da Coorte BRISA Pré-Natal, em São Luís (N=1.383), com dados coletados em três momentos: entre a 22ª e 25ª semanas de gestação, no nascimento no momento do parto, e no segundo ano de vida da criança. A análise da rede foi baseada no índice de Jaccard para identificar padrões de coocorrência, complementada pela caracterização com métricas de centralidade e medidas de agrupamento. A rede construída revelou alta conectividade entre os fatores analisados. Emergiram como hubs o consumo de alimentos ultraprocessados, bebidas ricas em açúcares, baixa condição socioeconômica e cárie dentária durante a gestação. O consumo de bebidas ricas em açúcares e a baixa condição socioeconômica na gestação apresentaram fortes vínculos com todos os desfechos adversos ao nascimento. Subsequentemente, no segundo ano de vida, novos hubs foram identificados: exposição a açúcares, alergias e aleitamento materno não exclusivo. Em relação ao início das DCNTs na infância, fatores como a ingestão materna de alimentos ultraprocessados e bebidas ricas em açúcares, baixa condição socioeconômica, anemia e cárie durante a gestação, juntamente com a exposição precoce a açúcares no segundo ano de vida, mostraram-se fortemente ligados ao desenvolvimento de alergias, excesso de peso/obesidade, asma e cárie em crianças. Esses achados reforçam que os fatores socioeconômicos, os riscos

comportamentais e as condições de saúde sistêmica e bucal durante a gestação exercem uma influência decisiva sobre desfechos adversos ao nascimento e surgimento precoce das DCNTs, evidenciando a importância de intervenções antecipadas para interromper o ciclo transgeracional dessas doenças. O CAPÍTULO 6 apresenta o artigo **“Global, regional, and national burden of high sugar-sweetened beverages consumption, 1990-2021, with projections up to 2050: a systematic analysis for the Global Burden of Disease Study 2021”**, publicado no *The American Journal of Clinical Nutrition* (Factor de Impacto 6.9, DOI: 10.1016/j.ajcnut.2025.07.033). O estudo investigou a carga global do consumo excessivo de bebidas ricas em açúcares de adição ao longo das três últimas décadas e a projeção até 2050, bem como seu impacto na carga de DCNTs. Utilizamos dados do *Global Burden of Disease Study 2021* para estimar a exposição populacional a um alto consumo dessas bebidas e a carga de DCNTs atribuída a este comportamento, incluindo doenças cardiovasculares, diabetes e doenças renais. Para avaliar os impactos, analisamos taxas de mortalidade, anos vividos com incapacidade (YLDs), anos de vida perdidos (YLLs) e anos de vida ajustados por incapacidade (DALYs). Projeções das taxas de exposição essas bebidas foram realizadas utilizando modelos de ensemble baseados no Índice Socioeconômico Demográfico (SDI). Os achados revelaram que, em 2021, o valor de exposição populacional global ao consumo elevado foi de 30,56%, sendo mais alto nas super-regiões de alta renda e América Latina e Caribe. Observou-se uma correlação entre o aumento do consumo de bebidas ricas em açúcares de adição e o SDI, com maiores taxas em países mais desenvolvidos. A carga global de DCNTs atribuída ao consumo de bebidas ricas em açúcares de adição incluiu uma taxa padronizada por idade de 0,89 mortes por 100.000 habitantes e 41,39 DALYs. As projeções indicam um aumento de +9,54% no consumo global dessas bebidas até 2050. Este estudo evidenciou o impacto crescente das bebidas ricas em açúcares de adição na carga global das DCNTs ao longo das últimas três décadas, apontando para um cenário ainda mais preocupante no futuro, caso medidas de saúde pública não sejam implementadas com eficácia. Os achados reforçam a urgência de políticas específicas voltadas à redução do consumo dessas bebidas, especialmente em regiões mais vulneráveis. O CAPÍTULO 7 desta tese apresenta a construção de um livro digital voltado à prevenção das DCNTs a partir dos primeiros mil dias fundamentada nas evidências da Teoria do Desenvolvimento das Origens da Saúde e da Doença (DOHaD) com enfoque na Odontologia, intitulado **“Os primeiros mil dias de vida: a odontologia na perspectiva DOHaD”**. O material foi elaborado em na versão em português (<https://ares.unasus.gov.br/acervo/handle/ARES/27271>) e em inglês (<https://ares.unasus.gov.br/acervo/handle/ARES/29558>). As publicações foram fundamentadas

em quatro premissas centrais informadas pelo arcabouço DOHaD: (1) a cárie dentária está associada a asma infantil, obesidade e é preditora de futuras doenças como diabetes e doenças cardiovasculares; (2) o consumo de alimentos ultraprocessados e de açúcar é um fator de risco importante para DCNTs bucais e sistêmicas; (3) a desequilíbrio do microbioma afeta a saúde bucal e sistêmica; e (4) o aleitamento materno exerce efeito protetor. A edição em português alcançou mais de 7.000 acessos no Brasil e em outros países, como Estados Unidos, Reino Unido, Alemanha, Irlanda, Suécia e Japão, impulsionando o lançamento da versão em inglês para ampliar seu alcance e impacto. Esta obra constitui o primeiro livro a abordar o arcabouço DOHaD no campo da Odontologia, contribuindo de maneira significativa para o avanço teórico da área. Como recurso educativo inovador, a publicação promove a formação profissional e o fortalecimento de práticas de atenção integral à saúde, destacando o valor de iniciativas interdisciplinares na disseminação do conhecimento orientado pelo DOHaD em escala global. A tese tem os açúcares de adição, em especial nas bebidas ricas em açúcares, um eixo comum nas redes complexas de saúde, associados a doenças bucais e outras DCNTs, destacando a necessidade urgente de políticas públicas coordenadas para redução deste consumo.

Palavras-chave: Doenças não transmissíveis; Cárie dentária; Periodontite; Bebidas ricas em açúcares de adição; Fatores comportamentais e metabólicos; Redes complexas.

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ABSTRACT

The complex network approach emerges as a promising tool to explore the intricate web of interactions among the risk factors for both oral and systemic non-communicable diseases (NCDs). This perspective allows for an understanding of how these connections are organized and evolve throughout the life course, from early years to adulthood, while also identifying strategic targets for the development of public policies and interventions aimed at reducing the burden of these diseases. This thesis is composed of seven chapters. The first two chapters provide an initial exploration of the relationship between periodontitis and behavioral and metabolic risk factors, with an emphasis on the consumption of sugar-sweetened beverages, the main source of discretionary calories in the Western diet. The next three chapters delve deeper into the investigation through the application of complex network analysis, aiming to explore the interrelationships between oral and systemic diseases, as well as their shared risk factors, across different stages of the life cycle. The sixth chapter broadens the scope of the thesis by examining the global spread of the consumption of sugar-sweetened beverages and projecting its impact through the year 2050. Finally, the last chapter is dedicated to translating the knowledge generated in this doctoral work to society through the development of a digital book for dentists, offering an unprecedented approach to the Developmental Origins of Health and Disease (DOHaD) theory as applied to Dentistry. CHAPTER 1 presents the hypothesis that the prevalence of periodontitis in Brazil has increased over the past three decades, accompanied by a rise in the consumption of beverages high in added sugars. This chapter resulted in the original article **“Behavioral and metabolic risk factors associated with periodontitis in Brazil, 1990–2019: a multidimensional analysis for the Global Burden of Disease Study 2019”**, published in the journal *Clinical Oral Investigations* (Impact Factor 3.1, DOI: 10.1007/s00784-023-05384-6). The aim of this study was to analyze the relationship between periodontitis and behavioral and metabolic risk factors common to NCDs among Brazilian adults over a 30-year period. To achieve this, data from the Global Burden of Disease Study 2019 were used. The analysis was conducted using Prais-Winsten regression to identify trends in time series, and fixed effects regression to investigate associations between variables. The results indicated that,

since 2005, the prevalence of periodontitis has been increasing in Brazil, even in the context of declining tobacco use. Moreover, periodontal disease was found to be associated with the consumption of sugar-sweetened beverages, overweight/obesity, dyslipidemia, and hyperglycemia. These findings offer a new perspective on the interconnection between periodontitis and NCDs, highlighting the importance of preventive strategies focused on behavioral and metabolic factors. This study also marked the beginning of my involvement with the Graduate Programs in Dentistry (PPGO-UFMA), Health Sciences (PPGCS-UFMA), and Computer Science (PPGCC-UFMA) within the scope of the Graduate Program Development Initiative in the Legal Amazon (PDPG Amazônia Legal–CAPES), through which I receive my doctoral scholarship. In addition, this study was a key milestone in establishing a partnership with a researcher from Duke-NUS Medical School in Singapore, who later became my co-supervisor. Following the publication of this first article, I had the opportunity to complete a doctoral exchange program at that institution, supported by the National Academic Cooperation Program in the Amazon (PROCAD Amazônia–CAPES). During this period, I deepened my analytical skills and advanced my understanding of the interrelations between behavioral and metabolic factors in periodontitis. The product of this internship is presented in CHAPTER 2 of this thesis, which corresponds to the original article entitled **“Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study”**, published in the *Journal of Clinical Periodontology* (Impact Factor 6.8, DOI: 10.1111/jcpe.13961). This study investigated the relationship between the consumption of sugar-sweetened beverages and periodontitis using data from the Third National Health and Nutrition Examination Survey (NHANES III), involving American adults aged 30 to 50 years. Beverage consumption was associated with periodontitis when individuals reported intake of ≥ 5 , ≥ 7 , and ≥ 14 times per week. The results contribute to a better understanding of the factors that influence oral health and highlight the importance of interventions aimed at preventing the excessive consumption of these beverages. These findings motivated us to deepen our understanding of the interconnections between oral and systemic NCDs, since sugar consumption appears to be a common link among them. This perspective led us to formulate the third hypothesis of this study: NCDs may be interconnected from the earliest years of life, with their complexity increasing as additional organs and systems are affected with age. To better understand the dynamics of these diseases and their interrelations, we sought a close collaboration with the Institute of Mathematics and Computer Sciences (ICMC/USP), which enabled the application of advanced analytical approaches in complex network analysis. CHAPTER 3 of this thesis is based on the original article entitled **“Caries Is the Hub of a**

Complex Network of Chronic Diseases across the Life Decades", published in the *Journal of Dental Research* (Impact Factor 5.9, DOI: 10.1177/00220345251317487). This study explored the interconnections among NCDs across all life stages using complex network analysis to uncover pathways that may support enhanced intervention strategies and improve NCD management from childhood through old age. The research used data from the 2011–2012 and 2013–2014 cycles of the National Health and Nutrition Examination Survey (NHANES), which included indicators of metabolic risk, diabetes, cancer, cardiovascular, autoimmune, respiratory, mental, and oral diseases. From early life, dental caries was closely linked to overweight/obesity and asthma. As age progressed, new diseases became interconnected, increasing the network's complexity. Depression played a central role in adulthood, while in old age, episodes of forgetfulness and mental confusion became more relevant. The centrality of diabetes, cardiovascular diseases, and cancer increased with age, peaking in individuals aged 60 and over, with diabetes emerging as the most prominent condition. The results showed that all age groups exhibited high clustering coefficients among NCDs, demonstrating the interdependence between diseases. Dental caries remained the central hub across the decades, with other health conditions orbiting around it. This study represented a significant advancement in the application of complex networks as an analytical tool, offering a clearer and more dynamic view of disease relationships. This, in turn, enabled more precisely targeted interventions to reduce the NCD burden in the population. The findings obtained in the previous chapter, which mapped the interconnections among NCDs throughout life, encouraged a deeper investigation—not only into the diseases themselves but also into their social determinants, in addition to behavioral and metabolic risk factors in Brazilian adolescents. Adolescence is a sensitive developmental period in which patterns shaping the development of NCDs can be identified, allowing for more impactful preventive interventions. Thus, CHAPTER 4 resulted in the original article entitled **"High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the Complex Network of Non-Communicable Diseases in Adolescents"**, published in *Diabetology & Metabolic Syndrome* (Impact Factor 3.9, DOI: 10.1186/s13098-024-01469-8). This study used data from the RPS Cohort Consortium in the city of São Luís, focusing on adolescents aged 18 to 19 years (n = 2,515). Through complex network analysis, we investigated how socioeconomic, behavioral, and metabolic variables, including income, diet, sleep quality, the TyG index (a marker of insulin resistance), and chronic conditions such as depression, asthma, caries, and periodontitis—interact and shape the dynamics of NCDs in this age group. To characterize the network, we applied metrics such as degree, betweenness, eigenvector centrality, local transitivity, Shannon

entropy, and clustering coefficients. The results highlighted three main hubs in the overall network: high free sugar intake, insulin resistance, and low socioeconomic status. Among boys, low fiber intake and a high triglyceride/HDL ratio stood out as cardiometabolic risk markers. Among girls, sedentary behavior and inadequate sleep were strongly associated with metabolic and psychological outcomes. In both sexes, dental caries reaffirmed the central role of oral health in its interaction with systemic conditions. These findings reinforce adolescence as a strategic period for integrated interventions that address the identified central elements. Understanding adolescence as a window of opportunity for the prevention of NCDs broadened our perspective on the importance of investigating earlier stages of life course. In this context, CHAPTER 5 deepens the investigation of the transgenerational roots of NCDs, exploring exposures during pregnancy and the early years of life, through the article **“Decoding the Complexity of Health-Related Factors Connections around the First Thousand Days of Life: Network Analysis”**. The manuscript will be submitted to the scientific journal *Pediatrics* (Impact Factor 6.4). This study used data from the BRISA Prenatal Cohort in São Luís (N = 1,383), with data collected at three time points: between the 22nd and 25th weeks of gestation, at birth, and during the child’s second year of life. Network analysis was based on the Jaccard index to identify patterns of co-occurrence, complemented by centrality metrics and clustering measures. The constructed network revealed high connectivity among the factors analyzed. The main hubs identified during pregnancy were the consumption of ultra-processed foods, sugar-sweetened beverages, low socioeconomic status, and dental caries. Sugar-sweetened beverage consumption and low socioeconomic status during pregnancy showed strong links with all adverse birth outcomes. Subsequently, in the child’s second year of life, new hubs emerged: sugar exposure, allergies, and non-exclusive breastfeeding. Regarding the onset of NCDs in childhood, factors such as maternal intake of ultra-processed foods and sugar-sweetened beverages, low socioeconomic status, anemia, and dental caries during pregnancy—together with early-life exposure to sugars—were strongly associated with the development of allergies, overweight/obesity, asthma, and dental caries in children. These findings reinforce that socioeconomic factors, behavioral risks, and systemic and oral health conditions during pregnancy exert a decisive influence on adverse birth outcomes and the early emergence of NCDs, highlighting the importance of early interventions to break the transgenerational cycle of these diseases. CHAPTER 6 presents the article **“Global, regional, and national burden of high sugar-sweetened beverages consumption, 1990–2021, with projections up to 2050: a systematic analysis for the Global Burden of Disease Study 2021”**, which was published in *The American Journal of Clinical Nutrition* (Impact Factor 6.9, DOI:

10.1016/j.ajcnut.2025.07.033). The study investigated the global burden of excessive consumption of sugar-sweetened beverages (SSBs) over the past three decades and projected trends through 2050, as well as its impact on the burden of NCDs. We used data from the Global Burden of Disease Study 2021 to estimate population exposure to high SSB consumption and the burden of NCDs attributable to this behavior, including cardiovascular diseases, diabetes, and kidney diseases. To assess the impacts, we analyzed mortality rates, years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life years (DALYs). Projections of SSB exposure rates were conducted using ensemble models based on the Socio-demographic Index (SDI). Findings revealed that, in 2021, the global population exposure to high SSB consumption was 30.56%, with the highest levels observed in high-income super-regions and Latin America and the Caribbean. A correlation was found between increased SSB consumption and SDI, with higher rates in more developed countries. The global burden of NCDs attributable to SSB consumption included an age-standardized rate of 0.89 deaths per 100,000 population and 41.39 DALYs. Projections indicate a +9.54% increase in global SSB consumption by 2050. This study highlights the growing impact of sugar-sweetened beverages on the global burden of NCDs over the past three decades, pointing to an even more concerning scenario in the future if effective public health measures are not implemented. The findings reinforce the urgency of targeted policies to reduce the consumption of these beverages, especially in more vulnerable regions. CHAPTER 7 of this thesis presents the development of a digital book focused on the prevention of NCDs starting from the first thousand days of life, based on evidence from the Developmental Origins of Health and Disease (DOHaD) theory, with an emphasis on Dentistry. The book is entitled **“The first thousand days of life: a DOHaD perspective to dentistry”**. The material was produced in both Portuguese (<https://ares.unasus.gov.br/acervo/handle/ARES/27271>) and English (<https://ares.unasus.gov.br/acervo/handle/ARES/29558>). The publications were grounded in four core premises derived from the DOHaD framework: (1) dental caries are associated with childhood asthma, obesity, and are predictive of future diseases such as diabetes and cardiovascular conditions; (2) the consumption of ultra-processed foods and sugar is a major risk factor for both oral and systemic NCDs; (3) microbiome imbalance affects both oral and systemic health; and (4) breastfeeding has a protective effect. The Portuguese edition has reached over 7,000 accesses in Brazil and other countries, including the United States, United Kingdom, Germany, Ireland, Sweden, and Japan, which prompted the release of the English version to expand its reach and impact. This work represents the first book to address the DOHaD framework within the field of Dentistry, making a significant contribution to the

theoretical advancement of the area. As an innovative educational resource, the publication promotes professional training and strengthens comprehensive health care practices, highlighting the value of interdisciplinary initiatives in the global dissemination of DOHaD-informed knowledge. Throughout this thesis, added sugars—especially those found in sugar-sweetened beverages—emerge as a common axis in complex health networks, associated with oral diseases and other NCDs, underscoring the urgent need for coordinated public policies aimed at reducing consumption.

Keywords: Non-communicable diseases; Dental caries; Periodontitis; Sugar-sweetened beverages; Behavioral and metabolic factors; Complex networks.

SUMÁRIO

1 INTRODUÇÃO	18
2 OBJETIVOS	20
3 REFERENCIAL TEÓRICO	22
3.1 Doenças Crônicas Não Transmissíveis	22
3.2 Consumo de Açúcares de Adição e Doenças Bucais e Sistêmicas	23
3.3 Interações Complexas entre DCNTs ao Longo da Vida	25
3.4 Análise de Redes Complexas	27
4 METODOLOGIA	29
4.1 Metodologia do Capítulo 1	29
4.2 Metodologia do Capítulo 2	31
4.3 Metodologia do Capítulo 3	34
4.4 Metodologia do Capítulo 4	37
4.5 Metodologia do Capítulo 5	40
4.6 Metodologia do Capítulo 6	45
4.7 Metodologia do Capítulo 7	47
5 RESULTADOS	50
5.1 Capítulo 1 - Fatores de risco comportamentais e metabólicos associados à periodontite no Brasil, 1990-2019: uma análise multidimensional para o <i>Global Burden of Disease Study 2019</i>	50
5.1.1 Material Suplementar do Capítulo 1	60
5.2 Capítulo 2 - Consumo de bebidas ricas em açúcares de adição e periodontite em adultos: Um estudo transversal de base populacional	65
5.2.1 Material Suplementar do Capítulo 2	76
5.3 Capítulo 3 - A cárie é o hub de uma rede complexa de doenças crônicas ao longo das décadas da vida	85
5.3.1 Material Suplementar do Capítulo 3	95
5.4 Capítulo 4 - Alto teor de açúcares livres, resistência à insulina e baixos indicadores socioeconômicos: os elementos centrais da complexa rede de doenças não transmissíveis em adolescentes	103
5.4.1 Material Suplementar do Capítulo 4	117
5.5 Capítulo 5 - Decodificando a complexidade das conexões entre fatores relacionados à saúde nos primeiros mil dias de vida: análise de rede	121
5.5.1 Material Suplementar do Capítulo 5	143
5.6 Capítulo 6 - Carga global, regional e nacional do consumo elevado de bebidas ricas em açúcares de adição, 1990-2021, com projeções até 2050: uma análise sistemática para o <i>Global Burden of Disease Study 2021</i>	147
5.6.1 Material Suplementar do Capítulo 6	158
5.7 Capítulo 7 – [Livro digital] Os primeiros mil dias de vida: a odontologia na perspectiva DOHaD	178
Versão em português	178
Versão em inglês	254
6 CONSIDERAÇÕES FINAIS	327
REFERÊNCIAS	330
APÊNDICE – Outras produções ao longo do doutorado	338

1 INTRODUÇÃO

As doenças crônicas não transmissíveis (DCNTs), incluindo doenças cardiovasculares, diabetes, cânceres, doenças respiratórias crônicas e condições bucais como a cárie e a periodontite, constituem hoje um dos maiores desafios de saúde pública global. Responsáveis por aproximadamente 71% de todas as mortes no mundo (GBD 2021 Diabetes Collaborators, 2023; Qaiser, Hj Ibrahim e Husain, 2018), as DCNTs não apenas impõem uma alta carga de morbidade e mortalidade, mas também geram impactos econômicos substanciais, pressionando sistemas de saúde e ampliando desigualdades sociais (World Health Organization, 2021). A crescente prevalência dessas condições reflete um complexo entrelaçamento de determinantes socioeconômicos, fatores de risco comportamentais e metabólicos, cuja interação é moldada desde os primeiros anos de vida e se perpetua ao longo do curso de vida (Alves-Costa *et al.*, 2025).

Entre esses fatores, o consumo excessivo de açúcares de adição, amplamente presente em alimentos ultraprocessados, e especialmente nas bebidas ricas em açúcares de adição, emerge como um dos principais contribuintes para o desenvolvimento de múltiplas DCNTs (Malik e Hu, 2022). Sua influência ultrapassa o âmbito das doenças metabólicas, como obesidade, resistência à insulina e hipertensão, estendendo-se também a doenças inflamatórias crônicas bucais, como a periodontite (Alves-Costa *et al.*, 2024). Mecanismos biológicos subjacentes a esse consumo incluem a indução de disfunções imunológicas (Ye, Jiang e Zhang, 2022), estados pró-inflamatórios sistêmicos (Lima *et al.*, 2018; Ribeiro *et al.*, 2018) e desequilíbrios da microbiota (Nyvad e Takahashi, 2020), afetando negativamente tanto a saúde bucal quanto a saúde sistêmica. Apesar dos avanços científicos e das políticas públicas que buscam reduzir o consumo de açúcares de adição, seus efeitos deletérios continuam presentes de forma alarmante, sobretudo em populações vulneráveis e em países de baixa e média renda, onde fatores socioeconômicos intensificam os riscos (Bridge, Groisman e Bedi, 2022; Corte *et al.*, 2021; Krieger *et al.*, 2021).

O reconhecimento de que fatores de risco como dieta inadequada, tabagismo, consumo abusivo de álcool e inatividade física são compartilhados entre diversas DCNTs mudou paradigmas na abordagem da prevenção e controle dessas doenças. No entanto, grande parte dos modelos tradicionais de análise epidemiológica falha em capturar a natureza dinâmica, não linear e multifatorial dessas inter-relações. As DCNTs não se desenvolvem isoladamente; elas coevoluem dentro de redes complexas de interações entre fatores individuais, sociais e ambientais. Assim, surge a necessidade de novas

abordagens metodológicas que consigam mapear, compreender e intervir nessa teia intrincada de fatores de risco e desfechos em saúde.

Nesse contexto, a análise de redes complexas desponta como uma ferramenta inovadora e promissora. Ao permitir a visualização e o entendimento das conexões entre múltiplos fatores de risco e condições de saúde, as redes complexas oferecem uma perspectiva mais realista da biologia e do comportamento humano, proporcionando insights que podem aprimorar estratégias de prevenção e manejo das DCNTs (Costa, Rodrigues e Cristino, 2008), inclusive em saúde bucal (Alves-Costa et al., 2025; Alves-Costa et al., 2024). Mais do que identificar associações isoladas, as redes revelam padrões estruturais e nós críticos que podem ser alvos prioritários para intervenções em saúde pública.

Esta tese se propõe a investigar a interconexão entre fatores comportamentais, metabólicos e doenças bucais e sistêmicas, utilizando a abordagem de redes complexas como eixo metodológico principal. Organizada em sete capítulos, a tese constrói um percurso de análise que se inicia na investigação da relação entre a periodontite e fatores de risco compartilhados das DCNTs, com ênfase no consumo de bebidas ricas em açúcares de adição, estendendo-se para uma análise global da carga de doença atribuível a esse consumo, e culminando na aplicação de métodos de redes para compreender as interações dessas variáveis ao longo do ciclo de vida.

2 OBJETIVOS

2.1 Objetivo geral

Investigar as inter-relações entre fatores comportamentais, metabólicos e socioeconômicos e as doenças não transmissíveis bucais e sistêmicas ao longo do ciclo de vida, utilizando abordagens epidemiológicas tradicionais e análise de redes complexas para identificar padrões, hubs e alvos estratégicos de intervenção.

2.2 Objetivos específicos

- Capítulo 1: Analisar a relação entre periodontite e riscos comportamentais (tabagismo, consumo de álcool, inatividade física, consumo de bebidas ricas em açúcares de adição) e metabólicos (sobrepeso/obesidade, dislipidemia, hiperglicemia e hipertensão) em adultos brasileiros de 25 a 49 anos, ao longo de três décadas (1990–2019).
- Capítulo 2: Investigar a associação entre consumo de bebidas ricas em açúcares de adição e periodontite em adultos norte-americanos, e avaliar em que medida o conhecimento prévio de diagnóstico de diabetes modifica essa relação.
- Capítulo 3: Modelar as conexões entre diferentes DCNTs e seus fatores de risco em toda a população dos Estados Unidos, desde a infância até a velhice, para identificar padrões de coocorrência e nodos centrais ao longo das décadas de vida.
- Capítulo 4: Investigar, por meio de análise de redes complexas, o conjunto de fatores socioeconômicos, comportamentais e metabólicos associados à presença de DCNTs em adolescentes brasileiros, identificando os principais hubs de risco nessa faixa etária.
- Capítulo 5: Investigar as interconexões entre fatores socioeconômicos, comportamentais e metabólicos durante a gestação e os primeiros dois anos de vida, e seu impacto sobre desfechos adversos ao nascimento (cesárea, macrossomia, prematuridade) e o surgimento precoce de DCNTs na infância.

- Capítulo 6: Realizar uma análise abrangente da carga global, regional e nacional atribuível ao alto consumo de bebidas ricas em açúcares de adição entre 1990 e 2021, com projeções até 2050, estimando a mortalidade, YLDs, YLLs e DALYs de DCNTs atribuíveis a este comportamento.
- Capítulo 7: Desenvolver um material educativo bilíngue (português e inglês), fundamentado no arcabouço DOHaD, para capacitar cirurgiões-dentistas quanto à prevenção das doenças não transmissíveis nos primeiros mil dias de vida, incorporando evidências sobre cárie dentária, consumo de ultraprocessados, desequilíbrio do microbioma e aleitamento materno.

3 REFERENCIAL TEÓRICO

3.1 Doenças Crônicas Não Transmissíveis

As doenças crônicas não transmissíveis (DCNTs) são condições crônicas de longa duração e progressão lenta, incluindo doenças cardiovasculares, câncer, diabetes e doenças respiratórias crônicas (World Health Organization, 2021). Representam uma das principais causas de mortalidade global, especialmente em países de baixa e média renda (Salam, 2016). Tradicionalmente, o termo DCNTs têm sido associadas a doenças como as cardiovasculares, câncer, diabetes e doenças respiratórias crônicas (World Health Organization, 2021). No entanto, há um crescente reconhecimento de que a definição de DCNTs deve ser ampliada para incluir outras condições crônicas, como doenças bucais, renais crônicas, hepáticas e distúrbios da tireoide (Salam, 2016; Wolf *et al.*, 2021). Esses problemas de saúde estão relacionados a fatores de risco comuns, como o uso de tabaco, abuso de álcool, dieta inadequada e inatividade física (Alves-Costa, et al., 2024; World Health Organization, 2021). A abordagem para o manejo das DCNTs está se voltando para estratégias integrativas e holísticas, com foco na complexidade de sistemas, considerando as DCNTs como expressões interconectadas de doença, o que exige estratégias abrangentes que lidem com determinantes sociais, econômicos e ambientais, além dos mecanismos moleculares e celulares (Bousquet *et al.*, 2014).

As DCNTs são responsáveis por 71% de todas as mortes no mundo, com impacto particularmente grave em países de baixa e média renda, onde ocorrem 86% das mortes prematuras por DCNTs (GBD 2021 Diabetes Collaborators, 2023; Qaiser, Hj Ibrahim e Husain, 2018). As principais causas de mortalidade por DCNTs são as doenças cardiovasculares, o câncer, as doenças respiratórias crônicas e o diabetes (The Lancet Diabetes & Endocrinology, 2024). Em resposta, esforços liderados pelas Nações Unidas visam reduzir as mortes prematuras por DCNTs em 30% até 2030 através da prevenção e tratamento (United Nations. Department of Economic and Social Affairs. Sustainable Development., 2024). O estudo *Global Burden of Disease* identificou fatores de risco tradicionais, como o uso de tabaco e hipertensão, e fatores não tradicionais, como a poluição do ar, como prioridades para os esforços de controle das DCNTs (Benziger, Roth e Moran, 2016). Além da mortalidade, as DCNTs têm implicações socioeconômicas substanciais, podendo aumentar o empobrecimento individual e familiar e prejudicar o desenvolvimento social e econômico (Qaiser, Hj Ibrahim e Husain, 2018).

A coocorrência dos principais fatores de risco de DCNTs, incluindo dieta não saudável, inatividade física, tabagismo e consumo de álcool, é predominante em várias populações. Estudos realizados em diferentes contextos apontam uma variação de 17,6 a 44,1% da população estudada acumulando dois ou mais fatores de risco de DCNTs (Haregu *et al.*, 2015; Ricardo *et al.*, 2019; Shayo, 2019). O acúmulo de fatores de risco é maior em determinados grupos demográficos, como meninas, adolescentes mais velhos e pessoas de nível socioeconômico mais baixo (Ricardo *et al.*, 2019; Shayo, 2019). É importante ressaltar que esses fatores de risco comuns estão associados a várias DCNTs, inclusive cânceres, doença coronariana, acidente vascular cerebral, diabetes mellitus e demência (Peters *et al.*, 2019; World Health Organization, 2021, 2023). Essa sobreposição sugere que intervenções direcionadas que abordam vários fatores de risco simultaneamente poderiam reduzir efetivamente a carga das DCNTs em vários resultados de saúde.

As DCNTs representam desafios significativos para os sistemas de saúde, especialmente em países de baixa e média renda (LMICs). Estima-se que, até 2030, as DCNTs representarão 75% da carga de doenças nesses países (World Health Organization, 2025). Essas doenças geram uma crescente carga econômica, com projeções de perdas cumulativas de US\$ 47 trilhões nas próximas décadas, particularmente em LMICs (Bloom *et al.*, 2011). O impacto econômico das DCNTs vai além dos custos médicos diretos, afetando a produtividade, as pressões fiscais e os níveis de pobreza (Qaiser, Hj Ibrahim e Husain, 2018). Sistemas de saúde em LMICs frequentemente enfrentam dificuldades para gerenciar as DCNTs, devido à falta de integração, coordenação e financiamento (Budreviciute *et al.*, 2020; Romdhane *et al.*, 2015). A adaptação dos sistemas de saúde para lidar com as DCNTs exige uma abordagem multissetorial, que envolva promoção da saúde, prevenção e estratégias de tratamento (Robinson e Hort, 2012). A carga financeira das DCNTs é particularmente grave para as famílias mais pobres, com estudos mostrando altas taxas de gastos catastróficos e empobrecimento devido aos custos relacionados ao tratamento das DCNTs (Thakur *et al.*, 2011). O enfrentamento efetivo das DCNTs exige uma combinação de intervenções populacionais e fortalecimento dos sistemas de saúde para garantir cobertura universal (Budreviciute *et al.*, 2020; Thakur *et al.*, 2011).

3.2 Consumo de Açúcares de Adição e Doenças Bucais e Sistêmicas

O papel dos açúcares de adição no desenvolvimento da cárie é amplamente reconhecido. Estudos recentes também destacam a associação entre o consumo de açúcar e a saúde periodontal. O consumo de bebidas açucaradas (SSBs) tem sido associado a um maior risco de periodontite, especialmente em níveis de consumo iguais ou superiores a cinco vezes por semana (Alves-Costa, et al., 2024). Uma revisão sistemática indicou que a ingestão frequente de alimentos ou bebidas contendo açúcares livres está associada a uma maior prevalência ou incidência de doenças periodontais, embora as evidências sejam limitadas devido ao desenho dos estudos (Gupta *et al.*, 2022; Kusama *et al.*, 2022). Dados do NHANES III sugerem que jovens adultos com alto consumo de açúcares de adição apresentam maior prevalência de doenças periodontais, possivelmente devido à inflamação sistêmica (Lula *et al.*, 2014). O consumo de SSBs também pode aumentar o sangramento gengival e o risco de periodontite, destacando a importância de incluir o consumo de açúcares na avaliação de risco periodontal (Gupta *et al.*, 2022).

A relação entre açúcares de adição e fatores metabólicos é complexa. Estudos sugerem que açúcares podem prejudicar a homeostase da glicose e aumentar a resistência à insulina em jovens com risco de obesidade (Ladeira *et al.*, 2022; Wang, J. *et al.*, 2014). Os efeitos metabólicos da frutose parecem ser dependentes da dose, sendo mais evidentes quando o consumo elevado de açúcar é acompanhado de excesso de calorias (Macdonald, 2016). Um mecanismo proposto relaciona o consumo excessivo de açúcar à deficiência de cobre, o que pode levar a sobrecarga de ferro hepático, doença hepática gordurosa e resistência à insulina (DiNicolantonio, Mangan e O'Keefe, 2018). Além disso, o excesso de frutose na dieta está associado à ativação da *lipogênese de novo* no fígado, um processo em que o excesso de açúcares é convertido em ácidos graxos, contribuindo para o acúmulo de gordura hepática, dislipidemia e aumento do risco de doenças metabólicas (Lustig, 2010; Stanhope, 2012).

As interações entre saúde oral e condições sistêmicas, como doenças cardiovasculares e síndrome metabólica, têm ganhado destaque. Doenças orais, como cárie dentária e periodontite, estão associadas a hormônios do estresse elevados, alterações imunológicas e aumento da carga alostática, especialmente em grupos socioeconomicamente desfavorecidos (Gomaa *et al.*, 2016). Essas conexões são mediadas por respostas inflamatórias, com as doenças bucais potencialmente vinculadas a distúrbios metabólicos e cardiovasculares (Carramolino-Cuellar, Tomas e Jimenez-Soriano, 2014; Ladeira *et al.*, 2022; Lima *et al.*, 2018; Ribeiro *et al.*, 2018, 2021).

Políticas públicas para reduzir o consumo excessivo de açúcares, especialmente por meio da redução do consumo de bebidas ricas em açúcares de adição, são cruciais para a promoção da saúde e a prevenção da obesidade (Malik e Hu, 2022). Estratégias como medidas fiscais, provisão de informações, mudanças nas opções padrão e restrição de disponibilidade têm sido propostas (Krieger *et al.*, 2021). Embora rotulagem calórica e a remoção de bebidas ricas em açúcares de adição das escolas tenham amplo apoio público, impostos e restrições de tamanho de porção enfrentam maior resistência (Gollust, Barry e Niederdeppe, 2014). Políticas eficazes incluem acordos comerciais que priorizem a saúde, reformulação de alimentos, regulamentação de publicidade, melhoria na rotulagem, fortalecimento das diretrizes alimentares e incentivo a escolhas saudáveis (Azaad Moonesar, Al-Alawy e Gaafar, 2024; Itria *et al.*, 2021). Tais medidas são especialmente relevantes para crianças e adolescentes, particularmente em comunidades de baixa renda e minorias, que são desproporcionalmente impactadas (Muth *et al.*, 2019). Uma abordagem integrada, adaptada às tendências emergentes e às novas evidências científicas, é essencial, pois nenhuma política isolada será suficiente para reduzir o consumo de SSBs a níveis saudáveis (Krieger *et al.*, 2021; Malik e Hu, 2022).

3.3 Interações Complexas entre DCNTs ao Longo da Vida

A interação entre doenças crônicas ao longo das diferentes fases da vida reflete uma complexa rede de fatores socioeconômicos, biológicos e comportamentais que contribuem para o desenvolvimento de condições de saúde interconectadas. Nos primeiros anos de vida, problemas como cárie dentária, asma e obesidade frequentemente compartilham fatores de risco comuns, como a exposição precoce a dietas ricas em açúcares de adição (Araújo *et al.*, 2024; Nascimento *et al.*, 2017). A obesidade infantil, por exemplo, não apenas está associada a alterações metabólicas que favorecem a resistência à insulina no futuro, mas também pode exacerbar condições inflamatórias, como a asma (Reyes-Angel *et al.*, 2022). Além disso, crianças em contextos de desigualdade socioeconômica tendem a enfrentar maior exposição a barreiras no acesso à saúde (Fekadu *et al.*, 2024), o que amplifica a vulnerabilidade a essas condições interligadas. Esse cenário inicial cria as bases para a persistência de doenças crônicas ao longo da vida.

Na juventude, a carga dessas condições se intensifica com a inclusão de novas patologias, como periodontite, resistência à insulina (Ladeira *et al.*, 2022) e depressão (Barbosa *et al.*, 2022), frequentemente interligadas por mecanismos inflamatórios e

metabólicos. A obesidade continua desempenhando um papel central (Alves-Costa *et al.*, 2025), exacerbando a inflamação sistêmica que pode contribuir tanto para a progressão da periodontite quanto para alterações metabólicas associadas à resistência à insulina (Ladeira *et al.*, 2022). A depressão, por sua vez, é frequentemente associada a comportamentos de risco, como o consumo elevado de açúcares (Barbosa *et al.*, 2022) e a negligência da higiene bucal (Stepović *et al.*, 2020), o que pode agravar a saúde bucal e metabólica. Jovens em condições socioeconômicas desfavoráveis estão mais expostos a fatores de risco, como insegurança alimentar e estresse crônico (Crielaard *et al.*, 2021), perpetuando um ciclo de vulnerabilidade às doenças crônicas.

Na vida adulta, a interação entre doenças crônicas se torna ainda mais evidente, com a emergência de doenças cardiovasculares, diabetes tipo 2 e o agravamento de condições pré-existentes, como a obesidade, cárie e a periodontite (Alves-Costa *et al.*, 2025). A cárie dentária, quando não tratada, pode levar à perda dentária, limitando a capacidade mastigatória e impactando negativamente a nutrição (Mark, 2020). Simultaneamente, o diabetes, as doenças cardiovasculares e a forma grave da periodontite se apresentam no indivíduo pela intensificação dos processos inflamatórios subjacentes a eles (Bodanese *et al.*, 2021; Nascimento *et al.*, 2018). Desigualdades socioeconômicas continuam a influenciar esse quadro, com populações vulneráveis enfrentando menor acesso a cuidados de saúde preventivos e maior exposição a ambientes obesogênicos e dietas ricas em açúcares, que perpetuam o risco de múltiplas doenças (Sigala e Stanhope, 2021; Stevens *et al.*, 2017).

Entre idosos, as interações entre doenças crônicas alcançam um ponto crítico, com a sobreposição de doenças cardiovasculares, diabetes, perdas dentárias, depressão e declínios cognitivos (Alves-Costa *et al.*, 2025). A inflamação crônica de baixo grau, amplamente presente em condições como o diabetes, doenças cardiovasculares e periodontite (Guarner e Rubio-Ruiz, 2015; Moutsopoulos e Madianos, 2006), pode acelerar processos neurodegenerativos e contribuir para o comprometimento cognitivo (Kosyrevá *et al.*, 2022; Lyman *et al.*, 2014). Além disso, a depressão em idosos é frequentemente agravada por fatores como isolamento social, perda de autonomia, falta de suporte familiar (Vishwakarma, Gaidhane e Bhoi, 2023) e saúde bucal comprometida (Silva *et al.*, 2019), esta última impactando a capacidade de alimentação e o estado nutricional. Ademias, evidências sugerem que a depressão na meia-idade pode aumentar o risco de Alzheimer, enquanto a depressão persistente pode preceder a demência (Kuring, Mathias e Ward, 2020). A desigualdade socioeconômica ao longo da vida exerce efeitos cumulativos,

amplificando os impactos na saúde bucal e sistêmica na velhice. Esses processos destacam a necessidade de abordagens integradas e contínuas que considerem as interações complexas entre condições crônicas em diferentes fases da vida, promovendo intervenções preventivas desde os primeiros anos até o envelhecimento.

3.4 Análise de Redes Complexas

As redes complexas são grafos com propriedades topológicas não triviais que se diferenciam de redes simples, como as cadeias de eventos (Chen e Lou, 2019). Elas têm despertado grande interesse nas últimas décadas devido à sua ampla presença em sistemas reais e tecnológicos (Ahuja e Sharma, 2014). Essas redes consistem em nós conectados por arestas, exibindo arquiteturas e topologias sofisticadas. A descoberta das propriedades de micromundos e de redes livres de escala impulsionou o entendimento dos princípios organizacionais dessas estruturas (Xiao Fan Wang e Guanrong Chen, 2003). A análise de redes complexas tem aplicações práticas, como melhorar o design de redes de computadores, compreender respostas populacionais a novos desafios, identificar vulnerabilidades e prever falhas em sistemas como redes elétricas (Ahuja e Sharma, 2014). Também é possível explorar a relação entre topologia e dinâmica da rede, como a propagação de epidemias e a sincronização de doenças (Vulliard e Menche, 2021).

No campo da saúde, as redes complexas emergem como ferramentas valiosas para compreender a organização e funcionalidade de sistemas biológicos e de saúde. Por exemplo, análises de redes têm sido aplicadas para mapear estruturas organizacionais em hospitais, identificando comunidades que otimizam a eficiência em relação a divisões tradicionais (Minerba *et al.*, 2008). Além disso, a análise de redes tem sido usada para examinar padrões de colaboração entre profissionais de saúde e seu impacto nos custos e na qualidade do atendimento (Wang, F. *et al.*, 2014). A metodologia também pode ser utilizada para investigar interações entre proteínas e transcrições gênicas, onde as interconexões entre entidades celulares, como proteínas, RNAs e DNA, influenciam diretamente processos biológicos essenciais, como a regulação gênica e a comunicação celular (Barabási e Oltvai, 2004). Tais redes são caracterizadas por propriedades como modularidade, organização hierárquica e resiliência estrutural. Análises recentes destacam que a compreensão da dinâmica e topologia dessas redes permite avanços significativos na predição de funções biológicas e no mapeamento de interações gênicas ou proteicas, mesmo diante de limitações relacionadas a dados incompletos ou ruidosos (Barabási e Oltvai, 2004; Costa, Rodrigues e Cristino, 2008).

As métricas de centralidade de redes complexas fornecem informações detalhadas sobre padrões e comportamentos. Métricas baseadas no grau incluem a centralidade de grau (degree), que quantifica as conexões diretas de um nó, refletindo sua influência local, e a centralidade de autovetor (eigenvector), que avalia não apenas a quantidade de conexões, mas também a importância dos nós conectados, refletindo influência em escala global na rede (Costa *et al.*, 2007). Métricas baseadas no caminho mais curto incluem a centralidade de intermediação (betweenness), que mede a frequência com que um nó participa de caminhos mais curtos entre outros pares, indicando seu papel na mediação de fluxos; a centralidade de proximidade (closeness), que avalia a distância média de um nó para os demais, indicando sua acessibilidade (Costa *et al.*, 2007).

A entropia de Shannon nos nós quantifica a diversidade das conexões de um nó (Wiesner e Ladyman, 2019), enquanto a transitividade local avalia o grau de interconexão entre os vizinhos de um nó, capturando padrões de agrupamento local (Costa *et al.*, 2007). Em escala global, métricas como a entropia de Shannon da rede caracterizam a diversidade estrutural em toda a rede (Softic *et al.*, 2017), a assortatividade (assortivity mixing) mede a tendência de nós semelhantes se conectarem, seja por grau ou outros atributos, e o coeficiente de agrupamento reflete a densidade de triângulos na rede, indicando interconectividade global (Costa *et al.*, 2007). Estudos mostram que métricas de centralidade baseadas em grau, como grau e autovetor, são altamente correlacionadas em várias redes, enquanto métricas baseadas em caminhos mais curtos apresentam correlação moderada (Meghanathan, 2015). Essas análises contribuem para o desenvolvimento de metodologias mais robustas para avaliar e interpretar redes complexas (Gaur *et al.*, 2019).

4 METODOLOGIA

4.1 Metodologia do Capítulo 1

Delineamento do Estudo

O presente estudo utiliza dados em painel de 26 estados brasileiros, abrangendo adultos (25 a 49 anos) ao longo de três décadas (1990 a 2019). Os dados foram obtidos do *Global Burden of Disease Study 2019* (GBD) (Global Burden of Disease Collaborative Network, 2020a) e do Instituto Brasileiro de Geografia e Estatística (IBGE). O GBD quantifica sistematicamente a carga global de doenças e fatores de risco em 204 países e territórios, permitindo comparações ao longo do tempo, entre populações e questões de saúde. A principal fonte de dados do GBD são pesquisas nacionais ou estaduais representativas, com imputação de dados ausentes (Murray *et al.*, 2020; Vos *et al.*, 2020). A Tabela S1 suplementar contém informações descritivas sobre os dados utilizados e suas fontes.

Desfecho

A doença periodontal fornecida pelo GBD foi a taxa de prevalência de periodontite (por 100.000 habitantes), definida no estudo como Índice de Necessidade de Tratamento Periodontal Comunitário (CPITN) código IV, perda de inserção clínica (CAL) >6 mm ou profundidade de sondagem (PPD) >5 mm (Global Burden of Disease Collaborative Network, 2020b).

Variáveis Comportamentais e Metabólicas

Os principais fatores de risco comportamentais e metabólicos para DCNTs foram selecionados com base nos fatores de risco para DCNTs definidos pela Organização Mundial da Saúde (OMS) (World Health Organization, 2021). Os fatores de risco comportamentais incluíram tabagismo, uso de álcool, dieta alta em bebidas ricas em açúcares de adição (SSB) e baixa atividade física. Os fatores de risco metabólicos foram índice de massa corporal (IMC) elevado como marcador de sobrepeso/obesidade, colesterol LDL elevado como indicador de dislipidemia, glicemia de jejum elevada como marcador de hiperglicemia e pressão arterial sistólica elevada como indicativo de hipertensão. Devido à alta colinearidade entre essas variáveis, cada uma foi utilizada separadamente nos modelos de regressão. Todas essas variáveis estavam disponíveis como *Summary Exposure Value* (SEV), que mede a exposição da população a um fator de risco, considerando a intensidade da exposição, com valores variando de 0% (não

exposto) a 100% (totalmente exposto). O índice de Gini de 2005 a 2019 (Fig. S1), que mede a distribuição do Produto Interno Bruto (PIB), representando desigualdade de renda (de 0, igualdade perfeita, a 1, desigualdade máxima), foi utilizado para ajustar os modelos.

Modelagem

Os modelos foram ajustados usando modelagem de efeitos fixos com nível de significância de 0,05. O agrupamento a nível estadual foi usado para relaxar os requisitos de autocorrelação e heterocedasticidade (Abadie *et al.*, 2022). Modelos de efeitos fixos são apropriados para avaliar desfechos em saúde, pois podem estimar efeitos de localização não observáveis que permanecem fixos ao longo do tempo, como fatores geográficos e históricos. As regressões lineares foram realizadas utilizando R e RStudio.

O modelo de regressão linear consistiu em uma abordagem bruta, considerando o desfecho explicado pelos fatores de risco e o efeito fixo não observável. Foi utilizada uma matriz de dados com 26 estados x 30 anos (1990-2019). O modelo bruto foi:

$$Periodontite_{it} = \beta_1 FatordeRisco_{it} + u_i + \varepsilon_{it} \quad t = 1990, \dots, 2019,$$

onde *Periodontite* é a taxa de prevalência de periodontite em um estado *i* no ano *t*. Os *FatordeRisco* representam o SEV dos fatores de risco comportamentais (tabagismo, uso de álcool, dieta rica em SSB e baixa atividade física) e fatores de risco metabólicos (sobrepeso/obesidade, dislipidemia, hiperglicemia e hipertensão). *u_i* é o efeito de localização não observável, e *ε_{it}* é o termo de erro.

Análises ajustadas foram realizadas usando o índice de Gini. Como no Brasil o índice de Gini não está disponível desde 1990, e há evidências de perturbação na estimativa da prevalência de periodontite no Brasil por volta dos anos 2000 (Fig. S2) (Costa Junior *et al.*, 2021), as análises de regressão foram conduzidas com uma matriz de dados com 26 estados x 15 anos (2005–2019). O índice de Gini foi escolhido por ser a série mais longa disponível para os estados brasileiros em formato de painel de dados e já ter sido associado a indicadores de saúde no país (Gaspar *et al.*, 2021). Assim, o modelo ajustado foi:

$$Periodontite_{it} = \beta_1 FatordeRisco_{it} + \beta_2 Gini_{it} + u_i + \varepsilon_{it} \quad t = 2005, \dots, 2019.$$

Como análise de sensibilidade, foram realizados modelos para os dois principais fatores de risco comportamentais, tabagismo e dieta rica em SSB, nos dois intervalos, 1990-2005 e 2005-2019.

As estimativas de Prais-Winsten foram realizadas para explorar tendências em séries temporais da prevalência de periodontite e o SEV resumido dos fatores de risco comportamentais e metabólicos. O GBD fornece prevalência e SEV de forma resumida para o Brasil; portanto, as matrizes de dados analisadas foram 1 país x 30 anos (1990-2019) e 1 país x 15 anos (2005-2019). Os resultados foram classificados como estacionários ($p > 0,05$), aumento ($\beta_1 > 0$), ou diminuição ($\beta_1 < 0$), com $p < 0,05$. A transformação logarítmica foi usada para reduzir a heterogeneidade da variância dos resíduos. A mudança percentual anual (APC) também foi calculada usando a fórmula: $100 \cdot (10^\beta - 1)$, sendo β o coeficiente da regressão de Prais-Winsten (Antunes e Cardoso, 2015).

4.2 Metodologia do Capítulo 2

Delineamento do Estudo

Este estudo transversal utilizou dados populacionais da *Third National Health and Nutrition Examination Survey* (NHANES III), que empregou uma estratégia de amostragem representativa complexa, multietapas e estratificada, abrangendo civis americanos não institucionalizados. O NHANES III foi escolhido porque oferece o maior conjunto de dados para exames periodontais e frequência de consumo de bebidas ricas em açúcares de adição (SSB). O estudo incluiu 33.994 indivíduos recrutados entre 1988 e 1994. Mulheres grávidas e participantes com risco de endocardite infecciosa, febre reumática e em diálise não foram examinados para condições periodontais devido ao risco de bacteremia. Participantes com idades entre 30 e 50 anos que realizaram exame periodontal foram elegíveis para este estudo ($N = 5.222$). A Figura 1 exibe o fluxograma deste estudo. A população não incluída neste estudo está descrita na Tabela S1.

Avaliação da Periodontite

Dois quadrantes (um superior e um inferior) foram selecionados aleatoriamente para exame periodontal. As superfícies vestibulares e mesiovestibulares de cada dente foram sondadas, exceto os terceiros molares. A profundidade de sondagem periodontal (PS) e o nível de inserção clínica (NIC) foram medidos em até 28 sítios. O NIC foi calculado somando-se (1) a distância da margem gengival livre até a junção cimento-

esmalte e (2) a distância da margem gengival até a base do sulco/bolsa (PS). Dentistas calibrados realizaram essas avaliações, resultando em coeficientes de correlação intraclasse que variaram de 0,75 a 0,97 para escores médios e de extensão de NIC e PS. Os coeficientes kappa específicos para confiabilidade interexaminadores em escores de prevalência em nível de sujeito variaram de 0,25 a 0,50, com kappa ponderado variando de 0,55 a 0,89.

A periodontite foi categorizada de acordo com os critérios definidos pelos Centros de Controle e Prevenção de Doenças e pela Academia Americana de Periodontia (CDC-AAP) (Eke *et al.*, 2012). Para fins analíticos, esta variável foi diferenciada em saudável (referência) e participantes com qualquer grau de periodontite. Como análise de sensibilidade, diferentes métricas periodontais foram consideradas como desfechos: categorização CDC-AAP como ordinal (saudável, leve, moderada e grave), classificação AAP/EFP (Tonetti, Greenwell e Kornman, 2018) como ordinal (saúde, estágio I, estágio II e estágio III/IV com base no maior CAL e PPD interproximal), proporção de sítios com $PPD \geq 4$ mm, proporção de sítios com $CAL \geq 3$ mm, CAL médio e proporção de sítios com sangramento à sondagem, todas como variáveis contínuas.

Consumo de Bebidas Ricas em Açúcares de Adição

A principal variável explicativa foi a frequência semanal de consumo de SSB com base nas respostas ao questionário de frequência alimentar. Neste estudo, SSB incluíram bebidas adoçadas artificialmente, como leite com chocolate e chocolate quente; Hi-C (Coca-Cola Foods), Tang (Kraft General Foods Inc.) e Kool-Aid (Kraft General Foods Inc.); e refrigerantes regulares consumidos mensalmente. O fator de correção para consumo de SSB foi 1 mês = 4,3 semanas (valores não arredondados) (Centers for Disease Control and Prevention, 1996). Considerando a ausência de consenso sobre um ponto de corte indicativo de um comportamento de consumo arriscado de SSB, três variáveis dicotômicas foram utilizadas como o número de SSB consumidos por semana: < 5 ou ≥ 5 vezes/semana, < 7 ou ≥ 7 vezes/semana e < 14 ou ≥ 14 vezes/semana. Como análise de sensibilidade, o consumo de SSB também foi considerado como variável ordinal (< 5 vezes/semana; ≥ 5 vezes a < 7 vezes/semana; ≥ 7 vezes a < 14 vezes/semana; e ≥ 14 vezes/semana) e como variável contínua. O consumo de SSB variou de 0 a 148, um intervalo que parecia irracional. Para abordar esta questão, os participantes que relataram consumir ≥ 50 vezes/semana foram excluídos com base na distribuição de dados (Figura S2).

Variáveis de Confundimento

Questionários foram utilizados para coletar dados sobre sexo, idade e raça/etnia (brancos não hispânicos, negros não hispânicos e mexicanos-americanos). As razões de pobreza da renda familiar foram calculadas comparando a renda familiar com a linha de pobreza ajustada anualmente pelo US Census Bureau (ano base: 1), conforme publicado anteriormente (Eke *et al.*, 2018; Rosinger, Bethancourt e Francis, 2019). Isso resultou em três categorias: baixa ($<1,3$), média ($\geq 1,3$ a $<3,5$) e alta ($\geq 3,5$). O nível de educação foi categorizado como $<9^{\circ}$ ano, 9° - 11° ano, ensino médio completo ou algum nível universitário. O diagnóstico prévio de diabetes foi autorrelatado como presente ou ausente. A ingestão total de calorias alimentares (kcal) nas 24 horas anteriores foi tratada como variável contínua. O comportamento de tabagismo foi dicotomizado em nunca, ex-fumante (uso prévio de ≥ 100 cigarros ao longo da vida)/ fumante atual. O uso de álcool foi categorizado de acordo com a ingestão autorrelatada nas 24 horas anteriores (sim ou não).

Análise Estatística

A Figura S1 apresenta o gráfico acíclico direcionado resumido utilizado para investigar a relação. Inicialmente, foi empregada uma regressão logística convencional, ajustando-se para a razão de pobreza da renda familiar, nível educacional, raça/etnia, sexo, idade, tabagismo e consumo de álcool, para explorar a associação entre periodontite e o consumo de SSBs. Posteriormente, o efeito médio do tratamento (ATE) das SSBs na periodontite foi estimado utilizando o método de ponderação por probabilidade inversa (IPW) com base no escore de propensão aplicado na regressão logística, balanceando os grupos expostos e não expostos. Após ajuste para confundidores, as estimativas foram obtidas para os casos completos ($N = 4.473$). Para abordar a variabilidade, os pesos foram estabilizados e truncados no percentil 99 (Chesnaye *et al.*, 2022). Os cálculos do *E-value* foram realizados para avaliar a confusão não mensurada. Um *E-value* alto indica que uma confusão não-mensurada substancial seria necessária para anular a estimativa do efeito (VanderWeele e Ding, 2017). Como análise de sensibilidade, essas estimativas foram obtidas usando imputação multivariada por cadeias de equações (MICE) para lidar com variáveis com mais de 5% de dados ausentes. O método de *bootstrap* foi aplicado aos parâmetros para refletir a variabilidade do modelo imputado. A metodologia detalhada de imputação de dados está disponível no material suplementar.

O estudo também examinou se a conscientização sobre diabetes poderia modificar a relação entre as SSBs e a periodontite. Isso foi realizado utilizando o IPW, assumindo um efeito não confundido das SSBs na periodontite dado os confundidores, com a conscientização sobre diabetes como um modificador, seguindo Vanderweele (2009). Adjusted ORs were reported for each stratum of SSB consumption and diabetes awareness. Razões de chances ajustadas (ORs) foram reportadas para cada estrato de consumo de SSB e conscientização sobre diabetes. A modificação do efeito foi avaliada tanto em escalas aditivas quanto multiplicativas, quantificada pelo excesso de risco relativo devido à interação para OR ($RERI_{OR}$) e pela razão das razões de chances entre os grupos com base no status de diabetes. Valores de $RERI_{OR} > 0$ indicam fortes indícios de que o efeito estimado na escala aditiva das SSBs com diabetes autodeclarado foi maior do que o efeito estimado das SSBs sem diabetes autodeclarado, indicando uma modificação positiva do efeito das SSBs nos estratos de diabetes autodeclarado em uma escala aditiva. Valores de $RERI_{OR} < 0$ indicam uma modificação negativa do efeito. Em uma escala multiplicativa, valores > 1 sugerem que o efeito das SSBs entre aqueles com diabetes autodeclarado é maior do que entre aqueles sem diabetes autodeclarado, enquanto valores < 1 indicam modificação do efeito na direção oposta; o valor 1 revela ausência de modificação do efeito (Knol e VanderWeele, 2012).

Para avaliar se a conscientização sobre diabetes difere de outras condições de saúde, uma análise de sensibilidade foi conduzida utilizando o status de peso percebido como um modificador, que tem sido sugerido como influente no consumo de SSBs (Malik e Hu, 2022). Usando o R 4.3.1, todas as análises foram realizadas com nível de significância de 5% para testes bicaudais. Pesos de amostra foram aplicados utilizando o pacote '*survey*'. Escores de propensão foram realizados utilizando o pacote '*WeightIt*', e o balanceamento das covariáveis foi avaliado com o pacote '*cobalt*'. Descrições detalhadas das estatísticas usadas para verificar o balanceamento podem ser encontradas no material suplementar.

4.3 Metodologia do Capítulo 3

Delineamento do Estudo

Este estudo analisou dados dos ciclos de 2011-2012 e 2013-2014 do *National Health and Nutrition Examination Survey* (NHANES), focando em civis não institucionalizados dos EUA, com idades entre 1 e 80 anos ($N = 19.134$). Esses ciclos foram selecionados por meio de um método detalhado de amostragem estratificada devido aos

seus dados abrangentes de saúde médica e bucal. Este estudo foi relatado de acordo com as diretrizes do *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE).

Coleta de Dados

Câncer, doenças cardiovasculares, artrite reumatoide, bronquite e enfisema foram autorrelatados (sim/não) por participantes com 20 anos ou mais. Dificuldades em pensar ou lembrar e experiências de confusão/problemas de memória também foram autorrelatadas, com perguntas separadas para participantes com 20+ e 60+ anos (respectivamente), posteriormente combinadas em uma única variável "esquecimento" (sim/não). Diabetes e pré-diabetes foram identificados por meio de questionário autorrelatado para indivíduos com 16+ anos ou pelo nível sérico de hemoglobina glicada para indivíduos com 12+ anos. Um nível de $\geq 6,5\%$ indicava diabetes, enquanto níveis entre 5,7% e 6,4% indicavam pré-diabetes. Risco de diabetes e psoríase foram autorrelatados por participantes com 16+ anos. Doença celíaca foi relatada por indivíduos com 6+ anos. Todos os participantes com 1+ anos foram questionados se tinham asma (sim/não).

Os participantes com 18+ anos foram avaliados quanto à depressão usando o questionário *Patient Health Questionnaire* de nove itens (PHQ-9), com pontuação de 0-27. Pontuações de 5+ indicaram sintomas depressivos.

A pressão arterial sistólica e diastólica foi medida em participantes sentados com 8+ anos, utilizando a média de três leituras após um descanso de 5 minutos. Participantes com idades entre 8 e 17 anos foram considerados hipertensos se a pressão arterial estivesse no percentil 95 ou acima, e aqueles com 18+ anos se a pressão arterial excedesse 140/90 mmHg.

O índice de massa corporal foi calculado a partir das medições realizadas e depois categorizado como eutrófico ou com sobrepeso/obesidade, usando um limite de 25 kg/m² para participantes com 20+ anos. Para participantes entre 2 e 19 anos, a classificação de sobrepeso/obesidade foi determinada a partir do percentil 85. Amostras de sangue foram coletadas por venopunção para participantes com 6+ anos para medir HDL-c e colesterol total. LDL-c e triglicerídeos foram medidos adicionalmente em participantes com 12+ anos. Os níveis foram categorizados com base em limites estabelecidos: ≤ 50 mg/dL para baixo HDL-c em mulheres com 25+ anos, e ≤ 40 mg/dL para baixo HDL-c em todas as crianças e homens adultos; ≥ 250 mg/dL para colesterol total elevado em participantes com 20+ anos e ≥ 200 mg/dL para mais jovens; ≥ 160 mg/dL para LDL-c elevado em

participantes com 20+ anos e ≥ 130 mg/dL para mais jovens; e ≥ 150 mg/dL para triglicérides elevados em participantes com 20+ anos, e ≥ 150 mg/dL em participantes de 12 a 19 anos.

A saúde periodontal foi avaliada por meio de periograma, abrangendo medições de recessão gengival e profundidade de bolsa. A periodontite foi classificada com base na classificação de 2018 da *American Academy of Periodontology/European Federation of Periodontology* (AAP/EFP), dicotomizada como nenhuma ou qualquer estágio para participantes com 30+ anos. Cárie dentária foi avaliada em participantes com 1+ anos, como cavidades não tratadas ou preenchidas em pelo menos uma superfície dental ou perda dentária devido a cárie. Análises de sensibilidade foram conduzidas, considerando participantes entre 1 e 5 anos, para focar exclusivamente na dentição primária.

Análise de Dados

A análise de redes complexas foi o principal procedimento analítico aplicado neste estudo, utilizando uma abordagem orientada por dados para examinar as relações entre condições (Costa *et al.*, 2007). Uma estrutura de grafo não direcionado foi construída a partir de uma matriz de coocorrência de doenças, com as doenças representadas como nós e as coocorrências como arestas; a espessura da aresta representa o número proporcional de coocorrências entre as duas doenças. Quatro modelos distintos foram estabelecidos com base em categorias de idade: 1 a 19 anos ($N = 7.805$), 20 a 39 anos ($N = 3.911$), 40 a 59 anos ($N = 3.786$) e 60 anos ou mais ($N = 3.632$). Essas categorias foram escolhidas para capturar transições chave de desenvolvimento e saúde, permitindo que nossa análise refletisse as dinâmicas sutis de mudanças relacionadas à idade, de acordo com Geifman *et al.* (2013).

Extraímos quatro medidas de centralidade específicas do nó para caracterizar a estrutura da rede: grau, intermediação do nó, centralidade do autovetor e transitividade local. O grau de um nó (doença) é a contagem do número de conexões (i.e., arestas) que ele possui, representando quão envolvida uma doença específica está na rede. A intermediação do nó é definida como o número de vezes que um nó (doença) atua como conexão nos caminhos mais curtos entre outros nós (doenças); uma doença com maior valor de intermediação sugere que ela age como mediadora/ponte entre outras doenças, indicando fisiopatologia ou fatores de risco compartilhados. A centralidade do autovetor de um nó (doença) foi obtida por meio de um processo recíproco em que a centralidade foi

atribuída proporcionalmente à soma das centralidades dos outros nós (doenças) aos quais está conectado, destacando jogadores influentes e atribuindo valores mais altos às doenças conectadas a muitas outras bem conectadas. A transitividade local de um nó (doença) foi calculada com base na razão entre o número de triângulos conectados a esse nó (doença) e o número de triplas centradas nesse nó (doença), indicando a probabilidade de duas doenças coocorrerem se ambas já estiverem ligadas a uma terceira (Costa *et al.*, 2007).

A entropia de Shannon específica do nó foi medida para verificar a diversidade das conexões de cada nó; valores mais altos indicam conexões mais diversas que um nó possui com outros na rede. A entropia de Shannon relacionada à rede também foi calculada, refletindo o nível de complexidade da estrutura (Wiesner e Ladyman, 2019).

Em relação às propriedades da rede complexa, calculamos a distribuição de graus para observar o padrão de conectividade. O coeficiente de cluster avalia a probabilidade de qualquer nó (doença) formar um triângulo com outros dois nós (doenças) na rede. Considerando que as DCNTs são comumente classificadas em grupos com base no sistema/órgão afetado, também determinamos a assortatividade, quantificando a preferência de nós (doenças) dentro de um grupo específico para se conectarem entre si (valores positivos) ou com doenças de outros grupos (valores negativos) (Costa *et al.*, 2007). Neste estudo, os grupos foram classificados como doenças autoimunes (artrite reumatoide, psoríase e doença celíaca), doenças mentais (depressão e esquecimento), riscos metabólicos (HDL-c baixo, LDL-c alto, colesterol total alto, triglicerídeos altos, sobrepeso/obesidade, hipertensão, pré-diabetes e risco de diabetes), DCNTs fatais (doenças cardiovasculares, diabetes e cânceres), doenças respiratórias (asma, enfisema e bronquite) e doenças bucais (cáries e periodontite). As análises para identificar e visualizar as redes complexas foram realizadas no R versão 4.2.1.

4.4 Metodologia do Capítulo 4

Delineamento do Estudo

Estudo transversal de base populacional aninhado no segmento de São Luís do consórcio de coortes Ribeirão Preto, Pelotas e São Luís (RPS) no Brasil, teve foco em indivíduos de 18 a 19 anos. Todos os participantes da coorte original foram convidados para o segundo seguimento ($n = 687$). Para aumentar o poder estatístico da amostra e minimizar perdas de seguimento, o acompanhamento também incluiu 1133 indivíduos nascidos em São Luís em 1997, identificados pelo Sistema de Informações sobre Nascidos Vivos (SINASC). Além disso, a amostra englobou 695 voluntários nascidos em

1997, identificados por escolas e universidades registradas no SINASC (Confortin *et al.*, 2021). Assim, a amostra do estudo foi composta por 2515 adolescentes, sendo 52,3% mulheres e 47,7% homens.

Aspectos Éticos

Este estudo foi aprovado pelo Comitê de Ética em Pesquisa do Hospital Universitário da Universidade Federal do Maranhão (CAAE #1302489). Todos os participantes assinaram o Termo de Consentimento Livre e Esclarecido.

Coleta de Dados

Para capturar e analisar padrões de coocorrência em redes complexas, as variáveis foram dicotomizadas para simplificar a representação e a interpretação das conexões entre condições de saúde e fatores relacionados.

Determinantes Socioeconômicos

Informações socioeconômicas foram coletadas por meio de questionário de avaliação. As variáveis incluíram baixa escolaridade do adolescente e do chefe pela família (até o ensino fundamental), baixa renda familiar ($\leq$ USD 270,76, com base no salário mínimo nacional do Brasil em 2016) e baixa classe socioeconômica (classes C-E), conforme os Critérios de Classificação Econômica do Brasil (classe A sendo a mais alta e classe E a mais baixa) (Association of Research Companies, 2008).

Fatores Comportamentais

O uso atual de tabaco e o uso atual ou anterior de outras drogas (maconha, cocaína, heroína, ecstasy, crack ou LSD) foram coletados por questionário autoadministrado confidencial. O alto consumo de álcool foi avaliado pelo questionário *Alcohol Use Disorders Identification Test* (AUDIT).

Informações dietéticas foram coletadas por meio de um Questionário de Frequência Alimentar (FFQ) de qualidade e quantidade, administrado por nutricionistas treinados, que investigaram a frequência, o tamanho das porções e a quantidade de alimentos consumidos nos últimos 12 meses. As variáveis dietéticas incluíram alto consumo de gorduras saturadas ($\geq$ 10% das calorias totais), lipídios ($\geq$ 30% das calorias

totais), sódio ($\geq 5\text{g}$) e açúcares livres ($\geq 5\%$ das calorias totais, limite ideal segundo a Organização Mundial da Saúde-OMS) (Ruanpeng *et al.*, 2017). Baixa ingestão de fibras foi definida como $< 25\text{g}$ para mulheres e $< 38\text{g}$ para homens. Baixa ingestão de proteínas foi considerada $< 0,8\text{g/kg}$ de peso corporal, enquanto alta ingestão de proteínas foi $> 2\text{g/kg}$. Análises de sensibilidade consideraram o alto consumo de açúcar livre como 10% (limite máximo da OMS) (Ruanpeng *et al.*, 2017) e 25g (recomendação máxima da *American Heart Association*) (Vos *et al.*, 2017).

Comportamento sedentário foi definido como < 150 minutos de atividade física por semana, avaliado pelo questionário SAPAC (*Self-Administered Physical Activity Checklist*). A má qualidade do sono foi identificada por escores > 5 no Índice de Qualidade do Sono de Pittsburgh (PSQI), e sonolência diurna excessiva foi definida por escores ≥ 9 na Escala de Sonolência de Epworth (ESS).

Condições Metabólicas

Sobrepeso/obesidade foram definidos como índice de massa corporal $> 25\text{kg/m}^2$ e percentual de gordura corporal elevado ($\geq 30\%$ em mulheres e $\geq 25\%$ em homens), utilizando um BOD POD e um estadiômetro (Altura Exata[®]). Hipertensão foi definida por pressão arterial $> 130/80$ mmHg e alta velocidade de onda de pulso ($\geq 90^\circ$ percentil da distribuição da amostra) (Zhao *et al.*, 2019). Outros marcadores incluíram níveis elevados de colesterol total (≥ 200 mg/dL), LDL-c (≥ 130 mg/dL), VLDL-c (≥ 30 mg/dL), triglicerídeos (≥ 150 mg/dL) e HDL-c baixo (< 40 mg/dL). A razão triglicerídeos/HDL-c $\geq 1,75$ (Shim *et al.*, 2016) e o índice TyG ≥ 7.94 (Reckziegel *et al.*, 2023) foram utilizados como marcadores de resistência à insulina.

DCNT na Adolescência

Asma foi autorrelatada com base em diagnóstico médico prévio. A capacidade pulmonar foi avaliada usando o Espirômetro KoKo PFT (Koko[®] Spirometer), considerando FEV₁ $< 80\%$ do valor previsto como anormal (Global Initiative for Chronic Obstructive Lung Disease, 2010).

Depressão e risco de suicídio foram avaliados pela *Mini-International Neuropsychiatric Interview* (MINI), diagnosticando episódios depressivos maiores e recorrentes. Alto risco de suicídio foi indicado por escores ≥ 6 .

A saúde bucal foi avaliada pelo número de dentes cariados (índice CPO-D) e pelo registro de lesões de cárie graves (caracterizadas por envolvimento visível da polpa,

ulceração causada por fragmentos dentários deslocados, fistula ou abscesso, pelo índice PUFA). A periodontite foi classificada conforme as diretrizes da *American Academy of Periodontology/European Federation of Periodontology* (AAP/EFP) de 2018 e dicotomizada como nenhuma ou qualquer periodontite. A presença de sangramento à sondagem (BoP) foi definida como >15% das superfícies afetadas (Ladeira *et al.*, 2023).

Análise dos Dados

Estruturou-se um grafo não direcionado com base em uma matriz de coocorrência, onde os nós representavam fatores/condições de saúde e as arestas suas coocorrências. A aresta foi ponderada pela proporção de coocorrências entre as condições. Modelos gerais e baseados em sexo foram construídos para análise.

Para descrever a estrutura da rede, calcularam-se quatro medidas de centralidade específicas para cada nó: grau, intermediação, centralidade do autovetor e transitividade local. O grau de um nó (condição) representa seu número de conexões (arestas), indicando seu envolvimento na rede. A intermediação mede quantas vezes um nó serve como ponte nos caminhos mais curtos entre outros nós; valores mais altos sugerem que o nó atua como mediador ou ponte entre condições, implicando mecanismos fisiopatológicos ou fatores de risco compartilhados. A centralidade do autovetor atribui um valor a cada nó com base na centralidade dos nós aos quais ele está conectado, identificando nós influentes. A transitividade local é a razão entre o número de triângulos conectados a um nó e o número de triplas centradas nele, indicando a probabilidade de duas condições coocorrerem se ambas já estiverem ligadas a uma terceira (Costa *et al.*, 2007).

A entropia de Shannon específica para cada nó foi medida para avaliar a diversidade de conexões de cada nó, com valores mais altos indicando conexões mais diversas (Eagle, Macy e Claxton, 2010). A entropia de Shannon para toda a rede também foi calculada para refletir a complexidade geral da estrutura da rede (Wiesner e Ladyman, 2019). O coeficiente de agrupamento também foi calculado para avaliar a probabilidade de que um nó forme um triângulo com outros dois, fornecendo informações sobre as características de agrupamento da rede.

4.5 Metodologia do Capítulo 5

Delineamento do Estudo

O Comitê de Ética em Pesquisa do Hospital Universitário da Universidade Federal do Maranhão, Brasil (#14771/2008–30), aprovou este estudo. Foi obtido consentimento

livre e esclarecido por escrito. Para participantes menores de 18 anos, um responsável adulto também assinou o termo de consentimento.

Utilizamos dados do estudo “Fatores Etiológicos do Nascimento Pré-Termo e Consequências de Fatores Perinatais na Saúde da Criança: Coorte Pré-Natal BRISA”, realizado em São Luís, Brasil. São Luís, capital do estado do Maranhão, na região Nordeste do país, tinha uma população de 1.014.837 habitantes e um Índice de Desenvolvimento Humano (IDH) de 0,768 em 2010.

As participantes foram gestantes atendidas em serviços de pré-natal públicos e privados. Como não havia registros abrangentes de gestantes, o tamanho da amostra foi calculado com base nas estimativas de prevalência das principais variáveis explicativas (de 10% a 50%), com margem de erro de 5% e poder estatístico de 80%, resultando em uma meta de 1.500 participantes. A elegibilidade exigia a realização de uma ultrassonografia obstétrica antes da 20ª semana gestacional para confirmação da idade gestacional. Gestantes com gravidez múltipla foram excluídas devido ao maior risco de nascimento pré-termo. A amostra final incluiu 1.383 díades mãe-filho. Mais detalhes sobre a coorte estão descritos em outra publicação (Silva, da *et al.*, 2014).

Coleta de dados

Para analisar padrões de conexão em redes complexas, transformamos as variáveis em formas dicotômicas para simplificar a interpretação dos vínculos entre condições de saúde e fatores de risco.

Durante a 22ª a 25ª semana de gestação, foi aplicado um questionário e realizado um exame odontológico como avaliações de linha de base. A idade materna foi categorizada como avançada para mulheres com 35 anos ou mais e como precoce para aquelas com menos de 20 anos. As participantes responderam se já haviam recebido diagnóstico de hipertensão ou diabetes, ou se haviam passado por cesarianas antes da gestação atual (sim/não). Também foram questionadas sobre o peso pré-gestacional, o qual, combinado com a altura medida, foi utilizado para calcular o IMC pré-gestacional, considerando-se $>25 \text{ kg/m}^2$ como sobrepeso/obesidade.

As variáveis socioeconômicas incluíram baixa escolaridade (até o ensino fundamental), baixa renda familiar ($\leq \text{USD } 290,00$, com base no salário mínimo nacional brasileiro em 2010) e baixa classe socioeconômica (classes C-E), conforme os Critérios

de Classificação Econômica do Brasil (sendo A a mais alta e E a mais baixa) (Association of Research Companies, 2008). A ocupação do chefe da família foi dicotomizada em não qualificada versus semiquificada/qualificada.

O consumo de álcool durante a gestação foi autorreferido com base no consumo semanal de cerveja, vinho e destilados. O tabagismo durante a gestação também foi autorreferido. O consumo semanal de bebidas açucaradas durante a gestação foi identificado quando as gestantes relataram o consumo de refrigerantes. O consumo semanal de alimentos ultraprocessados foi determinado quando as participantes relataram consumir mais de uma vez por semana qualquer um dos seguintes itens: hambúrgueres, cheeseburgers ou sanduíches; salsichas, cachorros-quentes, salame, presunto, mortadela ou outras carnes processadas; bacon ou linguiça; batatas fritas ou salgadinhos industrializados; sorvetes; ou produtos de panificação como biscoitos, doces, bolos, tortas ou folhados.

Os exames odontológicos foram realizados por seis dentistas calibrados. As lesões de cárie foram avaliadas utilizando-se o índice CPO-D (número de dentes Cariados, Perdidos por cárie e Obturados) (World Health Organization, 2013). Também foi realizado exame periodontal, analisado de acordo com o consenso de 2018 da *American Association of Periodontitis* e da *European Federation of Periodontitis* (Tonetti, Greenwell e Kornman, 2018). Posteriormente, a condição periodontal foi dicotomizada em saudável versus qualquer grau de periodontite.

O primeiro acompanhamento ocorreu 48 horas após o parto, momento em que os prontuários médicos foram coletados. Com base no diagnóstico médico, a ocorrência de anemia, diabetes e hipertensão durante a gestação foi dicotomizada como sim/não. Foram identificadas as crianças nascidas por cesariana, bem como aquelas classificadas como macrossômicas (≥ 4 kg). A idade gestacional foi determinada utilizando dois critérios: a data da última menstruação ou o exame de ultrassonografia realizado antes de 20 semanas de gestação. Se a idade gestacional baseada na última menstruação diferisse em até 10 dias daquela estimada pela ultrassonografia, a data da última menstruação era utilizada para calcular a idade gestacional. No entanto, se a diferença fosse superior a 10 dias, utilizava-se a estimativa da ultrassonografia (Verburg *et al.*, 2008). Partos prematuros foram definidos como aqueles ocorridos antes de 37 semanas de gestação.

O segundo acompanhamento ocorreu quando a criança tinha 2 anos de idade. As mães foram questionadas: “Até que idade seu bebê foi alimentado exclusivamente com leite materno, sem chá, água, outros leites, bebidas ou alimentos?” para identificar aquelas

que não amamentaram exclusivamente durante os primeiros seis meses. A interrupção precoce da amamentação (antes de um ano) também foi investigada por meio da pergunta: “O bebê mamou ontem? Se não, até que idade o bebê foi amamentado?” A ingestão alimentar foi avaliada utilizando recordatórios de 24 horas aplicados por nutricionistas treinados, detalhando todos os alimentos e bebidas consumidos, incluindo marca, preparo, tamanho da porção e volume, com o apoio de um álbum fotográfico. Os dados foram analisados no Virtual Nutri Plus® para estimar a ingestão energética e de nutrientes e calcular o consumo diário de açúcares adicionados. O consumo prejudicial foi definido como qualquer ingestão de açúcar adicionado (>0 g/dia) (Vos *et al.*, 2017).

A altura e o peso das crianças foram medidos para calcular o escore-z de IMC, sendo o sobrepeso/obesidade definidos como ≥ 1 escore-z (World Health Organization, 1995). A asma foi identificada por relato materno de diagnóstico médico, múltiplos episódios de chiado no peito ou visitas de emergência. As alergias foram definidas pelo relato materno de dermatite atópica, rinite ou contagem de eosinófilos no terceiro tercil. Exames intraorais identificaram cárie, incluindo lesões não cavitadas, utilizando o índice ceo-d (World Health Organization, 2013).

Abordagem analítica

Os dados faltantes foram imputados utilizando o método de Imputação Múltipla por Equações Encadeadas (MICE), com regressão logística como modelo de imputação. Esse procedimento preservou a estrutura binária dos dados ao imputar valores diretamente como 0 (ausência) ou 1 (presença), com base nas probabilidades preditas (Buuren e Groothuis-Oudshoorn, 2011).

Uma rede não direcionada foi construída a partir de uma matriz de similaridade, onde os nós representavam fatores de risco ou condições de saúde, e as arestas representavam suas relações (Comin *et al.*, 2020). Os pesos das arestas foram calculados utilizando o índice de Jaccard, que quantifica a similaridade de coocorrência como (Fletcher e Islam, 2018):

$$J(A, B) = \frac{|A \cap B|}{|A \cup B|}$$

onde A e B representam dois conjuntos de atributos, $|A \cap B|$ é o número de atributos em comum e $|A \cup B|$ é o número total de atributos presentes em qualquer um dos conjuntos.

Os valores variam de 0 (nenhuma sobreposição) a 1 (sobreposição perfeita), com valores mais altos indicando relações mais fortes (representadas por arestas mais espessas).

Para caracterizar a rede, calculamos cinco métricas de centralidade para cada nó. O grau representa a soma dos pesos das arestas conectadas a um nó, indicando sua participação geral na rede. A centralidade do autovetor (eigenvector) captura a importância de um nó com base em suas conexões com outros nós altamente conectados. A centralidade de proximidade (closeness) reflete a eficiência com que um nó pode alcançar todos os outros, sendo calculada como o inverso do comprimento médio dos caminhos mais curtos. A centralidade de intermediação (betweenness) quantifica a frequência com que um nó se encontra nos caminhos mais curtos entre outros nós, destacando seu papel como mediador ou ponte. Por fim, a transitividade local mede a proporção de triângulos fechados ao redor de um nó, indicando a probabilidade de que seus vizinhos também estejam conectados (Costa *et al.*, 2007).

A detecção de comunidades foi realizada utilizando o algoritmo de Louvain, que otimiza a modularidade (Q) para identificar grupos de nós com conexões internas densas e conexões externas esparsas. A modularidade é definida como (Blondel *et al.*, 2008):

$$Q = \frac{1}{2m} \sum_{ij} \left[A_{ij} - \frac{k_i k_j}{2m} \right] \delta(c_i, c_j)$$

onde A_{ij} é o peso da aresta entre os nós i e j ; k_i e k_j são seus respectivos graus; m é o peso total de todas as arestas, e $\delta(c_i, c_j)$ é igual a 1 se os nós pertencem à mesma comunidade, e 0 caso contrário. O algoritmo mescla comunidades iterativamente para maximizar (Blondel *et al.*, 2008).

Adicionalmente, a entropia de Shannon foi calculada para cada nó a fim de avaliar a diversidade de suas conexões, sendo que valores mais altos representam maior diversidade (Eagle, Macy e Claxton, 2010). A entropia de Shannon para toda a rede também foi calculada, medindo a complexidade geral da rede (Wiesner e Ladyman, 2019). Por fim, o coeficiente de agrupamento foi calculado para determinar a probabilidade de que um nó forme triângulos, oferecendo uma visão sobre o comportamento de agrupamento local (Costa *et al.*, 2007). Todas as análises foram realizadas no R e no RStudio.

4.6 Metodologia do Capítulo 6

Fonte de Dados

Este estudo utilizou estimativas do estudo *Global Burden of Disease* (GBD) 2021, produzido pelo *Institute for Health Metrics and Evaluation* (IHME) da Universidade de Washington. O projeto GBD coleta dados por meio de revisões sistemáticas, buscas direcionadas e contribuições de colaboradores locais e da Organização Mundial da Saúde. Detalhes abrangentes sobre os processos de aquisição de dados usados para produzir as estimativas do GBD 2021 estão disponíveis no manuscrito principal do GBD (Schumacher *et al.*, 2024). Este manuscrito segue as diretrizes do *Guidelines for Accurate and Transparent Health Estimates Reporting* (GATHER) (Stevens *et al.*, 2016).

O GBD 2021 fornece uma avaliação quantitativa da carga de doenças atribuível a 369 doenças e lesões, além de uma análise detalhada de 88 fatores de risco em 204 países e territórios e 811 localizações subnacionais de 1990 a 2021 (Schumacher *et al.*, 2024). A análise dos fatores de risco utilizou dados de mais de 54.000 fontes distintas para gerar estimativas epidemiológicas, identificando 631 pares de risco-desfecho. Esses pares foram derivados por meio de uma abordagem baseada em dados para avaliar associações de risco, permitindo estimativas específicas por idade, sexo, local e ano em níveis globais, regionais e nacionais (Brauer *et al.*, 2024).

Dieta Rica em SSBs

Uma dieta rica em SSBs foi definida como a ingestão média diária (em gramas por dia) de bebidas contendo ≥ 50 kcal por 226,8 gramas de porção, incluindo bebidas gaseificadas, refrigerantes, energéticos e sucos de fruta industrializados, mas excluindo sucos 100% naturais de frutas e vegetais. A Figura Suplementar 1 fornece detalhes sobre as entradas de dados, métodos de processamento e técnicas de modelagem utilizadas, incluindo a abordagem meta-regressão bayesiana regularizada e ajustada (MR-BRT) para cruzamento de dados, conforme descrito no manuscrito principal do GBD (Brauer *et al.*, 2024).

Apresentação de Dados

O *Summary Exposure Value* (SEV) representa o nível populacional de exposição a um risco específico à saúde, neste caso, uma dieta rica em SSBs. O SEV é expresso em

uma escala de 0 a 100, em que 100 indica que toda a população está no nível máximo possível de risco para doenças devido ao alto consumo de SSBs, e 0 indica risco mínimo ou inexistente. Os SEVs para uma dieta rica em SSBs de 1990 a 2021 foram apresentados globalmente e para 204 países, abrangendo sete super-regiões e 21 regiões. A análise inclui estimativas de SEV padronizadas por idade e estratificadas por grupos etários de cinco anos, variando de 25 a 95 anos ou mais (Brauer *et al.*, 2024).

Para contextualizar melhor esses achados, as estimativas de SEV para SSB foram relatadas de acordo com o índice sociodemográfico (SDI). O SDI é uma medida composta que combina renda *per capita* ajustada, anos médios de escolaridade e taxas de fertilidade total para indivíduos com menos de 25 anos. Os valores de SDI variam de 0 a 1, com valores mais altos refletindo maiores níveis de desenvolvimento (Schumacher *et al.*, 2024). A relação entre o alto consumo de SSB e o SDI foi explorada usando Locally Weighted Scatterplot Smoothing (LOWESS) no nível do país, para fornecer informações sobre como fatores socioeconômicos influenciam os padrões de consumo de SSBs e seus riscos associados (Nordhausen e Taskinen, 2021).

Carga de DNT atribuída a SSBs em 2021

O estudo GBD também fornece estimativas da carga de DCNTs atribuídas ao consumo de SSBs. Essas estimativas abrangem o impacto em todas as DCNTs agregadas (Nível 1), bem como separadamente para condições específicas (Nível 2), como doenças cardiovasculares e doenças renais e diabetes. As medidas quantificam a taxa por 100.000 habitantes para diversos indicadores de saúde, incluindo mortes, anos vividos com incapacidade (YLD), anos de vida perdidos (YLL) e anos de vida ajustados por incapacidade (DALY) diretamente atribuíveis ao consumo de SSBs. Métodos detalhados para essas estimativas estão disponíveis em outra fonte (Brauer *et al.*, 2024).

Projeção do SEV de uma dieta rica em SSB até 2050

As projeções do SEV de uma dieta rica em SSB até 2050 foram fornecidas pelo GBD. Os métodos detalhados estão descritos em outra fonte (Zhou e Shen, 2024). Resumidamente, as previsões foram geradas através de um modelo de conjunto que combinou seis modelos de taxas de variação anualizadas com seis modelos de MR-BRT considerando o SDI. Estes modelos incorporaram uma série de esquemas de ponderação da atualidade, desde a ponderação igual de todos os anos até a ponderação exponencial das tendências mais recentes.

Seguindo a hierarquia de fatores de risco do GBD, o consumo elevado de SSBs foi classificado como um risco de Nível 3, juntamente com outros 41 riscos desagregados, como fonte de água insegura, dieta pobre em leite e altos níveis de colesterol LDL (Brauer *et al.*, 2024). O risco de Nível 3 indica um impacto substancial na saúde pública, sugerindo que as SSBs contribuem significativamente para morbidade e mortalidade em escala populacional. Com base nos SEVs em 1990, 2021 e 2050, todos os riscos de Nível 3 foram classificados. Alterações percentuais totais (TPC) e anuais (APC) foram apresentadas para ilustrar as variações de 1990 a 2050.

As análises estatísticas e as figuras foram produzidas usando R (versão 4.2.1) e RStudio (versão 2024.04.2+76).

4.7 Metodologia do Capítulo 7

Este estudo descreve o processo de desenvolvimento de um e-book bilíngue (português e inglês) intitulado “Os Primeiros Mil Dias de Vida: A Odontologia na Perspectiva DOHaD”. A construção do material seguiu uma abordagem sistemática para garantir sua relevância científica, clareza pedagógica e acessibilidade ao público-alvo.

Concepção e Planejamento

Inicialmente, foi realizada uma revisão da literatura sobre a Teoria das Origens Desenvolvimentistas da Saúde e da Doença (DOHaD), enfatizando sua relação com as doenças não transmissíveis (DNT) e a saúde bucal nos primeiros mil dias de vida. A temática foi escolhida devido à relevância das DNT como problema de saúde pública global e ao papel estratégico da odontologia na identificação precoce de fatores de risco e promoção da saúde no ciclo vital.

Estruturação do Conteúdo

O e-book foi organizado em duas versões: português e inglês. A estrutura incluiu introdução, capítulos principais e considerações finais. Foram abordados os seguintes tópicos principais:

- Os primeiros mil dias de vida
- Teoria DOHaD e a Odontologia
- Atenção à saúde durante a gestação
- Estressores ambientais durante a gestação
- Atenção à saúde durante os dois primeiros anos de vida

- Estressores ambientais durante os primeiros dois anos
- Os primeiros mil dias na agenda de enfrentamento das DNT
- Programa Previne Brasil e os indicadores de desempenho da assistência durante os primeiros mil dias

Na versão em inglês, o último tópico foi suprimido, pois trata de uma temática específica do contexto brasileiro.

Redação e Tradução

O conteúdo foi redigido em português e posteriormente traduzido para o inglês, respeitando as nuances culturais e linguísticas de cada idioma. A tradução priorizou a fidelidade ao texto original e a clareza das ideias, visando alcançar tanto profissionais de saúde brasileiros quanto uma audiência internacional interessada na temática. A tradução foi revisada por um fluente na língua inglesa.

Design e Diagramação

O material foi diagramado em formato digital, utilizando software Word da Microsoft Office. Elementos gráficos, como ilustrações e tabelas, foram inseridos para facilitar a compreensão e destacar informações-chave. A escolha das cores e fontes seguiu um padrão amigável e acessível, adequado tanto para leitura em dispositivos móveis quanto em computadores.

Revisão e Validação

O e-book passou por um processo de revisão técnica e linguística realizado por especialistas da área de odontologia, nutrição e saúde coletiva. A validação buscou avaliar a clareza, relevância e aplicabilidade do conteúdo.

Distribuição

O material foi disponibilizado em formato PDF, permitindo fácil acesso e compartilhamento. As duas versões foram publicadas em plataformas digitais de acesso aberto, ampliando sua disseminação entre profissionais de saúde, pesquisadores e estudantes interessados na interseção entre DOHaD e odontologia.

Aspectos Éticos

Todas as informações utilizadas na elaboração do e-book foram provenientes de fontes confiáveis, e os direitos autorais dos materiais consultados foram devidamente respeitados. A iniciativa teve como objetivo a disseminação de conhecimento científico, sem fins lucrativos.

5 RESULTADOS

5.1 Capítulo 1 - Fatores de risco comportamentais e metabólicos associados à periodontite no Brasil, 1990-2019: uma análise multidimensional para o *Global Burden of Disease Study* 2019

“Behavioral and metabolic risk factors associated with periodontitis in Brazil, 1990–2019: a multidimensional analysis for the Global Burden of Disease Study 2019”

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Behavioral and metabolic risk factors associated with periodontitis in Brazil, 1990–2019: a multidimensional analysis for the Global Burden of Disease Study 2019

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Abstract

Objectives Periodontitis is a non-communicable disease (NCD) that may be linked to other NCDs through shared risk factors. Accordingly, we analyzed the relationship between periodontitis and behavioral and metabolic risks common to NCDs in Brazilian adults over three decades.

Methods Indicators of periodontitis, behavioral risks (smoking, alcohol use, sugar-sweetened beverages (SSB), and physical activity), and metabolic risks (overweight/obesity, dyslipidemia, hyperglycemia, and hypertension) in Brazilian adults (25–49 y-old) between 1990 to 2019 were obtained from the Global Burden of Disease Study 2019. Data were adjusted for Gini index. Fixed-effects and Prais-Winsten regressions were performed ($p < 0.05$).

Results The prevalence of periodontitis has increased among Brazilians since 2005. High-SSB diet, alcohol use, and metabolic risks increased between 1990–2019, whereas smoking decreased. In crude models, periodontitis prevalence increased with alcohol use (2545.1; 95%CI: 2307.9–2782.3), high-SSB diet (365.5; 95%CI: 322.5–408.4), low physical activity (1784.4; 95%CI: 763.7–2805.0), overweight/obesity (172.3; 95%CI: 156.3–188.4), dyslipidemia (734.5; 95%CI: 624.7–844.2), and hyperglycemia (1774.3; 95%CI: 1555.9–1992.7). After adjustment for the Gini index, periodontitis prevalence raised with a high-SBB diet (1416.0; 95%CI: 1120.2–1711.8), overweight/obesity (629.9; 95%CI: 573.1–686.8), dyslipidemia (2035.8; 95%CI: 1728.1–2343.5), and hyperglycemia (8918.1; 95%CI: 7979.8–9856.3).

Conclusions Periodontitis has increased in Brazil since 2005, despite the smoking reduction. Sugar-sweetened beverage was the behavioral risk that mostly accompanied the periodontal trend.

Clinical relevance Our results support upstream strategies targeting commercial, social, political, and structural determinants to tackle NCDs and reduce oral health inequities.

Keywords Periodontitis · Behavioral risk factors · Metabolic risk factors · Noncommunicable diseases

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Introduction

Noncommunicable diseases (NCDs), such as cardiovascular disease, cancers, respiratory diseases, and diabetes, are responsible for approximately 70% of deaths worldwide, comprising 85% of premature deaths in low- and middle-income countries [1]. Periodontitis is a chronic disease manifested as irreversible inflammatory destruction of teeth apparatus and is one of the most prevalent NCDs [2]. Although not directly linked to mortality, periodontitis can predict other fatal NCDs decades earlier, such as diabetes and cardiovascular diseases [3].

The American Academy of Periodontology and the European Federation of Periodontology point out that periodontitis results from the interaction between a dysbiotic microbiome and the host-dysregulated immune response. Furthermore, they recognize that smoking and diabetes are risk factors that affect the severity, extent, and treatment response of periodontitis. In contrast, obesity, physical activity, and nutrition were noted as emerging risk factors that need future confirmation as etiological factors for periodontitis [4].

Systematic reviews have shown that alcohol consumption [5], sugar intake [6], and metabolic risk factors, e.g., obesity and hyperglycemia [7], are associated with an increased risk for periodontitis. In contrast, physical activity has been associated with an opposite trend [8]. However, to the best of our knowledge, no nationally representative sample studies have investigated all of those major behavioral and metabolic risk factors for NCDs associated with the rate of periodontitis from a longitudinal perspective.

Brazil is a continental country with peculiarities that make it suitable for assessing trends in behavioral and metabolic risk factors associated with periodontal disease. Brazil's smoking rate has markedly declined over the past few years [9], resulting from an efficient tobacco control policy implemented at the end of the eighties [10]. Meanwhile, the prevalence of periodontitis in Brazil has grown above the global mean in the last three decades [11]. Besides that, other behavioral risk factors, such as added sugar and alcohol consumption, have escalated in the country [12]; so, have metabolic risk factors, i.e., overweight/obesity, hyperglycemia, hypertension, and dyslipidemia rates [9]. Sifting through the literature, studies investigating the prevalence of periodontitis and the risk factors for NCDs after all these transformations are not found. For instance, even though tobacco smoking is an acknowledged cause of periodontitis [4] and its reduction is expected to decrease the burden of periodontitis in the population, it remains uncertain whether other behavioral and metabolic risk factors can nullify the effect of a decrease in exposure to tobacco.

Thus, we hypothesize that the prevalence of periodontitis has been increasing in Brazil over the last three decades,

accompanied by added sugar and alcohol consumption and, consequently, overweight/obesity, hyperglycemia, hypertension, and dyslipidemia rates, despite the smoking reduction. Accordingly, we analyzed the prevalence of periodontitis over the last three decades (1990 to 2019) in Brazilian adults and estimated the association between the burden of behavioral and metabolic risk factors with periodontitis rate.

Methods

Study design

The present study uses panel data from 26 Brazilian states from adults (25 to 49 years) over three decades (1990 to 2019). The data were obtained from the Global Burden of Disease Study 2019 (GBD) [13] and the Brazilian Institute of Geography and Statistics (IBGE). The GBD systematically quantifies global disease and risk factor burdens across 204 countries and territories, enabling comparisons over time, among populations, and across health issues. The primary source of GBD data is national or state representative surveys, and it imputes missing data [14, 15]. Supplementary Table S1 contains descriptive information about the data herein used and its source.

Outcome

The periodontal disease provided by the GBD was the prevalence rate of periodontitis (per 100,000 inhabitants), defined in the study as a Community Periodontal Treatment Needs Index (CPITN) code IV, clinical attachment loss (CAL) > 6 mm, or probing pocket depth (PPD) > 5 mm [16].

Behavioral and metabolic variables

The main behavioral and metabolic risk factors for NCDs were chosen following the World Health Organization (WHO) risk factors for NCDs [1]. Accordingly, the behavioral risk factors were smoking, alcohol use, a diet high in sugar-sweetened beverages (SSB), and low physical activity. The metabolic risk factors were high body mass index (BMI) as an overweight/obesity marker, high LDL cholesterol as an indicator of dyslipidemia, high fasting plasma glucose as a hyperglycemia surrogate, and high systolic blood pressure as a proxy of hypertension. Due to their high collinearity, each independent variable was used in separate regression models. All these variables were available as the summary exposure value (SEV). The SEV measures a population's exposure to a risk factor that considers the intensity of exposure, whose value varies from 0% (non-exposure) to 100% (fully-exposed).

The Gini index from 2005 to 2019 (Fig. S1), which measures the distribution of the Gross Domestic Product (GDP) representing income inequality, ranging from 0 (perfect equality) to 1 (maximum inequality), was used to adjust the models.

Modeling approach

The models were fitted using fixed-effects modeling at a significance level of 0.05. State-level clustering was used to relax the autocorrelation and heteroskedasticity requirement [17]. Fixed-effect models are appropriate for assessing health outcomes because they can estimate unobservable location effects that remain fixed over time, i.e., geographic, and historical factors. Linear regressions were performed using R and RStudio.

The linear regression model consisted of a crude approach using the outcome explained by risk factors and the unobservable fixed-effect. A data matrix with 26 states $\times$ 30 years ($t = 1990\text{--}2019$) was used. The crude model was:

$$\text{Periodontitis}_{it} = \beta_1 \text{RiskFactors}_{it} + u_i + \varepsilon_{it},$$

in which *Periodontitis* is the prevalence rate of periodontitis in a state i in year t . The *RiskFactors* are the SEV of the behavioral risk factors (i.e., smoking, alcohol use, a diet high in sugar-sweetened beverages, and low physical activity) and the metabolic risk factors (i.e., overweight/obesity, dyslipidemia, hyperglycemia, and hypertension). u_i is the unobservable location effect, and ε_{it} is an error term.

Adjusted analysis was performed using the Gini index. As in Brazil the Gini index has not been present since 1990, and evidence suggests a disturbance in the prevalence of periodontitis estimation in Brazil around the 2000s (Fig. S2) [18], thus, regression analyses were conducted using a data matrix with 26 states $\times$ 15 years ($t = 2005\text{--}2019$). The Gini index was chosen because it is the longest series available for the Brazilian states in panel data format and has already been associated with health indicators in the country [19]. Hence, the adjusted regression model was:

$$\text{Periodontitis}_{it} = \beta_1 \text{RiskFactors}_{it} + \beta_2 \text{Gini}_{it} + u_i + \varepsilon_{it}.$$

As a sensitivity analysis, we performed models for the two main behavioral risk factors, smoking, and a diet high in SSB, in the two intervals, 1990–2005 and 2005–2019.

Prais-Winsten estimations were performed to explore trends in time series of the prevalence of periodontitis and the summarized SEV of behavioral and metabolic risk factors. The GBD gives prevalence and SEV in summary form for Brazil, thus, the data matrix analyzed were 1 country $\times$ 30 years (1990–2019) and 1 country $\times$ 15 years (2005–2019). Results were classified as stationary ($p > 0.05$), increased ($\beta_1 > 0$), or decreased ($\beta_1 < 0$), given a $p < 0.05$.

Logarithmic transformation was used to reduce the variance heterogeneity of the residuals. The annual percent change (APC) was also performed using the formula: $100 \cdot (10^\beta - 1)$, being β the coefficient of the Prais-Winsten regression [20].

Role of the funding source

This study was financed by the Coordination for the Improvement of Higher Education Personnel (CAPES). The funding agency did not influence the design, data collection, analysis, or publication decision. All authors had full access to the data and scientific independence to interpret them.

Results

The distribution of periodontitis in the Brazilian states among adults (25 to 49 years old) in 1990, 2005, and 2019 is depicted in Fig. 1. The prevalence of periodontitis significantly increased between 2005 to 2019 (APC: +3.4%; 95%CI: 1.9–5.0) in Brazil. However, over the three decades, an uptrend but non-significant prevalence (APC: +2.0%; 95%CI: -1.2–5.2) was observed. Rio de Janeiro and Rio Grande do Sul were the states that consistently showed the highest rates of periodontitis.

Table 1 shows the time series for each behavioral and metabolic risk factor in Brazil. There was an increase in the SEV of diet high in SSB (APC: +2.4%; 95%CI: 1.9–2.8) and alcohol use (APC: +1.5%; 95%CI: 0.9–2.2), in addition to the SEV of overweight/obesity (APC: +9.9%; 95%CI: 8.7–9.3), dyslipidemia (APC: +1.1%; 95%CI: 1.0–1.1) and hyperglycemia (APC: +3.1%; 95%CI: 2.2–4.1) over the three decades. The SEV of smoking decreased from 14.9% in 1990 to 6.3% (APC: -6.7%; 95%CI: -7.8–5.5). From 2005 to 2019, among the SEV of behavioral factors, only a diet high in SSB (APC: +1.3%; 95%CI: 1.1–1.5) increased, whereas smoking decreased (APC: -9.5%; 95%CI: -9.7–-9.2). In this period, all SEV of metabolic risk factors increased in the country, mainly overweight/obesity (APC: +4.6%; 95%CI: 3.5–5.7). Figure 2 displays the time series of behavioral and metabolic risk factors by state. An upward trajectory of SSB consumption was observed across all states, in contrast to smoking trends. Notably, the states of São Paulo, Rio de Janeiro, and Rio Grande do Sul exhibited the highest rates of SSB consumption in Brazil.

In the crude regression models, the SEV of behavioral risk factors alcohol use (365.5; 95%CI: 2307.9–2782.3), diet high in SSB (365.5; 95%CI: 322.5–408.4), and low physical activity (1784.4; 95%CI: 763.7–2805.0), and the metabolic risk factors overweight/obesity (172.3; 95%CI: 156.3–188.4), dyslipidemia (734.5; 95%CI: 624.7–844.2), and hyperglycemia (1774.3; 95%CI: 1555.9–1992.7) were



Fig. 1 Prevalence rate of periodontitis in Brazilian states among adults (25 to 49 y-old), 1990, 2005, and 2019

positively associated with an increase in the prevalence of periodontitis in Brazil. Conversely, the SEV of smoking was negatively associated with periodontitis prevalence (-398.3 ; 95%CI: $-473.6 - -323.0$) over the study period. The linear regression coefficients are given in Table 2.

Regarding the behavioral risk factors, when the models were adjusted for the Gini index (2005–2019), an increase in the prevalence rate of periodontitis was observed for each percentage increase in the SEV of a diet high in SBB (1416.0 ; 95%CI: $1120.2-1711.8$). The SEV of smoking was negatively associated with the prevalence of periodontitis (-1103.9 ; 95%CI: $-1433.2 - -774.5$). Concerning the metabolic risk factors, an increase in the prevalence rate of periodontitis accompanied the percentage increase in the SEV of overweight/obesity (629.9 ; 95%CI: $573.1-686.8$), dyslipidemia (2035.8 ; 95%CI: $1728.1-2343.5$), and hyperglycemia (8918.1 ; 95%CI: $7979.8-9856.3$). The linear regression coefficients for behavioral and metabolic risk factors adjusted for the Gini index from 2005 to 2019 are described in Table 3. The sensitivity analysis for smoking and SSB consumption in the two intervals (1990–2005 and 2005–2019) yielded consistent results (Table S2).

Discussion

Periodontitis rates have increased significantly among Brazilians since 2005, similar to increased consumption of sugar-sweetened beverages, overweight/obesity, dyslipidemia, and hyperglycemia. Furthermore, the prevalence of periodontitis rose despite the reduction of smoking. These findings reinforce the hypothesis that reducing smoking alone is not enough to reduce periodontitis burden. This

study has the advantage of using the GBD database, providing complete and standardized data, and making it possible to compare population parameters over time in panel analysis.

The prevalence of periodontitis has been linked to the consumption of SSBs in Brazil. This observation may be endorsed by the highest rates of periodontitis in the states of Rio de Janeiro and Rio Grande do Sul, which also have consistently exhibited elevated levels of SSB consumption. Trend analyses showed that sugar-sweetened beverages' consumption rates increased significantly in Brazil over the three decades analyzed. These beverages are the primary source of discretionary calories in the Western diet. Sugar-sweetened beverages have been associated with metabolic risks such as obesity, insulin resistance, and hypertension [21]. Sustained insulin resistance leads the liver into *de novo lipogenesis* and consequent low-grade inflammation [22]. Increasing evidence points to the role of reactive oxygen species in establishing an oxidative stress environment that underlies the pathogenesis of periodontitis [23]. Periodontitis is highly prevalent in patients with type 2 diabetes, smoking habits, and obesity. Moreover, sugar consumption has been associated with cardiovascular risk [24] and also periodontal disease in adolescents [25] and young adults [26]. Poor dietary habits can worsen clinical periodontal parameters, contributing to oral dysbiosis. Sugars function as local stressors for the oral biofilm, which can create a highly proteic feeding environment for gram-negative bacterial species [27]. Inflammation-induced loss of periodontal tissue further exacerbates this situation. Other causative factors such as genetic factors and smoking may also contribute to periodontal lesion chronification, leading to a positive feedback

Table 1 Time series trend analysis of the prevalence of periodontitis and each SEV of behavioral and metabolic risk factors separately among Brazilian adults (25 to 49 years) from 1990–2019

	1990	2019	β_1^a	APC ^b	95%CI	T ^c	R ²	2005	2019	β_1^a	APC ^b	95%CI	T ^c	R ²
Periodontitis	15708.4	19942.2	0.008	2.0	-1.2–5.2	●	0.99	16233.4	19942.2	0.015*	3.4	1.9–5.0	▲	0.99
Behavioral risk factors														
Smoking	14.9	6.3	-0.030*	-6.7	-7.8–-5.5	▼	0.95	11.4	6.3	-0.043*	-9.5	-9.7–-9.2	▼	0.99
Alcohol use	9.0	10.9	0.007*	1.5	0.9–2.2	▲	0.97	10.9	10.9	<0.001	<0.1	-0.1–0.0	●	0.99
Diet high in SSB	36.7	49.2	0.010*	2.4	1.9–2.8	▲	0.99	45.5	49.2	0.006*	1.3	1.1–1.5	▲	0.99
Low physical activity	11.9	12.0	0.001	<0.1	-0.6–0.6	●	0.99	12.2	12.0	-0.001	-0.3	-1.3–0.6	●	0.99
Metabolic risk factors														
Overweight/obesity	15.5	34.0	0.037*	9.9	8.7–9.3	▲	0.99	25.9	34.0	0.020*	4.6	3.5–5.7	▲	0.99
Dyslipidemia	35.1	40.1	0.005*	1.1	1.0–1.1	▲	0.99	37.3	40.1	0.005*	1.2	1.1–1.3	▲	0.99
Hyperglycemia	3.5	4.7	0.013*	3.1	2.2–4.1	▲	0.64	4.1	4.7	0.008*	2.0	1.5–2.4	▲	0.99
Hypertension	15.3	16.4	<0.001*	-0.1	-0.2–0.0	▼	0.14	15.5	16.4	0.004*	0.9	0.9–0.5	▲	0.99

Note: * $p < 0.05$ for Prais-Winsten regression; ^a β_1 - Obtained from Prais-Winsten regression; ^bAPC - Annual percent change (%); ^cT - Trend in time series: ● (stationary), ▲ (increased), and ▼ (decreased). The values presented refer to the trend analysis of the time series for each variable separately

loop that can worsen the deterioration of the tooth apparatus [28].

Our results from the crude analysis showed that an increase in alcohol consumption was associated with an increase in periodontitis burden over the last three decades, previous corroborating findings, including among Brazilians [29]. Alcohol use may reduce the immune response, favoring periodontitis development probably through maladaptive immunity [30]. Additionally, liver inflammation via acetaldehyde production may be observed, inducing *de novo* lipogenesis, and promoting hepatic insulin resistance, dyslipidemia, and hepatic steatosis, similar to the effects caused by added fructose [22]. Thus, alcohol use may result in or hasten low-grade systemic inflammation with oral consequences [22]. However, the alcohol use loss association after the model adjustment for the Gini index. Some hypotheses could explain this finding. First, the stationarity rate of alcohol use in the analyzed period (Table 1) could mask the association. Second, improving the Gini index (Fig. S1) in Brazil could mitigate the effects of alcohol consumption on periodontitis in the population since the alcohol harm paradox emphasizes that disadvantaged groups would be more exposed to alcohol-related problems [31]. Third, it is known that there is a consistent relationship between alcohol and periodontitis among males [5], whereas this study used an indicator for both sexes combined.

Similarly, low physical activity was also significantly associated in crude analysis with periodontitis prevalence. Physical activity could reduce the prevalence of periodontitis by reducing systemic inflammatory levels [8]. A study with obese individuals showed that weight loss induced by physical activity and a healthy diet might increase the expression of adiponectin receptors in adipose tissue and skeletal muscles [32]; an essential hormone regulator of insulin sensitivity and a biomarker for the risk of NCDs. However, the low physical activity rate in the Brazilian population did not account for the increase in periodontitis after adjustment for the Gini index. We suppose that the stationary level of this indicator between 2005 and 2019 was responsible for the loss of association after adjustment (Fig. 2 and Table 1).

Increased overweight/obesity also explained a greater periodontitis burden with the highest magnitude of association (R^2 within = 0.920) among all the explored metabolic risk factors. In this sense, studies hypothesize that the white adipose tissue secretes adipocytokines, which, combined with the hypoxia caused by the expanded adipose tissue [33], could alter the innate immune response, increasing the susceptibility to inflammation and bacterial infections in periodontitis [34]. Since metabolic alterations are usually associated, hyperglycemia and dyslipidemia also explained the increase in periodontitis from 2005 to 2019 (R^2 within > 0.820). A previous study has shown their association with periodontal disease [35]. Data suggest that the

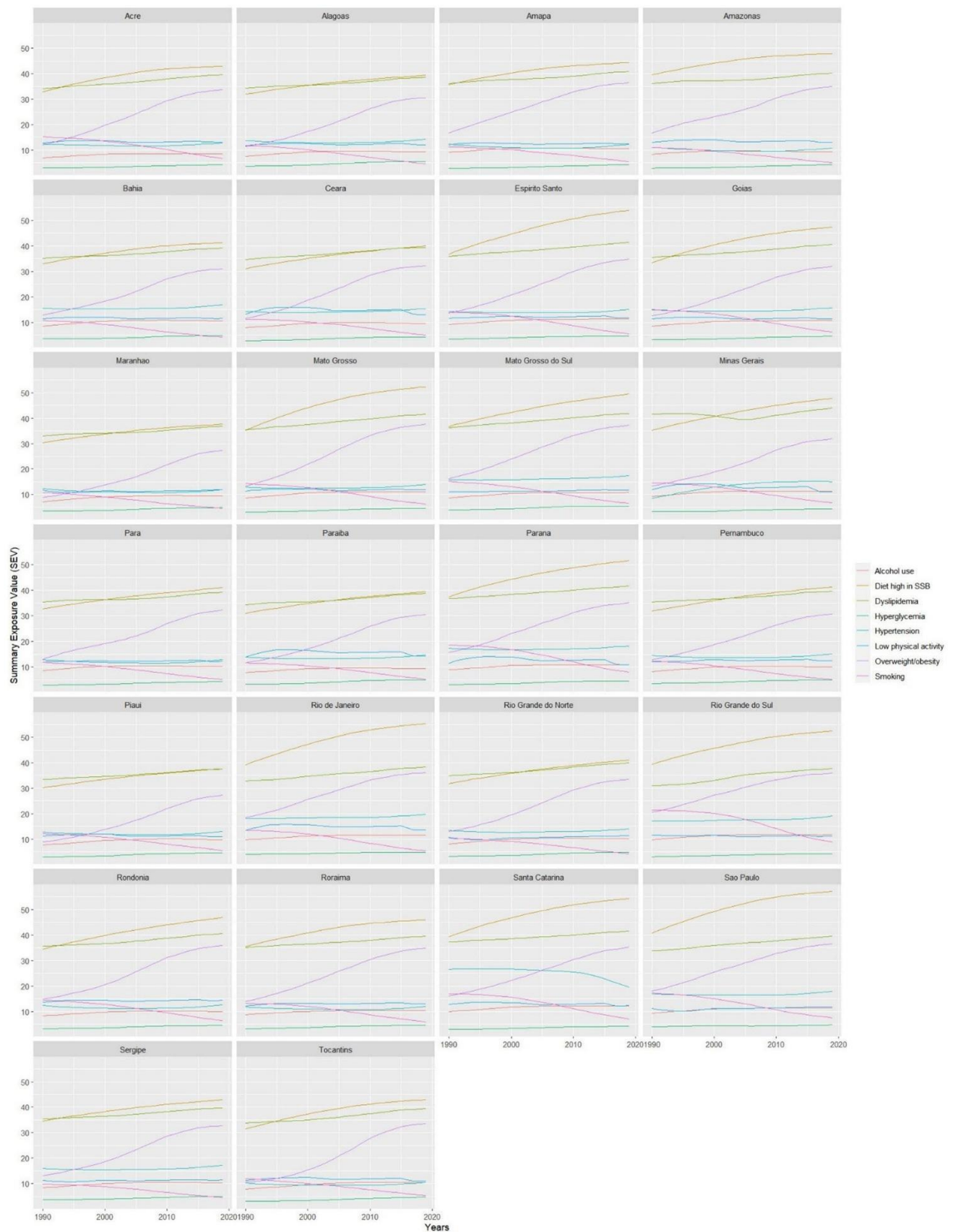


Fig. 2 Summary exposure value of behavioral and metabolic risk factors in Brazilian states among adults (25 to 49 years) between 1990 and 2019

Table 2 Crude linear regression β -coefficients of the SEV of behavioral and metabolic risk factors for the prevalence rate (per 100,000 inhabitants) of periodontitis in the 26 Brazilian states (1990–2019)

	β -coefficient ^a	95% CI ^b	R ² within
Behavioral risk factors			
Smoking	-398.3*	-473.6– -323.0	0.0870
Alcohol use	2545.1*	2307.9–2782.3	0.2107
Diet high in SSB ^c	365.5*	322.5–408.4	0.1387
Low physical activity	1784.4*	763.7–2805.0	0.0534
Metabolic risk factors			
Overweight/obesity	172.3*	156.3–188.4	0.1068
Dyslipidemia	734.5*	624.7–844.2	0.1027
Hyperglycemia	1774.3*	1555.9–1992.7	0.0637
Hypertension	195.8	-421.5–813.3	0.0015

Note: * $p < 0.05$; ^a β -coefficient – Obtained from fixed-effect regression; ^bCI – Confidence Interval; ^cSSB – sugar-sweetened beverages

Table 3 Gini index-adjusted linear regression β -coefficients of the SEV of behavioral and metabolic risk factors for the prevalence rate (per 100,000 inhabitants) of periodontitis in the 26 Brazilian states between 2005 and 2019

	β -coefficient ^a	95% CI ^b	R ² within
Behavioral risk factors			
Smoking	-1103.9*	-1433.2– -774.5	0.7145
Alcohol use	-6727.9	-13,754.4–298.5	0.1540
Diet high in SSB ^c	1416.0*	1120.2–1711.8	0.7460
Low physical activity	437.0	-644.3–1518.3	0.0998
Metabolic risk factors			
Overweight/obesity	629.9*	573.1–686.8	0.9208
Dyslipidemia	2035.8*	1728.1–2343.5	0.8286
Hyperglycemia	8918.1*	7979.8–9856.3	0.8787
Hypertension	1046.5	-1225.1–3318.1	0.1828

Note: * $p < 0.05$; ^a β -coefficient – Obtained from fixed-effect regression; ^bCI – Confidence Interval; ^cSSB – sugar-sweetened beverages

odds of periodontitis increase with the number of components of the metabolic syndrome present in an individual [35]. In fact, the progress of a hyperglycemic state together with a dyslipidemic profile can result in periodontal inflammation caused by systemic oxidative stress and a cascade of cytokines resulting from this process [23].

Surprisingly, our results demonstrate an inverse relationship, with periodontitis burden increasing despite reduced smoking rates. This unexpected outcome is likely linked to a substantial reduction in smoking (-58.14%) driven by Brazil's anti-smoking policies initiated in the 1980s [10]. The data suggests that targeting smoking reduction alone may not effectively mitigate the burden of periodontitis within the population, as it continued to rise. Therefore, we emphasize the necessity of proposing population-level policies addressing other behavioral and metabolic risk factors. In addition

to the variables examined in this study, it is essential to contextualize the observed increase in periodontitis in Brazil during the study period. Various factors may have contributed to this trend, including dietary changes, such as the rise in ultra-processed foods [36, 37], limited access to dental care services, especially in underserved areas [38], as well as socio-economic and cultural factors.

Our findings support upstream strategies targeting commercial, social, political, and structural determinants to tackle NCDs and also reduce oral health inequities. For example, regulatory market policies, labeling, and taxation of products rich in added sugars in connection with subsidies to encourage a healthy diet including more fruits and vegetables can be efficient measures to tackle and prevent NDCs, as learned from the smoking case, whose reduction was associated with a lower periodontitis burden.

As limitations, our findings may be affected by underreporting some indicators since we used secondary data. The primary data source for the GBD information is national or state surveys and missing data are estimated using a smoothing algorithm designed for the database. Additionally, the use of ecological data from Brazilian states for linear regression may not allow for individual-level interpretations due to potential ecological fallacy. Given the close relationship of the conditions under study (periodontitis, behavioral, and metabolic risk factors) to socioeconomic inequalities, our aggregate-level data provide average estimates for both poor and wealthy individuals, requiring cautious interpretation. Despite nearly 30 years of data, our approach may not fully capture the chronic nature of these conditions, particularly periodontitis. The influence of risk factors may require a time lag to manifest, necessitating longer analysis periods to assess cumulative effects fully. Lastly, causal inferences should not be drawn from our study, as despite using fixed effects and control variables, the presence of unobserved time-varying confounding factors cannot be entirely ruled out.

The rate of periodontitis has been increasing in Brazil since 2005, despite the smoking reduction. Sugar-sweetened beverage consumption was the behavioral risk factor that best explained this trend in Brazilians. This behavior is parallelly related to the increased accumulation of exposures to metabolic alterations, thus nullifying the beneficial effect of tobacco reduction. Therefore, interventions on upstream determinants of NDCs are of utmost importance to control metabolic and behavioral risk factors that influence periodontitis rates.

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1007/s00784-023-05384-6>.

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Author contribution SAC designed, performed statistical analyses, and wrote the manuscript; FRMLL designed, wrote the manuscript, and revised its final version; LLCL designed and wrote the manuscript; FLS designed and revised its final version; AMAP designed and revised its final version; BFS performed statistical analyses and revised its final version; GGN designed, performed statistical interpretation, and wrote the manuscript; CCCR coordinated the study, designed, performed statistical interpretation, wrote the manuscript. All authors contributed to the editing and approval of the final version of the manuscript.

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Data Availability The data utilized in this study is publicly available and can be freely accessed for download from <https://vizhub.healthdata.org/gbd-results/> and <https://sidra.ibge.gov.br/tabela/5939>.

Declarations

Ethics approval and consent to participate The University of Washington research ethics committee has approved the GBD study protocol. The GBD was performed in accordance with all relevant federal, state, and local laws, as well as University of Washington regulations and procedures. Participant consent does not apply to this study.

Conflict of interests The authors declare no conflict of interest.

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References

- World Health Organization (2021) Noncommunicable diseases. In: World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>. Accessed 13 Jan 2022
- Peres MA, Macpherson LMD, Weyant RJ et al (2019) Oral diseases: a global public health challenge. *The Lancet* 394:249–260. [https://doi.org/10.1016/S0140-6736\(19\)31146-8](https://doi.org/10.1016/S0140-6736(19)31146-8)
- Bengtsson VW, Persson GR, Berglund JS, Renvert S (2021) Periodontitis related to cardiovascular events and mortality: a long-time longitudinal study. *Clin Oral Invest* 25:4085–4095
- Tonetti MS, Greenwell H, Kornman KS (2018) Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *J Periodontol* 89:S159–S172. <https://doi.org/10.1002/JPER.18-0006>
- Pulikkotil SJ, Nath S, Muthukumaraswamy et al (2020) Alcohol consumption is associated with periodontitis. A systematic review and meta-analysis of observational studies. *Community Dent Health* 37:12–21. https://doi.org/10.1922/CDH_4569Pulikkotil10
- Gupta V, Dawar A, Bhadauria US et al (2022) Sugar-sweetened beverages and periodontal disease: A systematic review. *Oral Dis*. <https://doi.org/10.1111/ODI.14368>
- Salamonowicz M, Zalewska A, Maciejczyk M (2019) Oral consequences of obesity and metabolic syndrome in children and adolescents. *Dent Med Probl* 56:97–104. <https://doi.org/10.17219/dmp/102620>
- Railson de Ferreira O, Corrêa MG, Magno MB et al (2019) Physical activity reduces the prevalence of periodontal disease: Systematic review and meta-analysis. *Front Physiol* 10:234. <https://doi.org/10.3389/fphys.2019.00234>
- Gaspar RS, Rezende LFM, Laurindo FRM (2022) Analysing the impact of modifiable risk factors on cardiovascular disease mortality in Brazil. *PLoS ONE* 17:e0269549. <https://doi.org/10.1371/journal.pone.0269549>
- Portes LH, Machado CV, Turci SRB et al (2018) Tobacco Control Policies in Brazil: a 30-year assessment. *Ciênc Saúde Colet* 23:1837–1848. <https://doi.org/10.1590/1413-81232018236.05202018>
- Chen MX, Zhong YJ, Dong QQ et al (2021) Global, regional, and national burden of severe periodontitis, 1990–2019: An analysis of the Global Burden of Disease Study 2019. *J Clin Periodontol* 48:1165–1188. <https://doi.org/10.1111/jcpe.13506>
- Bryazka D, Reitsma MB, Griswold MG et al (2022) Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. *The Lancet* 400:185–235. [https://doi.org/10.1016/S0140-6736\(22\)00847-9](https://doi.org/10.1016/S0140-6736(22)00847-9)
- Global Burden of Disease Collaborative Network (2020) Global Burden of Disease Study 2019 (GBD 2019) Results. <https://vizhub.healthdata.org/gbd-results/>. Accessed 22 Oct 2023
- Vos T, Lim SS, Abbafati C et al (2020) Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 396:1204–1222. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9)
- Murray CJL, Aravkin AY, Zheng P et al (2020) Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 396:1223–1249. [https://doi.org/10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2)
- Global Burden of Disease Collaborative Network (2020) Periodontal diseases — Level 4 cause. In: Institute for Health Metrics and Evaluation. https://www.healthdata.org/results/gbd_summaries/2019/periodontal-diseases-level-4-cause. Accessed 22 Oct 2023
- Abadie A, Athey S, Imbens GW, Wooldridge JM (2022) When should you adjust standard errors for clustering? *Q J Econ* 138:1–35. <https://doi.org/10.1093/qje/qjac038>
- Costa Junior S da, Araujo PG, Frichembruder K, Hugo FN (2021) Brazilian Oral Health Policy: metasynthesis of studies on the Oral Health Network. *Rev Saúde Pública* 55:105. <https://doi.org/10.11606/s1518-8787.2021055003454>
- Gaspar RS, Rossi L, Hone T, Dornelles AZ (2021) Income inequality and non-communicable disease mortality and morbidity in Brazil States: a longitudinal analysis 2002–2017. *Lancet*

- Reg Health - Am 2:100042. <https://doi.org/10.1016/j.lana.2021.100042>
20. Antunes JLF, Cardoso MRA (2015) Using time series analysis in epidemiological studies. *Epidemiol Serv Saúde* 24:565–576. <https://doi.org/10.5123/S1679-49742015000300024>
 21. Lana A, Rodríguez-Artalejo F, Lopez-Garcia E (2014) Consumption of sugar-sweetened beverages is positively related to insulin resistance and higher plasma leptin concentrations in men and nonoverweight women. *J Nutr* 144:1099–1105. <https://doi.org/10.3945/JN.114.195230>
 22. Lustig RH (2010) Fructose: Metabolic, Hedonic, and Societal Parallels with Ethanol. *J Am Diet Assoc* 110:1307–1321. <https://doi.org/10.1016/j.jada.2010.06.008>
 23. Sczepanik FSC, Grossi ML, Casati M et al (2020) Periodontitis is an inflammatory disease of oxidative stress: We should treat it that way. *Periodontology* 2000 84:45–68. <https://doi.org/10.1111/prd.12342>
 24. Johnson RK, Appel LJ, Brands M et al (2009) Dietary Sugars Intake and Cardiovascular Health. *Circulation* 120:1011–1020. <https://doi.org/10.1161/CIRCULATIONAHA.109.192627>
 25. Moreira ARO, Batista RFL, Ladeira LLC et al (2021) Higher sugar intake is associated with periodontal disease in adolescents. *Clin Oral Investig* 25:983–991. <https://doi.org/10.1007/s00784-020-03387-1>
 26. Lula ECO, Ribeiro CCC, Hugo FN et al (2014) Added sugars and periodontal disease in young adults: an analysis of NHANES III data. *Am J Clin Nutr* 100:1182–1187. <https://doi.org/10.3945/ajcn.114.089656>
 27. Hajishengallis G (2014) The inflammophilic character of the periodontitis-associated microbiota. *Mol Oral Microbiol* 29:248–257. <https://doi.org/10.1111/omi.12065>
 28. Loos BG, Van Dyke TE (2020) The role of inflammation and genetics in periodontal disease. *Periodontology* 2000 83:26. <https://doi.org/10.1111/PRD.12297>
 29. Susin C, Wagner MC, Haas AN et al (2015) The association between alcohol consumption and periodontitis in southern Brazilian adults. *J Periodontal Res* 50:622–628. <https://doi.org/10.1111/jre.12242>
 30. Liangpunsakul S, Toh E, Ross RA et al (2017) Quantity of alcohol drinking positively correlates with serum levels of endotoxin and markers of monocyte activation. *Sci Rep* 7:4462. <https://doi.org/10.1038/s41598-017-04669-7>
 31. Boyd J, Sexton O, Angus C et al (2022) Causal mechanisms proposed for the alcohol harm paradox—a systematic review. *Addiction* 117:33–56. <https://doi.org/10.1111/add.15567>
 32. Christiansen T, Paulsen SK, Bruun JM et al (2010) Diet-induced weight loss and exercise alone and in combination enhance the expression of adiponectin receptors in adipose tissue and skeletal muscle, but only diet-induced weight loss enhanced circulating adiponectin. *J Clin Endocrinol Metab* 95:911–919. <https://doi.org/10.1210/jc.2008-2505>
 33. Guerreiro VA, Carvalho D, Freitas P (2022) Obesity, adipose tissue, and inflammation answered in questions. *J Obes* 2022:1–11. <https://doi.org/10.1155/2022/2252516>
 34. Iwashita M, Hayashi M, Nishimura Y, Yamashita A (2021) The link between periodontal inflammation and obesity. *Curr Oral Health Rep* 8:76–83. <https://doi.org/10.1007/S40496-021-00296-4>
 35. Lamster IB, Pagan M (2017) Periodontal disease and the metabolic syndrome. *Int Dent J* 67:67–77. <https://doi.org/10.1111/IDJ.12264>
 36. Cassiano LS, Peres MA, Motta JVS et al (2022) Periodontitis is associated with consumption of processed and ultra-processed foods: findings from a population-based study. *Nutrients* 14:3735. <https://doi.org/10.3390/nu14183735>
 37. da Costa Louzada ML, Martins APB, Canella DS et al (2015) Ultra-processed foods and the nutritional dietary profile in Brazil. *Rev Saude Publica* 49:38. <https://doi.org/10.1590/S0034-8910.2015049006132>
 38. Bastos TF, de Paula Barbosa Medina L, da Silva Sousa NF et al (2019) Income inequalities in oral health and access to dental services in the Brazilian population: National health survey, 2013. *Rev Bras Epidemiol* 22:E190015.SUPL.2. <https://doi.org/10.1590/1980-549720190015.supl.2>

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5.1.1 Material Suplementar do Capítulo 1

Journal: Oral Clinical Investigations

Title: Behavioral and metabolic risk factors associated with periodontitis in Brazil, 1990-2019: a multidimensional analysis for the Global Burden of Disease Study 2019.

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Table S1. Variables and data sources descriptions used in the analysis^a.

Variable name	Input data	Case definition	Measure	Source
Periodontitis	Periodontal diseases	Community Index of Periodontal Treatment Needs (CPITN) code IV, clinical attachment loss (CAL) > 6 mm, or periodontal pocket depth (PPD) >5mm.	Prevalence rate (per 100,000 habitants)	Institute for Health Metrics and Evaluation/ Global Health Data Exchange Available at: https://vizhub.healthdata.org/gbd-results/
Smoking	Smoking	Current daily or occasional use of any smoked tobacco product.		
Alcohol use	Alcohol use	Current drinkers as individuals consuming at least one alcoholic beverage in the past year. Among current drinkers, was estimated the level of exposure based on average grams of pure alcohol consumed per day.		
Diet high in sugar-sweetened beverages	Diet high in sugar-sweetened beverages	Any intake (in grams per day) of beverages with ≥50 kcal per 226 .8 gram serving, including carbonated beverages, sodas, energy drinks, and fruit drinks, but excluding 100% fruit and vegetable juices.	Summary Exposure Value (SEV) - A measure of a population’s exposure to a risk factor that takes into account the extent of exposure by risk level and the severity of that risk’s contribution to disease burden. SEV takes the value zero when no excess risk for a population exists and the value one when the population is at the highest level of risk; we report SEV on a scale from 0% to 100% to emphasize that it is risk-weighted prevalence.	
Low physical activity	Low physical activity	It was measured in total metabolic equivalents (METs) and was defined as average weekly physical activity (at work, home, transport-related, and recreational) of less than 3000–4500 MET minutes per week.		
Overweight/obesity	High body-mass index	It was defined as body-mass index (BMI) greater than 20–25 kg/m².		
Dyslipidemia	High LDL cholesterol	It was obtained estimating blood concentration of low-density lipoprotein (LDL) greater than 0 .7 and 1 .3 mmol/L.		
Hyperglycemia	High fasting plasma glucose	It was defined as serum fasting plasma glucose of greater than 4 .8–5 .4 mmol/L.		
Hypertension	High systolic blood pressure	It was defined as systolic blood pressure above 110-115 mm Hg.		
Gini index	Gini index	Gini index of gross domestic product at current prices - Reference year 2010.	Gini index - Gini index measures the extent to which the distribution of income (or, in some cases, consumption expenditure) among individuals or households within an economy deviates from a perfectly equal distribution. A Lorenz curve plots the cumulative percentages of total income received against the cumulative number of recipients, starting with the poorest individual or household. The Gini index measures the area between the Lorenz curve and a hypothetical line of absolute equality, expressed as a percentage of the maximum area under the line. Thus, a Gini index of 0 represents perfect equality, while an index of 1 implies perfect inequality.	

^a All data were obtained in a summarized form for Brazil and detailed for each Brazilian state, excluding the Federal District.

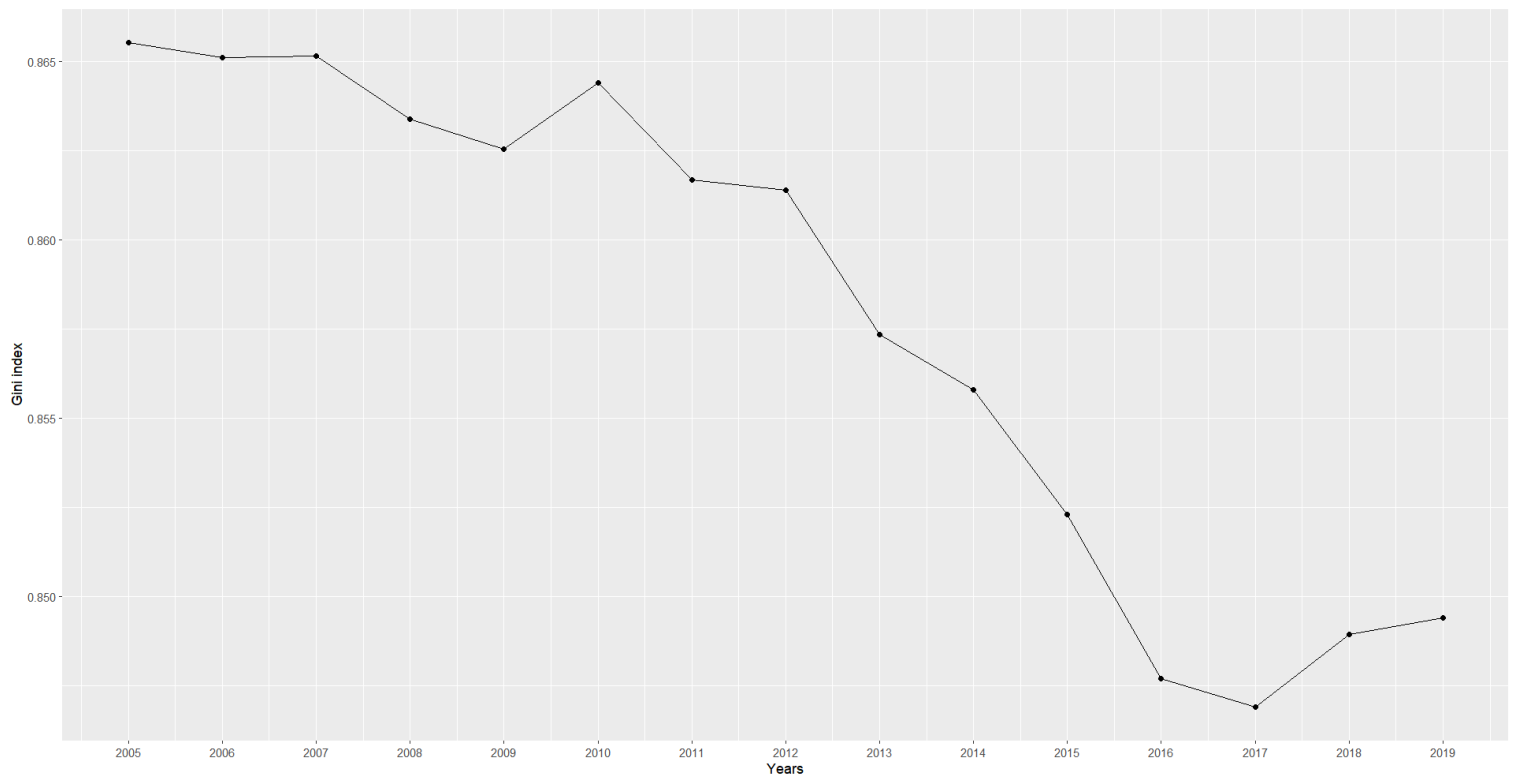
Fig. S1 Gini index of the Gross Domestic Product distribution in Brazil (2005-2019).

Fig. S2 Prevalence rate (per 100,000) of periodontitis among Brazilian adults (25 to 49 years old) between 1990 to 2019.



Table S2. Crude linear regression β -coefficients of the SEV of smoking and SSB consumption for the prevalence rate (per 100,000 habitants) of periodontitis in the 26 Brazilian states during two distinct time periods (1990-2005 and 2005-2019).

	1990-2005		2005-2019	
	β - coefficient ^a	SE ^b	β - coefficient ^a	SE ^b
Smoking	-1773.46*	80.0	-1072.21*	157.5
		9		6
Diet high in SSB ^c	870.94*	50.2	1408.19*	146.1
		2		9

Note: * $p < 0.05$; ^a β -coefficient – Obtained from fixed-effect regression; ^bSE – Standardized Error; ^cSSB - sugar-sweetened beverages.

5.2 Capítulo 2 - Consumo de bebidas ricas em açúcares de adição e periodontite em adultos: Um estudo transversal de base populacional

“Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study”

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ORIGINAL ARTICLE

Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study

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Abstract

Aim: Investigating the association between sugar-sweetened beverages (SSBs) and periodontitis and whether the awareness of diabetes modifies this relationship.

Materials and Methods: Cross-sectional analysis was conducted using the National Health and Nutrition Examination Survey (NHANES III) data involving US adults aged 30–50. Periodontitis was classified according to the Centers for Disease Control and Prevention and American Academy of Periodontology (CDC-AAP), and SSB consumption as dichotomous (<5 or ≥5, <7 or ≥7 and <14 or ≥14 times/week), ordinal and continuous variables. Confounders included family income poverty ratio, education, race/ethnicity, sex, age, food energy intake, smoking and alcohol. Odds ratios (ORs) were obtained by logistic regressions using inverse probability weighting. Effect modification analysis was performed considering self-reported diabetes.

Results: Among 4473 cases analysed, 198 self-reported diabetes. SSBs were associated with periodontitis when individuals consumed ≥5 (OR 1.64; 95% confidence interval [CI] = 1.30–2.06), ≥7 (OR 1.92; 95% CI = 1.50–2.46) and ≥14 (OR 2.19; 95% CI = 1.50–3.18) times/week. The combined effect of consuming SSBs (≥5 and ≥14 times/week) and self-reported diabetes had less impact than the cumulative effect.

Conclusions: SSB consumption was associated with higher odds of periodontitis, and the estimates were reduced among those with awareness of diabetes.

KEYWORDS

diabetes mellitus, non-communicable diseases, periodontitis, sugar-sweetened beverages

Clinical Relevance

Scientific rationale for study: Sugar-sweetened beverage (SSB) consumption increases the risk for non-communicable diseases (NCDs), including periodontitis. Prior investigations have not

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considered important factors, including age groups, diversity of beverages consumed and awareness of a diabetes diagnosis that may modify a person's relationship with sugar consumption.

Principal findings: SSB intake was associated with higher odds of periodontitis in US adults. This association may be modified by the awareness of a diabetes diagnosis.

Practical implications: Dentists should counsel patients to reduce SSB consumption as a preventive measure for periodontitis and other NCDs. Oral care professionals are essential members of teams dedicated to the prevention of NCDs.

1 | INTRODUCTION

Sugar-sweetened beverages (SSBs) account for about 24% of added sugar intake in the North American diet (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2020). These beverages are characterized by artificial sweetening with mono- or disaccharides, including sucrose, high-fructose corn syrup and fruit juice concentrates (Malik & Hu, 2022). Their consumption has become a public health concern due to its association with the increased prevalence of cardiometabolic risk factors and non-communicable diseases (NCDs) (Malik & Hu, 2022). Given that efforts to limit their intake vary by country and are generally soft (von Philipsborn et al., 2019), international SSB consumption trends have remained stable or slightly increased over three decades (Corte et al., 2021).

Periodontitis is one of the most common NCDs (Peres et al., 2019). It is possible that the same inflammatory mechanisms underlying the relationship between SSBs and NCDs could also explain the development of periodontitis (Sczepanik et al., 2020). This interaction involves rapid glucose absorption from SSBs, causing acute hyperinsulinemia, insulin resistance and increased free fatty acids (Giugliano et al., 2006). Acute hyperglycaemia hampers vasodilation and reduces nitric oxide in tissues (Giugliano et al., 1997; Williams et al., 1998), leading to the unrestricted generation of free radical and proinflammatory cytokines, such as interleukin (IL)-6, IL-8 and TNF- α (Esposito et al., 2002). Endothelial cell insulin resistance may impact periodontitis by disrupting VCAM1 expression and leucocyte interactions (Zeze et al., 2023). Furthermore, excess fructose can incite hepatic de novo lipogenesis and foster the accumulation of visceral adipose tissue (Chen et al., 2017; Lustig, 2010). Sugar metabolism by-products may inhibit immune cell function, interfering with glycolysis in effector CD4⁺ T cells and reducing their chemotaxis towards CXCL10, perpetuating inflammation (Ye et al., 2022). Another mechanism involves the impact of glucose and fructose on diminishing the absorption of vitamin D (Lin et al., 2023), which may influence periodontal health. Besides that, early stages of periodontitis may be influenced locally by SSBs. Oral bacteria could transform sugars into short-chain carboxylic acids, for example, potentially contributing to inflammation (Kashket et al., 1998). Additionally, the damage to periodontal tissues creates a subgingival protein-rich environment for the biofilm (Hajishengallis, 2014) in a feedback loop worsening periodontitis lesion (Loos & Van Dyke, 2020). All these mechanisms co-occur and accumulate, potentially contributing to periodontitis progression (Marchetti et al., 2012; Sczepanik et al., 2020).

Studies have highlighted the association between SSB intake and periodontitis in adolescents aged 17–18 (Carmo et al., 2018; Moreira et al., 2021) and young adults spanning from 18 to 39 years old (Kim et al., 2017; Lula et al., 2014). A systematic review detected six studies that investigated such a relationship (Gupta et al., 2022). However, a meta-analysis could not be conducted due to variations in measurement methods and SSB definition (Gupta et al., 2022). Variations included the study population's age range, which was limited to adolescents in some cases (Carmo et al., 2018) or young- and middle-aged adults (Fann et al., 2016; Song et al., 2016), the use of a convenience sample of hospitalized subjects (Almozno et al., 2020), and the focus solely on sweetened coffee consumption as the explanatory variable (Han et al., 2016; Kim & Nam, 2019). Despite the absence of a meta-analysis, these studies consistently found a positive association between SSBs and periodontitis. Caution, however, must be applied to interpreting these findings. Most studies used the presence of periodontal probing depth (PPD) ≥ 4 mm to diagnose periodontitis, but the experience of periodontitis is not exclusively linked to PPD deepening, rendering this measurement potentially inaccurate in identifying periodontitis progression (Mdala et al., 2014).

Previous studies also did not adequately consider the complex relationship between SSB, periodontitis and age. While the prevalence of periodontitis rises with age (Eke et al., 2016, 2020), SSB consumption may decrease (Rosinger et al., 2017). For example, upon medical recommendation or a disease diagnosis, individuals may adopt healthier lifestyle behaviours, introducing a temporal bias in the relationship between SSBs and NCDs, including periodontitis (Szklo & Nieto, 2014). Adults diagnosed with diabetes in the United States exhibit a higher proportional consumption of diet soda and other sugar-free beverages as a strategy to reduce added sugar intake (Nettleton et al., 2009). In this context, one might argue that the association between SSBs and periodontitis could be attenuated or influenced by reverse causality through dietary pattern modifications aimed at addressing conditions like diabetes (Drouin-Chartier et al., 2019).

In sum, the association between SSB intake and periodontitis cannot be taken for granted, considering that current studies have limitations in accounting for those specificities. The null hypothesis posits that there is no relationship between SSBs and periodontitis. Thus, our objective was to explore the association between SSB consumption and periodontitis within a representative sample of the US adult population. Furthermore, we assessed whether awareness of a diabetes diagnosis influences this relationship.

2 | METHODS

2.1 | Study design

This cross-sectional study utilized population-based data from NHANES III, which used a complex, multi-stage, stratified representative sampling strategy encompassing non-institutionalized American civilians. NHANES III was chosen because it offers the largest dataset for periodontal examinations and frequency of SSB consumption. The study included 33994 individuals recruited between 1988 and 1994. Pregnant women and participants with a risk of infectious endocarditis, rheumatic fever and under dialysis were not examined for periodontal conditions due to the risk of bacteraemia. Participants aged 30–50 years with periodontal examination were eligible for this study ($N = 5222$). Figure 1 displays the study flow chart. The population not included in this study is described in Table S1.

2.2 | Periodontitis assessment

Two quadrants (one upper and one lower) were randomly selected for periodontal examination. Each tooth's buccal and mesiobuccal surfaces were probed except for the third molars. The PPD and clinical attachment level (CAL) were measured. CAL was calculated by summing (1) the distance from the free gingival margin to the cemento-enamel junction and (2) the distance from the gingival margin to the base of the sulcus/pocket (PPD). Calibrated dentists performed these assessments, yielding intra-class correlation coefficients ranging from

0.75 to 0.97 for mean and extent scores of CAL and PPD. The specific kappa coefficients for inter-examiner reliability in subject-level prevalence scores ranged from 0.25 to 0.50, with weighted kappa spanning 0.55 to 0.89.

Periodontitis was categorized according to the criteria outlined by the CDC-AAP (Eke et al., 2012). For analytical purposes, this variable was further differentiated into healthy (reference) and participants with any periodontitis. As a sensitive analysis, different periodontal metrics were considered as outcomes: CDC-AAP categorization as ordinal (healthy, mild, moderate and severe), AAP/EFP classification (Tonetti et al., 2018) as ordinal (health, stage I, stage II and stage III/IV based on greatest inter-proximal CAL and PPD), the proportion of sites with PPD ≥ 4 mm, the proportion of sites with CAL ≥ 3 mm, mean CAL, and the proportion of sites exhibiting bleeding on probing, both continuous variables.

2.3 | Sugar-sweetened beverage intake

The main explanatory variable was the weekly frequency of SSB intake based on the responses to the food-frequency questionnaire. In this study, SSBs encompassed artificially sweetened beverages such as chocolate milk and hot cocoa; Hi-C (Coca-Cola Foods), Tang (Kraft General Foods Inc.) and Kool-Aid (Kraft General Foods Inc.); and regular colas and sodas consumed monthly. The correction factor for SSB intake was 1 month = 4.3 weeks (unrounded values) (Centers for Disease Control and Prevention, 1996). Considering the absence of consensus regarding a cut-off point indicative of a risky SSB consumption

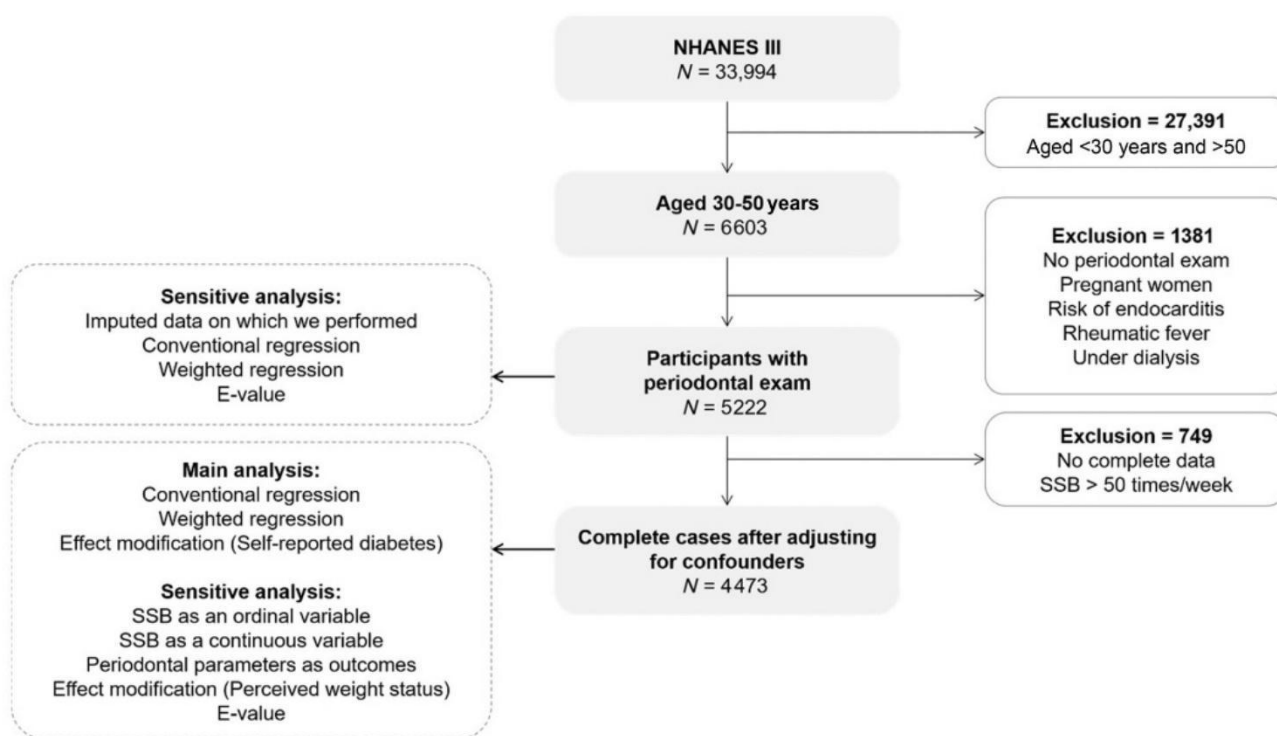


FIGURE 1 Study's flow chart.

behaviour, three dichotomous variables were utilized as the number of SSBs consumed per week: <5 or ≥ 5 times/week, <7 or ≥ 7 times/week and <14 or ≥ 14 times/week. As a sensitivity analysis, the consumption of SSBs was also considered as an ordinal variable (<5 times/week; ≥ 5 times to <7 times/week; ≥ 7 times to <14 times/week; and ≥ 14 times/week) and as a continuous variable. SSB consumption spanned from 0 to 148, a range that appeared irrational. To address this, participants who reported consuming ≥ 50 times/week were excluded based on the data distribution (Figure S2).

2.4 | Confounder assessment

Questionnaires were used to collect data on sex, age and race/ethnicity (non-Hispanic white, non-Hispanic black and Mexican-American). Family income poverty ratios were computed by comparing family income to the annually adjusted poverty line set by the US Census Bureau (base year: 1) (Eke et al., 2018; Rosinger et al., 2019). This led to three categories: low (<1.3), middle (≥ 1.3 to <3.5) and high income (≥ 3.5). Education level was categorized as less than 9th grade, 9th–11th grade, high school graduate or some college. Previous diabetes diagnosis was self-reported as presence or absence. Total food energy intake (kcal) over the prior 24 h was treated as a continuous variable. Smoking behaviour was dichotomized into never and former (previous use of ≥ 100 cigarettes in the lifetime) or current. Alcohol use was categorized according to self-reported intake in the previous 24 h (yes or no).

2.5 | Statistical analysis

Figure S1 displays the summarized directed acyclic graph used to investigate the relationship. Initially, conventional logistic regression was used, adjusting for family income poverty ratio, education level, race/ethnicity, sex, age, smoking and alcohol to explore the association between periodontitis and SSB intake. Subsequently, the average treatment effect (ATE) of SSBs on periodontitis was estimated using inverse probability weighting (IPW) from the propensity score applied in the logistic regression, balancing the exposed and unexposed groups. After adjusting for confounders, estimates were obtained for complete cases ($N = 4473$). To address variability, the weights were stabilized and truncated at the 99th percentile (Chesnaye et al., 2022). E-value calculations were performed to evaluate unmeasured confounding. A high E-value means that substantial unmeasured confounding is required to nullify the effect estimate (VanderWeele & Ding, 2017). As a sensitivity analysis, these estimates were obtained using multivariate imputation by chained equations (MICE) to handle variables with over 5% missing data. The bootstrap method was applied to parameters to reflect imputed model variability. Detailed data imputation methodology is provided in the Supplementary Material.

The study further examined whether diabetes awareness could modify the relationship between SSBs and periodontitis. This was accomplished using IPW, assuming an unconfounded effect of SSBs on periodontitis given the confounders, with diabetes awareness as a modifier, following Vanderweele (2009). Adjusted ORs were reported for each stratum of SSB consumption and diabetes awareness. Effect modification was assessed through both additive and multiplicative scales, quantified by the relative excess risk due to interaction for OR ($RERI_{OR}$) and the ratio of odds ratios between groups based on diabetes status. $RERI_{OR}$ values >0 mean that there are strong indications that the estimated effect on the additive scale of SSB with self-reported diabetes was larger than the estimated effect of SSB without self-reported diabetes, thus indicating positive effect modification of SSB across strata of self-reported diabetes on an additive scale. $RERI_{OR}$ values <0 indicate a negative effect modification. On a multiplicative scale, values >1 suggest that the effect of SSB among those with self-reported diabetes is larger than among those without self-reported diabetes, while values <1 indicate effect modification in the opposite direction and 1 reveals no effect on modification (Knol & VanderWeele, 2012). To evaluate if diabetes self-awareness differed from other health conditions, a sensitivity analysis was conducted using perceived weight status as a modifier, which has been suggested to influence SSB consumption (Malik & Hu, 2022). Using R 4.3.1, all analyses were conducted with 5% significance level for two-sided tests. Survey weights were applied using the 'survey' package. Propensity scores were performed using the 'WeightIt' package, and 'cobalt' was utilized to assess covariate balance. Detailed descriptions of the statistics used to check balance can be found in the Supplementary Material.

3 | RESULTS

Population characteristics are presented in Table 1. The sample included adults aged 30–50 who underwent periodontal examination (36.2% of those examined). The prevalence of any periodontitis was 27.4% (mild: 4.2%; moderate: 19.8%; and severe: 3.4%). SSB consumption ranged from 0 to 49.8 times/week, with 36.3% consuming ≥ 5 , 23.4% ≥ 7 and 10.7% ≥ 14 times/week. Among these participants, 2.9% self-reported diabetes. Regarding the population not included in the study (Table S1), the prevalence of periodontitis, SSB consumption, awareness of diabetes diagnosis, age and total food energy intake differed. However, no discrepancies were observed in the distribution by sex, educational level, race/ethnicity, smoking and alcohol consumption.

Table 2 displays odds ratios from conventional regressions and IPW-weighted ATE. A positive association between SSBs and periodontitis is noted in models using conventional regressions and IPW. Positive associations between SSBs and periodontitis were noted in both conventional regressions and IPW models. IPW models revealed that consuming SSBs ≥ 5 (OR 1.81; 95% CI = 1.43–2.30), ≥ 7 (OR 1.94; 95% CI = 1.50–2.52) or ≥ 14 (OR 2.19; 95% CI = 1.50–

TABLE 1 Characteristics of the US population: NHANES III (N = 5222).

	Unweighted N (%)	Weighted % ^a
Periodontitis		
Yes	1751 (33.5)	27.4
No	3471 (66.5)	72.6
Missing	-	
SSB (times/w) ^b		
<5	2803 (53.7)	63.7
≥5	2391 (45.8)	36.3
<7	3562 (68.2)	76.6
≥7	1632 (31.3)	23.4
<14	4572 (87.6)	89.3
≥14	622 (11.9)	10.7
Missing	28 (0.5)	
Family income poverty ratio		
Low income (<1.3)	1482 (28.4)	14.4
Middle income (≥1.3 to <3.5)	2086 (39.9)	42.4
High income (≥3.5)	1263 (24.2)	43.2
Missing	391 (7.5)	
Race/ethnicity		
Non-Hispanic white	1672 (32.0)	81.0
Non-Hispanic black	1682 (32.2)	12.7
Mexican-American	1646 (31.5)	6.3
Missing	222 (4.3)	
Education level		
Less than 9th grade	891 (17.1)	6.4
9–11th grade	711 (13.6)	9.0
High school graduate	1695 (32.5)	32.6
Some college	1890 (36.2)	52.0
Missing	35 (0.7)	
Sex		
Male	2394 (45.8)	49.3
Female	2828 (54.2)	50.7
Missing	-	
Age, year		
Mean ± SD ^c	38.5 ± 0.2	38.5 ± 0.3
Missing	-	
Self-reported diabetes		
Yes	231 (4.4)	2.9
No	4981 (95.4)	97.1
Missing	10 (0.2)	
Total food energy intake, kcal		
Mean ± SD ^c	2235.1 ± 28.7	2310.2 ± 52.4
Missing	133 (2.6)	
Smoking		
Never	2576 (49.3)	47.2

(Continues)

TABLE 1 (Continued)

	Unweighted N (%)	Weighted % ^a
Former or current	2641 (50.6)	52.8
Missing	5 (0.1)	
Alcohol use		
Yes	1396 (26.7)	30.6
No	3693 (70.7)	69.4
Missing	133 (2.5)	

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aWeighted distribution not considering missing values.

^bSugar-sweetened beverages (SSBs) in different forms: <5 or ≥5, <7 or ≥7 and <14 or ≥14 times/week.

^cMean and standard deviation (SD).

3.18) times/week increased the odds of periodontitis. *E*-value analysis indicated that unmeasured confounding must be 3.0–3.8 times greater to nullify these associations. Sensitivity analysis with multiple imputations showed similar results but with attenuated magnitudes (Table S2). In weighted regressions, ORs ranged from 1.26 (95% CI = 1.01–1.59) for SSB consumption and ≥5 to 1.67 (95% CI = 1.17–2.39) for SSB ≥14 times/week. Sensitivity analysis showed a dose–response gradient in the association between SSB consumption and periodontitis, ≥7 to <14 (OR 1.51; 95% CI = 1.11–2.05) and ≥14 times/week (OR 1.84; 95% CI = 1.74–2.57) in IPW models (Table S3). Moreover, the SSB consumption as a continuous variable demonstrated statistical associations with the CDC–AAP ordinal classification (OR 1.03; 95% CI = 1.01–1.05), the proportion of sites with PPD ≥ 4 mm (OR 1.02; 95% CI = 1.01–1.03) and the proportion of sites with CAL ≥ 3 mm (OR 1.02; 95% CI = 1.01–1.05). It also showed marginal associations with the AAP/EFP ordinal classification (OR 1.01; 95% CI = 1.00–1.02), mean CAL (OR 1.00; 95% CI = 0.99–1.01) and the proportion of sites with bleeding on probing (OR 1.01; 95% CI = 0.99–1.02) (Table S4).

Analyses of the effect modification by diabetes awareness on the SSB–periodontitis association are outlined in Tables 3 and 4. Both diabetes diagnosis and higher SSB consumption independently raised the odds of periodontitis (Table 3). However, SSB consumption was associated with a greater likelihood of periodontitis only among those who reported not having diabetes (Table 4). The combined effect of SSB consumption ≥5 (RERI_{OR} −0.83; 95% CI = −2.11 to −0.45) and SSB ≥14 (RERI_{OR} −1.25; 95% CI = −2.67 to −0.17) times/week and diabetes awareness was less than the cumulative additive effect (Table 3). On a multiplicative scale, the effect modification was in the same direction, but marginally significant for consumption ≥5 (OR 0.56; 95% CI = 0.3–1.03) and SSB ≥14 (OR 0.39; 95% CI = 0.14–1.00) times/week (Table 4). In sensitivity analysis, the odds of the association of SSB–periodontitis according to the perceived weight status increased, displaying an inverse pattern, especially for consumption ≥5 times/week (OR 1.33; 95% CI = 1.05–1.68) on the multiplicative scale (Table S6).

TABLE 2 Estimates of sweetened sugar intake on periodontitis in the US adults using either conventional regression-based adjustment or inverse probability weighting: NHANES III.

SSB (times/week) ^a	Conventional regression-based adjustment ^b		Inverse probability weighted regression ^c	
	OR (95% CI)	E-value (CI)	OR (95% CI)	E-value (CI)
<5 (reference)	1.0		1.0	
≥5	1.33 (1.04–1.70)	1.99 (1.24)	1.81 (1.43–2.30)	3.02 (2.21)
<7 (reference)	1.0		1.0	
≥7	1.56 (1.20–2.03)	2.50 (1.69)	1.94 (1.50–2.52)	3.29 (2.37)
<14 (reference)	1.0		1.0	
≥14	1.68 (1.19–2.38)	2.75 (1.66)	2.19 (1.50–3.18)	3.80 (2.37)

Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

^aThe models were tested by having sugar-sweetened beverages (SSBs) in different forms: < 5 or ≥5, < 7 or ≥7 and <14 or ≥14 times/week; Odds ratios (ORs) were obtained from logistic regression models adjusted for confounders: family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, smoking and alcohol use. Estimates for complete cases ($N = 4473$).

^bLogistic regression models adjusted for confounders using the conventional method.

^cLogistic regression models adjusted by the inverse probability weighting (IPW) method.

TABLE 3 Analysis of biological interactions between sugar-sweetened beverages (SSBs) and self-reported diabetes on periodontitis among US adults: NHANES III.

Additive interaction terms	N with/without periodontitis	OR	95% CI
SSB < 5 and no diabetes	633/1620	1.0	
SSB ≥ 5 and no diabetes	756/1266	1.62	1.44–1.82
SSB < 5 and diabetes	64/70	2.27	1.68–3.06
SSB ≥ 5 and diabetes	30/34	2.05	1.20–3.48
Measure of additive interaction: $RERI_{OR}$ (95% CI) = -0.83 (-2.11 to -0.45)			
SSB < 7 and no diabetes	859/2031	1.0	
SSB ≥ 7 and no diabetes	530/855	1.53	1.35–1.75
SSB < 7 and diabetes	80/75	2.03	1.51–2.72
SSB ≥ 7 and diabetes	19/24	2.35	1.28–4.33
Measure of additive interaction: $RERI_{OR}$ (95% CI) = -0.2 (-1.74 to 1.33)			
SSB < 14 and no diabetes	1164/2578	1.0	
SSB ≥ 14 and no diabetes	225/308	1.60	1.34–1.90
SSB < 14 and diabetes	88/95	2.02	1.50–2.71
SSB ≥ 14 and diabetes	6/9	1.37	0.52–3.38
Measure of additive interaction: $RERI_{OR}$ (95% CI) = -1.25 (-2.67 to -0.17)			

Note: Odds ratios (ORs) weighted propensity score adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, smoking and alcohol use. Estimates for complete cases ($N = 4473$). The models were tested having SSBs in different forms: < 5 or ≥5, < 7 or ≥7 and <14 or ≥14 times/week. $RERI_{OR}$ means the relative excess risk due to interaction for OR on an additive scale.

Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

4 | DISCUSSION

The study found associations between the consumption of SSBs and periodontitis. Besides, this relationship may be modified by the awareness of a diagnosis of diabetes, which may mask this relationship from a reverse causality perspective. The results provide valuable information about the contributing causes of periodontitis.

The study presents certain limitations. The half-mouth periodontal protocol may have underestimated the periodontitis prevalence (Albandar, 2011). Moreover, self-reported variables (diabetes, weight,

smoking, diet, alcohol) could be influenced by recall and social desirability biases. People may forget information and/or tend to underreport their weight and harmful habits to make a good impression about their health profile (Althubaiti, 2016). Nonetheless, the use of underestimated variables could indicate the magnitude of the associations could be greater. Regarding the effect modification analyses, although results were significant for individuals who consumed more SSBs (≥5 and ≥7) and also reported diabetes, the limited sample in these categories hinders accurate interpretation of the estimate for these groups. Additionally, interpreting causal inferences from cross-

	Diabetes		No diabetes	
	OR	95% CI	OR	95% CI
SSB < 5	1.0		1.0	
SSB ≥ 5	0.91	0.49–1.65	1.62	1.44–1.82
Effect modification on a multiplicative scale: OR (95% CI) = 0.56 (0.3–1.03)				
SSB < 7	1.0		1.0	
SSB ≥ 7	1.16	0.60–2.26	1.53	1.35–1.75
Effect modification on a multiplicative scale: OR (95% CI) = 0.76 (0.38–1.5)				
SSB < 14	1.0		1.0	
SSB ≥ 14	0.64	0.23–1.61	1.65	1.39–1.95
Effect modification on a multiplicative scale: OR (95% CI) = 0.39 (0.14–1.00)				

Note: Odds ratios (ORs) weighted propensity score adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, smoking and alcohol use. Estimates for complete cases ($N = 4473$). The models were tested having SSBs in different forms: < 5 or ≥ 5, < 7 or ≥ 7 and < 14 or ≥ 14 times/week. Effect modification on a multiplicative scale was obtained from the ratio of ORs. Abbreviations: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

TABLE 4 Analysis of effect modification of sugar-sweetened beverages (SSBs) on periodontitis by self-reported diabetes among US adults: NHANES III.

sectional design requires caution, though graphs (Figure S1) clarify the assumed relationships among variables.

SSBs increased the chance of periodontitis across tested models. Remarkably, SSB consumption has been associated with NCDs and cardiometabolic risk factors such as overweight/obesity and insulin resistance in various populations (Gupta et al., 2022; Meng et al., 2021; Szczepanik et al., 2020). SSB consumption activates the dopamine reward system, leading to excess calorie intake and weight gain, and together with rapid glucose absorption, promotes hyperinsulinemia and insulin resistance (Chen et al., 2017; Malik & Hu, 2022). Additionally, added fructose is metabolized into fatty acids and triglycerides (Lustig, 2010; Softic et al., 2017) and ectopic lipid accumulation and very-low-density lipoprotein cholesterol secretion are observed, causing insulin signalling impairment, increased oxidative stress and inflammation (Chen et al., 2017). Reactive oxygen species may induce apoptosis of periodontal cells and provide favourable conditions for local inflammation, increasing the risk of periodontitis (Marchetti et al., 2012; Szczepanik et al., 2020). Concomitantly, as endothelial cells are deficient in across-membrane glucose transport, glucose in SSBs induces harmful glucose levels in the intracellular environment (Hansen et al., 2017). This triggers a propensity for oxidative stress and the synthesis of advanced glycosylation end products, promoting inflammation and microvascular alterations in periodontal tissues (Nyvad & Takahashi, 2020). Not surprisingly, inflammatory markers such as IL-1 β , IL-6 and TNF- α , underlying other NCDs, have been associated with early signs of periodontitis (Ribeiro et al., 2021). These early stages are also affected locally by SSBs. Oral bacteria can convert sugars into short-chain carboxylic acids, which can contribute to gingival inflammation (Kashket et al., 1998). Oral microbial metabolites affect tissue immune response and repair, but the precise mechanisms causing bone loss remain unclear (Basic & Dahlén, 2023). Further research exploring the roles of metabolites on tissues is necessary to bridge this knowledge gap. Furthermore, the destruction of periodontal tissue creates a highly protein-nourishing environment for the biofilm (Hajishengallis, 2014), establishing a feedback loop that

exacerbates periodontitis (Loos & Van Dyke, 2020). Therefore, limiting free-sugar intake seemed to reduce gingival inflammation (Woelber et al., 2023).

The analysis revealed an intriguing pattern: acknowledging a diabetes diagnosis altered the association between SSBs and periodontitis, but notably, this association was statistically significant only among those without a diabetes diagnosis. These findings were consistent, especially in the additive interaction analyses. Our hypothesis posits that the diagnosis of diabetes may serve as a turning point where individuals alter their SSB consumption habits, yet the signs of periodontitis persist because this condition, like other NCDs, develops slowly over time. It is worth to note that the literature lacks robust insights into behavioural changes following a diabetes diagnosis, leaving this conjecture as a potential explanation for the reverse causality phenomenon often observed in cross-sectional studies, including this one (Drouin-Chartier et al., 2019; Malik & Hu, 2022). Additionally, the same phenomenon did not hold for perceived overweight (Tables S5 and S6).

The appropriate method for measuring SSB consumption remains debatable. Here, SSB intake was assessed by the frequency of weekly consumption, a commonly employed approach in research examining the link between SSBs and various health conditions, including periodontitis (Gupta et al., 2022), hyperglycaemia (Lana et al., 2014) and diabetes (Drouin-Chartier et al., 2019). In this study, SSB consumption was assessed in various ways because there is no clear consensus on the threshold at which behaviour becomes a risk factor, and studies tend to use arbitrary cut-off points (Carmo et al., 2018; Song et al., 2016). International health organizations have offered guidelines defining cut-off points in terms of the percentage of total daily energy from added sugar, ranging from 5% to 10%, for preventing NCDs (World Health Organization, 2015), but these recommended amounts do not protect against periodontitis (Ladeira et al., 2022).

Focusing on individuals aged 30–50 helps clarify the connection between SSB intake and periodontitis by reducing the influence of

potential confounders. Older people tend to have more advanced stages and grades of periodontitis, and tend to reduce their sugar intake due to various factors like changing taste preferences, using prosthetic replacements, health conditions requiring less sugar, lifestyle changes, economic factors and oral health concerns. Younger individuals tend to consume more SSBs but are less likely to have periodontitis or diabetes, which obscures the relationships examined in this study.

The strengths should also be emphasized. This study employed the conservative CDC-AAP classification for periodontitis, integrating multiple inter-proximal site thresholds, including CAL ≥ 3 to 6 mm and PPD ≥ 4 to 5 mm, thus enhancing sensitivity in identifying true cases (Eke et al., 2012). Moreover, the study used IPW, a technique that offers advantages in controlling for confounders, such as equalizing the distribution of measured confounders between participants with varying SSB consumption, thereby mitigating confounding bias. Furthermore, IPW preserved most individuals in the analysis, bolstering the effective sample size (Chesnaye et al., 2022). The study also innovatively demonstrated reverse causality related to the awareness of a diabetes diagnosis. Finally, results showed external validity in sensitivity analyses on multiple imputation data and for unmeasured confounders.

Consuming SSBs increased periodontitis risk. These findings underscore the need to analyse factors contributing to periodontitis, supporting preventive measures targeting SSB intake, including commercial, social, political and structural factors. This approach can help prevent periodontitis and other NCDs while integrating dentists into multidisciplinary healthcare teams for NCD prevention.

AUTHOR CONTRIBUTIONS

Silas Alves-Costa: Conception, data analysis, data interpretation and drafting of the work, data acquisition and critical review. **Marco A. Peres:** Design of the work, data interpretation and critical review. **Huihua Li:** Data analysis, data interpretation and critical review. **Susilena Arouche Costa:** Data acquisition and critical review. **Gustavo G. Nascimento:** Conception, data interpretation and critical review. **Cecilia Claudia Costa Ribeiro:** Conception and critical review. **Fábio Renato Manzolli Leite:** Conception, design of the work, data interpretation and critical review. All authors have read and agreed to the final version of the manuscript and can be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in National Center for Health Statistics at <https://wwwn.cdc.gov/nchs/nhanes/nhanes3/>.

ETHICS STATEMENT

The NHANES protocol received approval from the National Center for Health Statistics Research Ethics Review Board, and informed consent was obtained from all participants. No further ethical approvals were necessary for analyzing the data for public use.

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REFERENCES

- Albandar, J. M. (2011). Underestimation of periodontitis in NHANES surveys. *Journal of Periodontology*, 82(3), 337–341. <https://doi.org/10.1902/JOP.2011.100638>
- Almoznino, G., Gal, N., Levin, L., Mijiritsky, E., Weinberg, G., Lev, R., Zini, A., Touger-Decker, R., Chebath-Taub, D., & Shay, B. (2020). Diet practices, body mass index, and oral health-related quality of life in adults with periodontitis – A case-control study. *International Journal of Environmental Research and Public Health*, 17(7), 2340. <https://doi.org/10.3390/IJERPH17072340>
- Althubaiti, A. (2016). Information bias in health research: Definition, pitfalls, and adjustment methods. *Journal of Multidisciplinary Healthcare*, 9, 211–217. <https://doi.org/10.2147/JMDH.S104807>
- Basic, A., & Dahlén, G. (2023). Microbial metabolites in the pathogenesis of periodontal diseases: A narrative review. *Frontiers in Oral Health*, 4, 1210200. <https://doi.org/10.3389/froh.2023.1210200>
- Carmo, C. D. S., Ribeiro, M. R. C., Teixeira, J. X. P., Alves, C. M. C., Franco, M. M., França, A. K. T. C., Benatti, B. B., Cunha-Cruz, J., & Ribeiro, C. C. C. (2018). Added sugar consumption and chronic oral disease burden among adolescents in Brazil. *Journal of Dental Research*, 97(5), 508–514. <https://doi.org/10.1177/0022034517745326>
- Centers for Disease Control and Prevention. (1996). *Third National Health and Nutrition Examination Survey (NHANES III), 1988–94*. Centers for Disease Control and Prevention. <https://wwwn.cdc.gov/nchs/data/nhanes3/1a/ADULT-acc.pdf>
- Chen, Z., Yu, R., Xiong, Y., Du, F., & Zhu, S. (2017). A vicious circle between insulin resistance and inflammation in nonalcoholic fatty liver disease. *Lipids in Health and Disease*, 16(1), 203. <https://doi.org/10.1186/s12944-017-0572-9>
- Chesnaye, N. C., Stel, V. S., Tripepi, G., Dekker, F. W., Fu, E. L., Zoccali, C., & Jager, K. J. (2022). An introduction to inverse probability of treatment weighting in observational research. *Clinical Kidney Journal*, 15(1), 14–20. <https://doi.org/10.1093/CKJ/SFAB158>
- Corte, K. D., Fife, J., Gardner, A., Murphy, B. L., Kleis, L., Corte, D. D., Schwingshackl, L., Lecheminant, J. D., & Buyken, A. E. (2021). World trends in sugar-sweetened beverage and dietary sugar intakes in children and adolescents: A systematic review. *Nutrition Reviews*, 79(3), 274–288. <https://doi.org/10.1093/NUTRIT/NUAA070>
- Drouin-Chartier, J.-P., Zheng, Y., Li, Y., Malik, V., Pan, A., Bhupathiraju, S. N., Tobias, D. K., Manson, J. E., Willett, W. C., & Hu, F. B. (2019). Changes in consumption of sugary beverages and artificially sweetened beverages and subsequent risk of type 2 diabetes: Results from three large prospective U.S. cohorts of women and men. *Diabetes Care*, 42(12), 2181–2189. <https://doi.org/10.2337/dc19-0734>

- Eke, P. I., Borgnakke, W. S., & Genco, R. J. (2020). Recent epidemiologic trends in periodontitis in the USA. *Periodontology* 2000, 82(1), 257–267. <https://doi.org/10.1111/PRD.12323>
- Eke, P. I., Page, R. C., Wei, L., Thornton-Evans, G., & Genco, R. J. (2012). Update of the case definitions for population-based surveillance of periodontitis. *Journal of Periodontology*, 83(12), 1449–1454. <https://doi.org/10.1902/jop.2012.110664>
- Eke, P. I., Thornton-Evans, G. O., Wei, L., Borgnakke, W. S., Dye, B. A., & Genco, R. J. (2018). Periodontitis in US adults: National Health and Nutrition Examination Survey 2009–2014. *Journal of the American Dental Association*, 149, 576–588. <https://doi.org/10.1016/J.ADAJ.2018.04.023>
- Eke, P. I., Wei, L., Borgnakke, W. S., Thornton-Evans, G., Zhang, X., Lu, H., McGuire, L. C., & Genco, R. J. (2016). Periodontitis prevalence in adults ≥ 65 years of age, in the USA. *Periodontology* 2000, 72(1), 76. <https://doi.org/10.1111/PRD.12145>
- Esposito, K., Nappo, F., Marfella, R., Giugliano, G., Giugliano, F., Ciotola, M., Quagliaro, L., Ceriello, A., & Giugliano, D. (2002). Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans. *Circulation*, 106(16), 2067–2072. <https://doi.org/10.1161/01.CIR.0000034509.14906.AE>
- Fann, J. C. Y., Lai, H., Chiu, S. Y. H., Yen, A. M. F., Chen, S. L. S., & Chen, H. H. (2016). A population-based study on the association between the intake of soft drinks and periodontal disease in Taiwanese adults aged 35–44 years (KCIS no. 33). *Public Health Nutrition*, 19(8), 1471–1478. <https://doi.org/10.1017/S13688980015002608>
- Giugliano, D., Ceriello, A., & Esposito, K. (2006). The effects of diet on inflammation. *Journal of the American College of Cardiology*, 48(4), 677–685. <https://doi.org/10.1016/j.jacc.2006.03.052>
- Giugliano, D., Marfella, R., Coppola, L., Verrazzo, G., Acampora, R., Giunta, R., Nappo, F., Lucarelli, C., & D'Onofrio, F. (1997). Vascular effects of acute hyperglycemia in humans are reversed by L-arginine. *Circulation*, 95(7), 1783–1790. <https://doi.org/10.1161/01.CIR.95.7.1783>
- Gupta, V., Dawar, A., Bhadauria, U. S., Purohit, B. M., & Nilima, N. (2022). Sugar-sweetened beverages and periodontal disease: A systematic review. *Oral Diseases*, 29, 3078–3090. <https://doi.org/10.1111/odi.14368>
- Hajishengallis, G. (2014). The inflammophilic character of the periodontitis-associated microbiota. *Molecular Oral Microbiology*, 29(6), 248–257. <https://doi.org/10.1111/omi.12065>
- Han, K., Hwang, E., & Park, J. B. (2016). Association between consumption of coffee and the prevalence of periodontitis: The 2008–2010 Korea National Health and Nutrition Examination Survey. *PLoS One*, 11(7), e0158845. <https://doi.org/10.1371/JOURNAL.PONE.0158845>
- Hansen, N. W., Hansen, A. J., & Sams, A. (2017). The endothelial border to health: Mechanistic evidence of the hyperglycemic culprit of inflammatory disease acceleration. *IUBMB Life*, 69(3), 148–161. <https://doi.org/10.1002/iub.1610>
- Kashket, S., Zhang, J., & Niederman, R. (1998). Gingival inflammation induced by food and short-chain carboxylic acids. *Journal of Dental Research*, 77(2), 412–417. <https://doi.org/10.1177/00220345980770021001>
- Kim, S., Park, S., & Lin, M. (2017). Permanent tooth loss and sugar-sweetened beverage intake in U.S. young adults. *Journal of Public Health Dentistry*, 77(2), 148–154. <https://doi.org/10.1111/jphd.12192>
- Kim, Y. R., & Nam, S. H. (2019). Comparison of periodontal status according to the additives of coffee: Evidence from Korean National Health and Nutrition Examination Survey (2013–2015). *International Journal of Environmental Research and Public Health*, 16(21), 4219. <https://doi.org/10.3390/IJERPH16214219>
- Knol, M. J., & VanderWee, T. J. (2012). Recommendations for presenting analyses of effect modification and interaction. *International Journal of Epidemiology*, 41(2), 514–520. <https://doi.org/10.1093/IJE/DYR218>
- Ladeira, L. L. C., Nascimento, G. G., Leite, F. R. M., Alves-Costa, S., Thomaz, E. B. A. F., Alves, C. M. C., Cury, J. A., & Ribeiro, C. C. C. (2022). Sugar intake above international recommendations and oral disease burden: A population-based study. *Oral Diseases*, 1–9. <https://doi.org/10.1111/ODI.14464>
- Lana, A., Rodríguez-Artalejo, F., & Lopez-Garcia, E. (2014). Consumption of sugar-sweetened beverages is positively related to insulin resistance and higher plasma leptin concentrations in men and nonoverweight women. *The Journal of Nutrition*, 144(7), 1099–1105. <https://doi.org/10.3945/JN.114.195230>
- Lin, W.-T., Gonzalez, G. V., Kao, Y.-H., Lin, H.-Y., Li, M. S., Seal, D. W., Lee, C.-H., Hu, C., Chen, L.-S., & Tseng, T.-S. (2023). Mediation of BMI on 25-hydroxyvitamin D levels in U.S. adults with sugar-sweetened beverages consumption. *Nutrients*, 15(15), 3291. <https://doi.org/10.3390/nu15153291>
- Loos, B. G., & Van Dyke, T. E. (2020). The role of inflammation and genetics in periodontal disease. *Periodontology* 2000, 83(1), 26. <https://doi.org/10.1111/PRD.12297>
- Lula, E. C. O., Ribeiro, C. C. C., Hugo, F. N., Alves, C. M. C., & Silva, A. A. M. (2014). Added sugars and periodontal disease in young adults: An analysis of NHANES III data. *The American Journal of Clinical Nutrition*, 100(4), 1182–1187. <https://doi.org/10.3945/ajcn.114.089656>
- Lustig, R. H. (2010). Fructose: Metabolic, hedonic, and societal parallels with ethanol. *Journal of the American Dietetic Association*, 110(9), 1307–1321. <https://doi.org/10.1016/j.jada.2010.06.008>
- Malik, V. S., & Hu, F. B. (2022). The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. *Nature Reviews Endocrinology*, 18(4), 205–218. <https://doi.org/10.1038/s41574-021-00627-6>
- Marchetti, E., Monaco, A., Procaccini, L., Mummolo, S., Gatto, R., Tetè, S., Baldini, A., Tecco, S., & Marzo, G. (2012). Periodontal disease: The influence of metabolic syndrome. *Nutrition & Metabolism*, 9, 88. <https://doi.org/10.1186/1743-7075-9-88>
- Mdala, I., Olsen, I., Haffajee, A. D., Socransky, S. S., Thoresen, M., & De Blasio, B. F. (2014). Comparing clinical attachment level and pocket depth for predicting periodontal disease progression in healthy sites of patients with chronic periodontitis using multi-state Markov models. *Journal of Clinical Periodontology*, 41(9), 837–845. <https://doi.org/10.1111/JCPE.12278>
- Meng, Y., Li, S., Khan, J., Dai, Z., Li, C., Hu, X., Shen, Q., & Xue, Y. (2021). Sugar- and artificially sweetened beverages consumption linked to type 2 diabetes, cardiovascular diseases, and all-cause mortality: A systematic review and dose-response meta-analysis of prospective cohort studies. *Nutrients*, 13(8), 2636. <https://doi.org/10.3390/nu13082636>
- Moreira, A. R. O., Batista, R. F. L., Ladeira, L. L. C., Thomaz, E. B. A. F., Alves, C. M. C., Saraiva, M. C., Silva, A. A. M., Brondani, M. A., & Ribeiro, C. C. C. (2021). Higher sugar intake is associated with periodontal disease in adolescents. *Clinical Oral Investigations*, 25(3), 983–991. <https://doi.org/10.1007/s00784-020-03387-1>
- Nettleton, J. A., Lutsey, P. L., Wang, Y., Lima, J. A., Michos, E. D., & Jacobs, D. R. (2009). Diet soda intake and risk of incident metabolic syndrome and type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care*, 32(4), 688–694. <https://doi.org/10.2337/dc08-1799>
- Nyvad, B., & Takahashi, N. (2020). Integrated hypothesis of dental caries and periodontal diseases. *Journal of Oral Microbiology*, 12(1), 1710953. <https://doi.org/10.1080/20002297.2019.1710953>
- Peres, M. A., Macpherson, L. M. D., Weyant, R. J., Daly, B., Venturelli, R., Mathur, M. R., Listl, S., Celeste, R. K., Guarnizo-Herreño, C. C., Kearns, C., Benzan, H., Allison, P., & Watt, R. G. (2019). Oral diseases: A global public health challenge. *The Lancet*, 394(10194), 249–260. [https://doi.org/10.1016/S0140-6736\(19\)31146-8](https://doi.org/10.1016/S0140-6736(19)31146-8)
- Ribeiro, C. C. C., Carmo, C. D. S., Benatti, B. B., Casarin, R. V. C., Alves, C. M. C., Nascimento, G. G., & Moreira, A. R. O. (2021). Systemic circulating inflammatory burden and periodontitis in adolescents. *Clinical Oral Investigations*, 25(10), 5855–5865. <https://doi.org/10.1007/s00784-021-03891-y>

- Rosinger, A., Bethancourt, H., & Francis, L. A. (2019). Association of Caloric Intake from Sugar-Sweetened Beverages with Water Intake among US children and young adults in the 2011-2016 National Health and Nutrition Examination Survey. *JAMA Pediatrics*, 173(6), 602-604. <https://doi.org/10.1001/JAMAPEDIATRICS.2019.0693>
- Rosinger, A., Herrick, K., Gahche, J., & Park, S. (2017). Sugar-sweetened beverage consumption among U.S. adults, 2011-2014. *NCHS Data Brief*, 270, 1-8.
- Sczepanik, F. S. C., Grossi, M. L., Casati, M., Goldberg, M., Glogauer, M., Fine, N., & Tenenbaum, H. C. (2020). Periodontitis is an inflammatory disease of oxidative stress: We should treat it that way. *Periodontology* 2000, 84(1), 45-68. <https://doi.org/10.1111/prd.12342>
- Softic, S., Gupta, M. K., Wang, G.-X., Fujisaka, S., O'Neill, B. T., Rao, T. N., Willoughby, J., Harbison, C., Fitzgerald, K., Ilkayeva, O., Newgard, C. B., Cohen, D. E., & Kahn, C. R. (2017). Divergent effects of glucose and fructose on hepatic lipogenesis and insulin signaling. *Journal of Clinical Investigation*, 127(11), 4059-4074. <https://doi.org/10.1172/JCI94585>
- Song, I.-S., Han, K., Ko, Y., Park, Y.-G., Ryu, J.-J., & Park, J.-B. (2016). Associations between the consumption of carbonated beverages and periodontal disease: The 2008-2010 Korea national health and nutrition examination survey. *Medicine*, 95(28), e4253. <https://doi.org/10.1097/MD.0000000000004253>
- Szklo, M., & Nieto, F. J. (2014). *Epidemiology: Beyond the basics* (3rd ed.). Jones & Bartlett Learning. www.jblearning.com
- Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Periodontology*, 89, S159-S172. <https://doi.org/10.1002/JPER.18-0006>
- U.S. Department of Agriculture, & U.S. Department of Health and Human Services. (2020). *Dietary guidelines for Americans, 2020-2025* (Issue 9). dietaryguidelines.gov
- Vanderweele, T. J. (2009). On the distinction between interaction and effect modification. *Epidemiology*, 20(6), 863-871. <https://doi.org/10.1097/EDE.0b013e3181ba333c>
- VanderWeele, T. J., & Ding, P. (2017). Sensitivity analysis in observational research: Introducing the E-value. *Annals of Internal Medicine*, 167(4), 268-274. <https://doi.org/10.7326/M16-2607>
- von Philipsborn, P., Stratil, J. M., Burns, J., Busert, L. K., Pfadenhauer, L. M., Polus, S., Holzapfel, C., Hauner, H., & Rehfuss, E. (2019). Environmental interventions to reduce the consumption of sugar-sweetened beverages and their effects on health. *Cochrane Database of Systematic Reviews*, 2019(6), CD012292. <https://doi.org/10.1002/14651858.CD012292.pub2>
- Williams, S. B., Goldfine, A. B., Timimi, F. K., Ting, H. H., Roddy, M.-A., Simonson, D. C., & Creager, M. A. (1998). Acute hyperglycemia attenuates endothelium-dependent vasodilation in humans in vivo. *Circulation*, 97(17), 1695-1701. <https://doi.org/10.1161/01.CIR.97.17.1695>
- Woelber, J. P., Gebhardt, D., & Hujel, P. P. (2023). Free sugars and gingival inflammation: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, 50, 1188-1201. <https://doi.org/10.1111/jcpe.13831>
- World Health Organization. (2015). *Guideline: Sugars intake for adults and children*. WHO. <https://apps.who.int/iris/handle/10665/149782>
- Ye, L., Jiang, Y., & Zhang, M. (2022). Crosstalk between glucose metabolism, lactate production and immune response modulation. *Cytokine & Growth Factor Reviews*, 68, 81-92. <https://doi.org/10.1016/j.cytogfr.2022.11.001>
- Zeze, T., Shinjo, T., Sato, K., Nishimura, Y., Imagawa, M., Chen, S., Ahmed, A.-K., Iwashita, M., Yamashita, A., Fukuda, T., Sanui, T., Park, K., King, G. L., & Nishimura, F. (2023). Endothelial insulin resistance exacerbates experimental periodontitis. *Journal of Dental Research*, 102(10), 1152-1161. <https://doi.org/10.1177/00220345231181539>

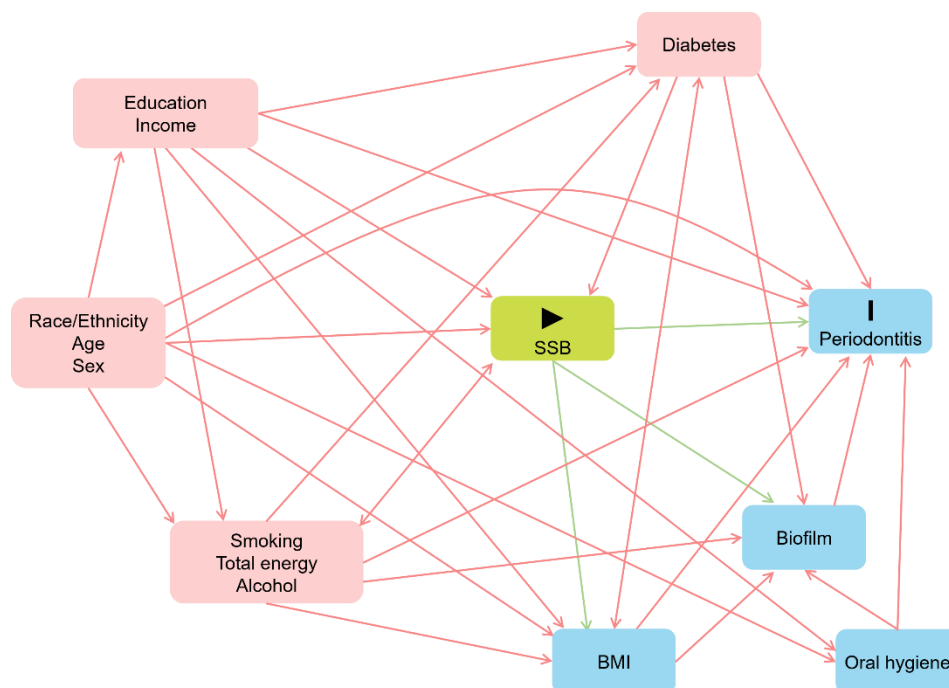
SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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5.2.1 Material Suplementar do Capítulo 2

Figure S1. Full directed acyclic graph used to investigate the relationship between SSB and periodontitis.

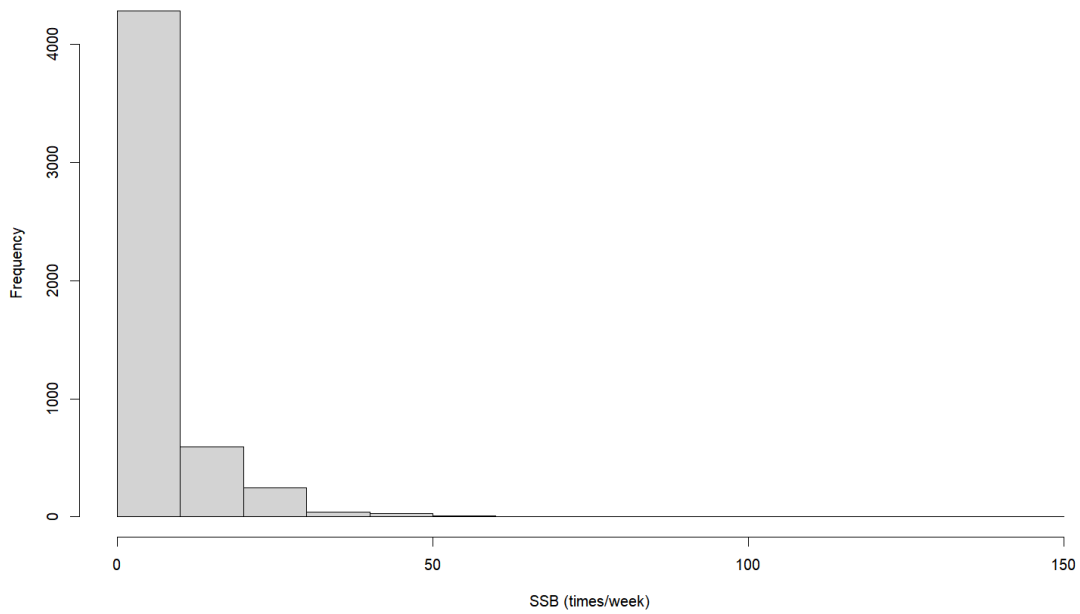


Note: This theoretical model was built based on literature and served to choose the confounding variables for the relationship between sugar-sweetened beverages (SSBs) and periodontitis. The sociodemographic variables income, educational level, and race/ethnicity are consistently associated with SSBs and periodontitis, particularly among men (Eke et al., 2020; Roesler et al., 2021; Rosinger et al., 2017). SSB intake seems to decrease with age, but the opposite is observed for periodontitis prevalence (Eke et al., 2020; Kit et al., 2013). It is well established that smoking, total food energy, and alcohol consumption increase the risk of periodontitis (Leite et al., 2018; Pulikkotil et al., 2020; Martinon et al., 2021) and there is evidence that both form with sugar a construct of addictive behaviors that could influence each other (Kearns et al., 2018; Pepino & Mennella, 2007). BMI - body mass index.

Reference

- Eke, P. I., Borgnakke, W. S., & Genco, R. J. (2020). Recent epidemiologic trends in periodontitis in the USA. *Periodontology* 2000, 82(1), 257–267.
- Kearns, C. E., Lisha, N. E., & Ling, P. M. (2018). Soda intake and tobacco use among young adult bar patrons: A cross-sectional study in seven cities. *Preventive Medicine Reports*, 10, 195.
- Kit, B. K., Fakhouri, T. H., Park, S., Nielsen, S. J., & Ogden, C. L. (2013). Trends in sugar-sweetened beverage consumption among youth and adults in the United States: 1999–2010. *The American Journal of Clinical Nutrition*, 98(1), 180–188.
- Leite, F. R. M., Nascimento, G. G., Scheutz, F., & López, R. (2018). Effect of smoking on periodontitis: A systematic review and meta-regression. *American Journal of Preventive Medicine*, 54(6), 831–841.
- Martinon, P., Fraticelli, L., Giboreau, A., Dussart, C., Bourgeois, D., & Carrouel, F. (2021). Nutrition as a key modifiable factor for periodontitis and main chronic diseases. *Journal of Clinical Medicine*, 10(2), 197.
- Pepino, M. Y., & Mennella, J. A. (2007). Effects of Cigarette Smoking and Family History of Alcoholism on Sweet Taste Perception and Food Cravings in Women. *Alcoholism, Clinical and Experimental Research*, 31(11), 1891.
- Pulikkotil, S. J., Nath, S., Muthukumaraswamy, Dharamarajan, L., Jing, K. T., & Vaithilingam, R. D. (2020). Alcohol consumption is associated with periodontitis. A systematic review and meta-analysis of observational studies. *Community Dental Health*, 37(1), 12–21.
- Roesler, A., Rojas, N., & Falbe, J. (2021). Sugar-sweetened beverage consumption, perceptions and disparities by race, ethnicity, and socioeconomic status in children and adolescents. *Journal of Nutrition Education and Behavior*, 53(7), 553.
- Rosinger, A., Herrick, K., Gahche, J., & Park, S. (2017). Sugar-sweetened beverage consumption among U.S. adults, 2011–2014. *NCHS Data Brief*, 270, 1–8.

Figure S2. Histogram of the frequency distribution of the consumption of sugar-sweetened beverages among US adults. NHANES III.



Note: SSB - Sugar-sweetened beverage.

Table S1. Distribution of characteristics of the population excluded from the study. NHANES III.

	13 to 29 y-old	51 to 90 y-old
	N (%)	N (%)
Periodontitis		
Yes	554 (9.5)	2,103 (62.0)
No	5,252 (90.5)	1,290 (38.0)
Missing	-	-
SSB (times/ w)[†]		
<5	1,494 (25.7)	2,602 (76.7)
≥5	2,767 (47.7)	778 (22.9)
<7	2,098 (36.1)	2962 (87.3)
≥7	2,163 (37.3)	419 (12.3)
<14	3,346 (57.6)	3244 (95.6)
≥14	915 (15.8)	136 (4.0)
Missing	1,545 (26.6)	13 (0.4)
Family income poverty ratio		
Low income (<1.3)	2,245 (38.7)	770 (22.7)
Middle income (≥1.3 to <3.5)	2,269 (39.1)	1,311 (38.6)
High income (≥3.5)	710 (12.2)	975 (28.7)
Missing	582 (10.0)	337 (9.9)
Race/ethnicity		
Non-Hispanic white	1,499 (25.8)	1,752 (51.6)
Non-Hispanic black	1,912 (32.9)	687 (20.2)
Mexican American	2,118 (36.5)	837 (24.7)
Missing	277 (4.8)	117 (3.4)
Education level		
Less than 9th grade	534 (9.2)	1050 (30.9)
9-11th grade	1,159 (20.0)	471 (13.9)
High school graduate	1,485 (25.6)	906 (26.7)
Some college	1,107 (19.1)	930 (27.4)
Missing	1,521 (26.2)	36 (1.1)
Gender		
Male	2,727 (47.0)	1,729 (51.0)
Female	3,079 (53.0)	1,664 (49.0)
Missing	-	-
Age, year		
Mean ± SD [‡]	20.8 ± 0.1	65.3 ± 0.3
Missing	-	-
Self-reported diabetes		
Yes	54 (0.9)	428 (12.6)
No	4,251 (73.2)	2,955 (87.1)
Missing	1,501 (25.9)	10 (0.3)
Total food energy intake, kcal		
Mean ± SD [‡]	2,385.0 ± 31.1	1,807.4 ± 27.5
Missing	156 (2.7)	118 (3.5)
Smoking		
Never	2,843 (49.0)	1,634 (48.2)
Former or current	1,467 (25.3)	1,751 (51.6)
Missing	1,496 (25.8)	8 (0.2)
Alcohol use		
Yes	1,000 (17.2)	607 (17.9)
No	4,651 (80.1)	2,668 (78.6)
Missing	155 (2.7)	118 (3.5)

Note: Periodontal exam was performed among people aged 13 to 90 y-old. [†] Sugar-sweetened beverages (SSBs) in different forms: <5 or ≥5, <7 or ≥7, and <14 or ≥14 times/week. [‡] Mean and standard deviation (SD). NHANES – National Health and Nutrition Examination Survey.

Table S2. Estimates of sweetened sugar intake on periodontitis in the US adults using either conventional regression-based adjustment or inverse probability weighting from multiple imputation data. NHANES III.

SSB (times/ week) [†]	Conventional regression-based adjustment [‡]		Inverse probability weighted regression [§]	
	OR (95% CI)	E-value (CI)	OR (95% CI)	E-value (CI)
< 5 (reference)	1.0		1.0	
≥ 5	1.27 (1.01 – 1.61)	1.86 (1.11)	1.26 (1.01 – 1.59)	1.83 (1.11)
< 7 (reference)	1.0		1.0	
≥ 7	1.48 (1.14 – 1.90)	2.32 (1.54)	1.48 (1.17 – 1.88)	2.32 (1.62)
< 14 (reference)	1.0		1.0	
≥ 14	1.61 (1.14 – 2.29)	2.60 (1.54)	1.71 (1.24 – 2.39)	2.81 (1.79)

Note: Odds ratios (OR) were obtained from multiple imputation data (N = 5,222) using logistic regression models adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, self-reported diabetes, smoking, and alcohol use. [†] Sugar-sweetened beverages (SSB) in different forms: <5 or ≥5, <7 or ≥7, and <14 or ≥14 times/week. [‡] Logistic regression models adjusted for confounders using the conventional method. [§] Logistic regression models adjusted by the inverse probability weighting (IPW) method. CI – Confidence interval. NHANES – National Health and Nutrition Examination Survey.

Sensitive analyses using multiple imputation

We created a list of missing data predictors with a minimum Pearson correlation of 0.1 and at least 50% of the useful data and then imputed from the less missing variable to the most missing. We used multiple imputation by chained equations (MICE) with predictive mean matching as the univariate imputation method, from which we simulated five imputed datasets (van Buuren & Groothuis-Oudshoorn, 2011). Among the imputed variables, we included the ‘family income poverty ratio’ variable with the other confounders, both in the conventional logistic regressions and the IPW fit, since it was the only one with more than 5% missing data (Tabachnick & Fidell, 2007). Each dataset generated an estimate, and we used Bootstrap (1000 times) to address the variability (Schomaker & Heumann, 2018).

References

- Buuren, S. van, & Groothuis-Oudshoorn, K. (2011). mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software*, 45(3).
- Schomaker, M., & Heumann, C. (2018). Bootstrap inference when using multiple imputation. *Statistics in Medicine*, 37(14), 2252–2266.
- Tabachnick, B. G., & Fidell, L. S. (2007). Using multivariate statistics (Fifth ed.). Boston: *Pearson Education, Inc.*

Table S3. Estimates of sugar-sweetened beverages (ordinal) on periodontitis among US adults with and without inverse probability weighting. NHANES III.

SSB (times/ week) [†]	N (%)	Conventional regression-based adjustment [‡]		Inverse probability weighted regression [§]	
		OR (95% CI)	E-value (CI)	OR (95% CI)	E-value (CI)
< 5 (reference)	2,387 (53.4)	1.0		1.0	
≥ 5 to < 7	658 (14.7)	0.98 (0.71 – 1.37)	1.16 (1.00)	0.96 (0.70 – 1.32)	1.25 (1.00)
≥ 7 to < 14	880 (19.7)	1.37 (0.98 – 1.90)	2.08 (1.00)	1.51 (1.11 – 2.05)	2.39 (1.46)
≥ 14	548 (12.3)	1.78 (1.23 – 2.57)	2.96 (1.76)	1.74 (1.18 – 2.57)	2.87 (1.64)

Note: Odds ratios (OR) were obtained from ordinal logistic regression models adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, self-reported diabetes, total energy intake, smoking, and alcohol use. [†] Sugar-sweetened beverages (SSB) in ordinal categories (times/week). Estimates for complete cases (N = 4,473). [‡] Logistic regression models adjusted for confounders using the conventional method. [§] Logistic regression models adjusted by the inverse probability weighting (IPW) method. CI – Confidence interval. NHANES – National Health and Nutrition Examination Survey.

Table S4. Regression models of sugar-sweetened beverages on periodontal metrics among US adults. NHANES III.

	Model 1 [†]	Model 2 [†]	Model 3 [‡]	Model 4 [‡]	Model 5 [§]	Model 6 [§]
	CDC-AAP (2012) classification	AAP/EFP (2018) classification	Proportion of sites with PPD ≥ 4 mm	Proportion of sites with CAL ≥ 3 mm	Mean CAL	Proportion of sites with B
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
SSB consumption	1.03	1.00	1.02	1.02	1.00	1.01
(times/week)	(1.01 – 1.05)	(0.99 – 1.02)	(1.01 – 1.03)	(1.01 – 1.05)	(0.99 – 1.01)	(0.99 – 1.0)

Note: Odds ratios (OR) were obtained from models adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, self-reported diabetes, total food energy intake, smoking, and alcohol use. CDC-AAP – Centers for Disease Control and Prevention and American Academy of Periodontology. AAP/EFP – American Academy of Periodontology and European Federation of Periodontology. PPD – Periodontal probing depth. CAL – Clinical attachment level. BoP – Bleeding on probing. Sugar-sweetened beverages (SSB) as a continuous variable (times/week). [†] Model analyzed by ordinal logistic regression. [‡] Model analyzed by quasibinomial regression. [§] Model analyzed by multiple linear regression. Estimates for complete cases (N = 4,473). CI – Confidence interval. IPW – Inverse probability weighting. NHANES – National Health and Nutrition Examination Survey.

Table S5. Analysis of biological interactions between sugar-sweetened beverages and perceived weight status on periodontitis among US adults. NHANES III.

Additive interaction terms	N with/without Periodontitis	OR	95% CI
SSB < 5 and under/normal weight	633/1,620	1.0	
SSB ≥ 5 and under/normal weight	756/1,266	1.28	1.07 – 1.54
SSB < 5 and overweight	64/70	0.60	0.52 – 0.70
SSB ≥ 5 and overweight	30/34	1.02	0.87 – 1.21
Measure of additive interaction: $RERI_{OR}$ (95% CI) = 0.14 (-0.1 – 0.38)			
SSB < 7 and under/normal weight	859/2,031	1.0	
SSB ≥ 7 and under/normal weight	530/855	1.31	1.08 – 1.59
SSB < 7 and overweight	80/75	0.70	0.61 – 0.81
SSB ≥ 7 and overweight	19/24	1.13	0.95 – 1.36
Measure of additive interaction: $RERI_{OR}$ (95% CI) = 0.13 (-0.16 – 0.42)			
SSB < 14 and under/normal weight	1164/2578	1.0	
SSB ≥ 14 and under/normal weight	225/308	1.34	1.04 – 1.73
SSB < 14 and overweight	88/95	0.71	0.62 – 0.81
SSB ≥ 14 and overweight	6/9	1.22	0.97 – 1.54
Measure of additive interaction: $RERI_{OR}$ (95% CI) = 0.17 (-0.25 – 0.59)			

Note: Odds ratios (OR) weighted propensity score adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, smoking, and alcohol use. Estimates for complete cases (N = 4,473). The models were tested having sugar-sweetened beverages (SSB) in different forms: < 5 or ≥ 5, < 7 or ≥ 7, and < 14 or ≥ 14 times/week. $RERI_{OR}$ means the relative excess risk due to interaction for OR on an additive scale. CI – Confidence interval. NHANES - National Health and Nutrition Examination Survey.

Table S6. Analysis of effect modification of sugar-sweetened beverages on periodontitis by perceived weight status among US adults. NHANES III.

	Overweight		Under/normal weight	
	OR	95% CI	OR	95% CI
SSB < 5	1.0		1.0	
SSB ≥ 5	1.70	1.46 – 1.99	1.28	1.07 – 1.54
Effect modification on a multiplicative scale: OR (95% CI) = 1.33 (1.05 – 1.68)				
SSB < 7	1.0		1.0	
SSB ≥ 7	1.62	1.36 – 1.91	1.31	1.08 – 1.59
Effect modification on a multiplicative scale: OR (95% CI) = 1.24 (0.96 – 1.60)				
SSB < 14	1.0		1.0	
SSB ≥ 14	1.73	1.37 – 2.17	1.34	1.04 – 1.73
Effect modification on a multiplicative scale: OR (95% CI) = 1.28 (0.91 – 1.80)				

Note: Odds ratios (OR) weighted propensity score adjusted for family income poverty ratio, education level, race/ethnicity, sex, age, total food energy intake, smoking, and alcohol use. Estimates for complete cases (N = 4,473). The models were tested having sugar-sweetened beverages (SSB) in different forms: < 5 or ≥ 5, < 7 or ≥ 7, and < 14 or ≥ 14 times/week. Effect modification on a multiplicative scale was obtained from the ratio of odds ratios. CI – Confidence interval. NHANES - National Health and Nutrition Examination Survey.

Balance check statistic when SSBs was considered as binary variable

The standardized mean difference was the balance statistic used for continuous covariables, calculated as the difference in means divided by a measure of spread, known as an effect size measure. When it comes to binary covariables, the default balance statistic was the raw difference in proportion. All standardized mean differences were < 0.1 .

Balance check statistic when SSBs was considered as ordinal variable

There were two main components checked: the two-group treatment comparisons and the balance summary. The two-group treatment comparisons were comparisons in which each SSB category was considered as a group taken two by two. The balance summary was, for each variable, the greatest imbalance across all two-group comparisons. All standardized mean differences were < 0.1 .

5.3 Capítulo 3 - A cárie é o hub de uma rede complexa de doenças crônicas ao longo das décadas da vida

“Caries Is the Hub of a Complex Network of Chronic Diseases across the Life Decades”

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Abstract

Caries precedes periodontitis; both may predict fatal noncommunicable diseases (NCDs) decades in advance. However, the complex network of relationships between these and other NCDs remains unclear. Understanding the intricate nonlinear connections among NCDs from the early life stages holds profound significance for public health management strategies to prevent NCDs. Accordingly, we modeled the connections among NCDs and identified the underlying patterns in the US population from childhood to elderhood. Indicators of metabolic risks, diabetes, and cancer, as well as cardiovascular, autoimmune, mental, respiratory, and oral diseases, were collected from National Health and Nutrition Examination Survey data (2011–2012 and 2013–2014 cycles), encompassing 4 age groups of Americans aged 1 to ≥60 y. Diseases were represented as nodes in the complex network analysis, and edges indicated their co-occurrences. To characterize the networks, we computed degree, betweenness, eigenvector, local transitivity, assortative mixing, Shannon entropy, and cluster coefficients. Caries was the central hub in all models. Caries and obesity were linked since the first years of life, and with age, new diseases became connected, increasing network complexity with Shannon entropy from −2.79 to −4.07. Depression plays an essential role in adult life; however, episodes of forgetting and mental confusion surpass depression's significance in elderhood. The centrality of diabetes, cardiovascular disease, and cancer increases with age, peaking at ≥60 y, with diabetes being the most prominent. All groups had coefficients indicating that NCDs were highly connected, with cluster coefficients of 0.85 to 0.98 and assortativity mixing of −0.23 to −0.06. Caries was the central element over the decades, with the other diseases orbiting around it. It was mainly linked to overweight/obesity from early childhood. Integrated strategies targeting shared risk factors for caries and obesity can boost childhood health and potentially affect the development of other NCDs later.

Keywords: noncommunicable diseases, oral health, obesity, metabolic syndrome, dyslipidemia, prediabetes

Introduction

Noncommunicable diseases (NCDs) are the leading cause of premature death worldwide, with the greatest impact on economically disadvantaged and minority populations. These diseases include cardiovascular conditions, diabetes, chronic respiratory diseases, cancers (World Health Organization [WHO] 2021), as well as neurodegenerative diseases such as Alzheimer and Parkinson, autoimmune diseases (Ballerini et al. 2022), and depression (Pryor et al. 2017). Among the most prevalent ones are caries and periodontitis (Naghavi et al. 2024), which often co-occur throughout life (Costa et al. 2023), serving as early indicators of systemic inflammation (Lima et al. 2018; Ribeiro et al. 2021) and showing patterns of association with cardiometabolic conditions (Alves-Costa, de Souza, et al. 2024), underscoring their significance within the broader landscape of NCDs.

Despite advances in understanding these diseases' cellular and molecular mechanisms (Padrón-Monedero 2023), purely mechanistic approaches have limited effectiveness in addressing the causes of NCDs (Wang et al. 2014). NCDs often share social, economic, and behavioral risk factors and can lead to

co-occurring or sequential diseases, particularly in older age (WHO 2021). For instance, worse oral health conditions could

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A supplemental appendix to this article is available online.

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predict diabetes and cardiovascular diseases 2 or more decades before (Demmer et al. 2008; Liu et al. 2022). Traditionally, relationships among NCDs are modeled linearly (Groenwold and Dekkers 2023) despite the complexity of living organisms, marked by nonlinear interconnections and interdependencies in systems composing the human body (Padrón-Monedero 2023).

Complex network analysis offers a way to study these interconnections, as shown in studies of populations in India (Puri and Singh 2022), Japan (Higa et al. 2022), Brazil (Alves-Costa, de Souza, et al. 2024), and the United Kingdom (Kuan et al. 2023). In the United States, 60% of adults have at least 1 NCD and 40% have 2 or more, accounting for \$4 trillion in annual health care costs (National Center for Chronic Disease Prevention and Health Promotion 2022). Despite this, few studies have simultaneously investigated the nonlinear interactions of NCDs in the country; to our knowledge, none have incorporated oral NCDs into complex network models.

We hypothesized that NCDs are interconnected from early life with increasing complexity, as new organs and systems are affected with age. Our aim was to explore NCD interconnections across life stages in the United States using complex network analysis to reveal pathways for improved intervention strategies, enhancing NCD management from childhood through old age.

Methods

Study Design

This study analyzed data from the 2011–2012 and 2013–2014 cycles of the National Health and Nutrition Examination Survey, focusing on noninstitutionalized US civilians aged 1 to 80 y ($N = 19,134$). These cycles were selected through a detailed, stratified sampling method for their comprehensive medical and oral health data. This study was reported according to the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology).

Data Collection

Cancer, cardiovascular diseases, rheumatoid arthritis, bronchitis, and emphysema were self-reported (yes/no) among participants aged ≥ 20 y. Difficulties in thinking or remembering and experience of confusion/memory problems were also auto-reported, with separate questions for participants aged ≥ 20 and ≥ 60 y, respectively, later combined into a single “forgetting” variable (yes/no). Diabetes and prediabetes were identified through a self-report questionnaire for those aged ≥ 16 y or by the serum level of glycated hemoglobin for those aged ≥ 12 y. A level $\geq 6.5\%$ indicated diabetes, while levels between 5.7% and 6.4% indicated prediabetes. Diabetes risk and psoriasis were self-reported by participants aged ≥ 16 y. Celiac disease was reported by participants aged ≥ 6 y. All participants aged ≥ 1 y were asked if they had asthma (yes/no).

Participants aged ≥ 18 y were screened for depression with the 9-item Patient Health Questionnaire, scoring 0 to 27. Scores ≥ 5 indicated depressive symptoms.

Systolic and diastolic blood pressure were measured in seated participants aged ≥ 8 y, with the average of 3 readings after a 5-min rest period. Participants aged 8 to 17 y were considered hypertensive if their blood pressure was ≥ 95 th percentile and for those aged ≥ 18 y, when blood pressure exceeded 140/90 mm Hg.

Body mass index was calculated from the measurements and categorized as eutrophic or overweight/obese, with a 25-kg/m² threshold for participants aged ≥ 20 y. For participants aged between 2 and 19 y, overweight/obese classification was determined from the 85th percentile. Blood samples were drawn via venipuncture for participants aged ≥ 6 y to measure high-density lipoprotein cholesterol (HDL-c) and total cholesterol. Low-density lipoprotein cholesterol (LDL-c) and triglycerides were additionally measured in participants aged ≥ 12 y. Levels were then categorized by established thresholds: for low HDL-c, ≤ 50 mg/dL in women aged ≥ 25 y and ≤ 40 mg/dL in all children and adult men; for high total cholesterol, ≥ 250 mg/dL in participants aged ≥ 20 y and ≥ 200 mg/dL in younger; for high LDL-c, ≥ 160 mg/dL in participants aged ≥ 20 y and ≥ 130 mg/dL in younger; and for high triglycerides, ≥ 150 mg/dL in participants aged ≥ 20 y and ≥ 150 mg/dL in participants aged 12 to 19 y.

Periodontal status was assessed via full-mouth evaluations, encompassing gingival recession and pocket depth measurements. Periodontitis was classified by the 2018 American Academy of Periodontology/European Federation of Periodontology classification, dichotomized as none or any stage for participants aged ≥ 30 y. Dental caries was evaluated in participants aged ≥ 1 y as untreated or filled cavities on at least 1 tooth surface or tooth loss due to caries. Sensitivity analyses were conducted, considering participants between the ages of 1 and 5 y to focus solely on primary dentition.

Data Analysis

Complex network analysis was the main analytical procedure applied in this study, employing a data-driven approach centered on examining the relationships among conditions (Costa et al. 2007). An undirected graph structure was constructed from a disease co-occurrence matrix, with diseases represented as nodes and co-occurrences as edges; the thickness of the edge represents the proportional number of co-occurrences between the diseases. Four distinct models were established by age categories: 1 to 19 y ($n = 7,805$), 20 to 39 y ($n = 3,911$), 40 to 59 y ($n = 3,786$), and ≥ 60 y ($n = 3,632$). These categories were chosen to capture key developmental and health transitions, allowing our analysis to reflect the nuanced dynamics of age-related health changes according to Geifman et al. (2013).

We extracted 4 node-specific centrality measures to characterize the network's structure: degree, node betweenness,

eigenvector centrality, and local transitivity. The degree of a node (disease) is the count of the number of connections (i.e., edges) that it holds, representing how involved a specific disease is in the network. Node betweenness is defined as the number of times that a given node (disease) has acted as a connection in the shortest paths between other nodes (diseases); hence, a disease with a greater betweenness value means that it acts as a mediator/bridge between other diseases, suggesting shared physiopathology or risk factors. Eigenvector centrality of a node (disease) was obtained through a reciprocal process wherein the centrality was assigned a value proportional to the sum of the centralities of the other nodes (diseases) to which it is connected, thus highlighting influential players and attributing higher values to diseases connected to many other well-connected diseases. Local transitivity of a node (disease) was calculated by the ratio between the number of triangles connected to that node (disease) and the number of triples centered on that node (disease); specifically, it indicates the likelihood of 2 diseases co-occurring if both are already linked to a third (Costa et al. 2007).

Shannon entropy–node specific was measured to check the diversity of each node's connections: the higher the value, the more diverse the connections that a node has with other nodes in the network. Shannon entropy–network related was also calculated, reflecting the structure's complexity level (Wiesner and Ladyman 2019).

Regarding the properties of the complex network, we have computed the degree distribution to observe the connectivity pattern. The cluster coefficient assesses the likelihood of any given node (disease) forming a triangle with 2 other nodes (diseases) in the network. Given that NCDs are commonly classified in groups by the affected system/organ, we also determined the assortativity mixing, quantifying the preference for nodes (diseases) within the specific group to link with each other (positive values) or with those diseases from other groups (negative values; Costa et al. 2007). In this study, groups were classified as autoimmune diseases (rheumatoid arthritis, psoriasis, and celiac disease), mental diseases (depression and forgetting), metabolic risks (low HDL-c, high LDL-c, high total cholesterol, high triglycerides, overweight/obesity, hypertension, prediabetes, and diabetes risk), fatality NCDs (cardiovascular diseases, diabetes, and cancers), respiratory diseases (asthma, emphysema, and bronchitis), and oral diseases (caries and periodontitis). Analyses for identifying and visualizing the complex networks were conducted in R version 4.2.1.

Results

Population characteristics are presented in Appendix Table 1. Our findings delineate the undirected complex network of co-occurrence among diseases (Fig. 1), wherein the edge thickness corresponds to the frequency of co-occurrence between 2 diseases (nodes). Notably, caries and overweight/obesity exhibited the most frequent co-occurrence across all age groups, with an escalation in the quantity and diversity of connections with age. Figure 2 illustrates the frequency of co-occurrences between diseases within each age group. In the

age range of 1 to 19 y, prominent connections were as follows: caries–overweight/obesity (20.3%), caries–asthma (10.5%), overweight/obesity–asthma (8.4%), overweight/obesity–low HDL-c (5.8%), and caries–low HDL-c (5.0%). This pattern shifted in the age group of 20 to 39 y, where caries–overweight/obesity (11.3%), caries–low HDL-c (5.6%), overweight/obesity–low HDL-c (5.4%), caries–depression (3.8%), and caries–periodontitis (3.3%) emerge as primary connections. Among individuals aged 40 to 59 y, caries–overweight/obesity (7.7%), caries–periodontitis (4.0%), caries–low HDL-c (3.6%), overweight/obesity–low HDL-c (3.4%), and caries–prediabetes (3.3%) exhibited the strongest co-occurrences. Finally, in participants aged ≥ 60 y, caries–overweight/obesity (5.9%), caries–prediabetes (3.6%), overweight/obesity–prediabetes (2.8%), and caries–periodontitis (2.5%) were the most frequent connections.

Node-specific centrality measures were extracted, including degree, betweenness, eigenvector centrality, and local transitivity (Fig. 3, Appendix Table 2). These measures evaluate aspects of the centrality of diseases in the network. Caries consistently held the highest degree across all age groups, followed by overweight/obesity (Fig. 3A), which indicates that these diseases have a greater number of connections linked to them. While the absolute number of connections with caries increased with age, its relative degree (node size; Fig. 1) actually decreased. Regarding the betweenness centrality, caries obtained the highest coefficients (Fig. 3B), indicating a mediation role, especially between the ages of 20 and 39 y (4.22; Appendix Table 2). The eigenvector values follow a similar pattern, showing caries and overweight/obesity as the most relevant diseases across all ages, followed by asthma in ages 1 to 19 y, low HDL-c in 20 to 59 y, and prediabetes in ≥ 60 y (Fig. 3C). Most diseases exhibited a local transitivity probability hovering near 1.0, suggesting a high likelihood of 2 diseases being interconnected if both shared a connection with them, forming a triangular relationship (Appendix Table 2). In general, the node-specific entropy of all diseases increases with age, which means that the diversity among the links increases (Fig. 3D). For a sensitivity analysis, we calculated these same measures among children aged 1 to 5 y to see if the centrality observed for caries was related to something linked to higher disease prevalence with aging, since the dentition changes entirely from age 6 y. We observed that caries was also the central condition for this age group, even in the primary dentition, with a similar connection pattern between caries and overweight/obesity (Appendix Fig. 1).

The properties of the complex networks were computed to characterize the observed patterns in each network and compare their differences as age progresses. Appendix Figure 2 shows the box plot of the degree distribution, suggesting that the complexity of the network, as measured by the number of disease connections, intensifies as age progresses.

Figure 4 presents assortativity mixing values and Shannon entropy. Interestingly, while assortativity mixing values trended upward with age, all remained negative, indicating that diseases are more connected with diseases in other groups (Fig. 4A). As one ages, Shannon entropy deviates from zero,

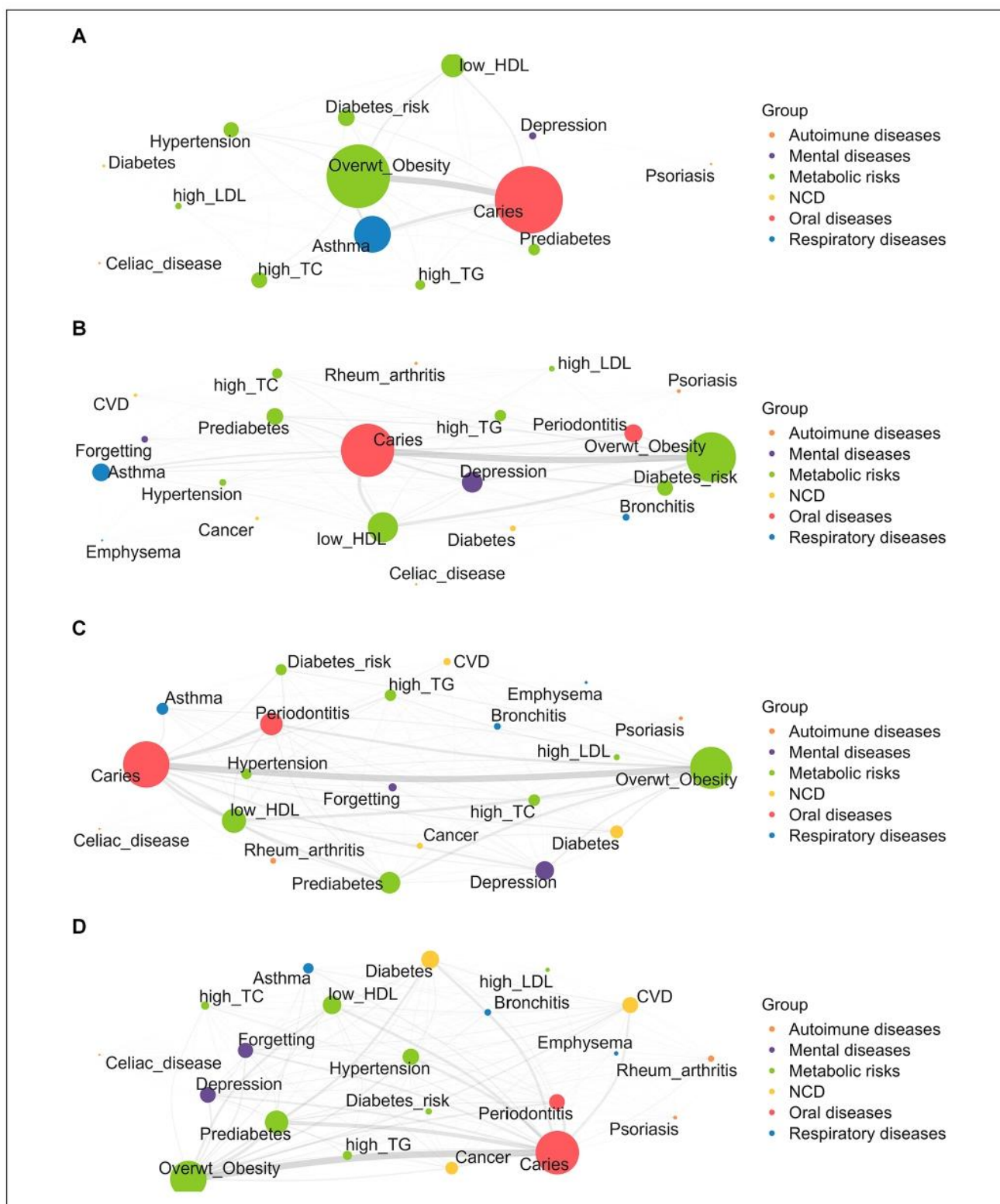


Figure 1. Noncommunicable diseases complex networks by age group in the US population. National Health and Nutrition Examination Survey, 2011 to 2014. Ages: (A) 1 to 19 y, (B) 20 to 39 y, (C) 40 to 59 y, and (D) ≥ 60 y. CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NCD, noncommunicable disease; Overwt_Obesity, overweight/obesity; TC, total cholesterol; TG, triglycerides.

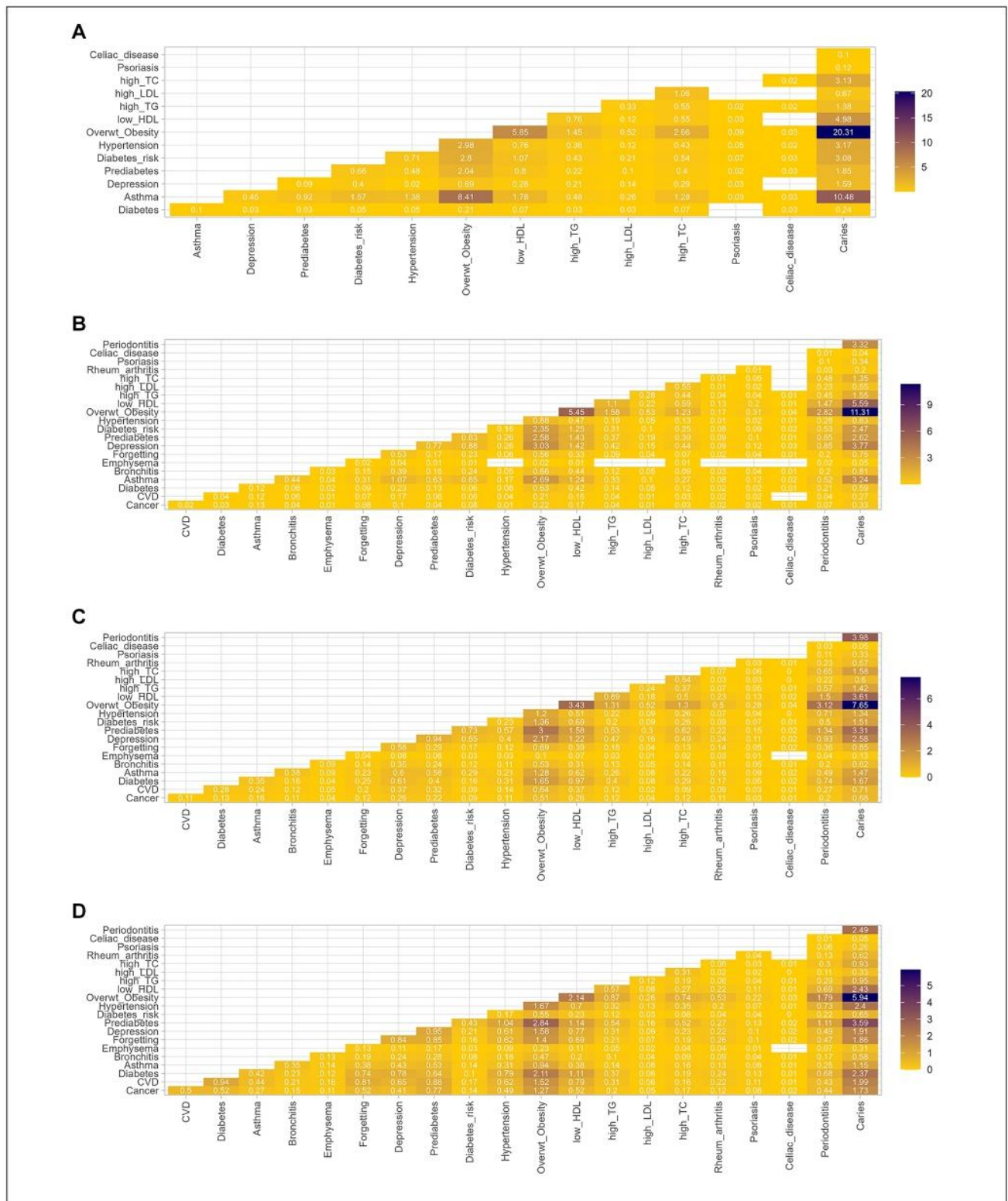


Figure 2. Disease co-occurrence strength by age group in the US population. National Health and Nutrition Examination Survey, 2011 to 2014. Ages: (A) 1 to 19 y, (B) 20 to 39 y, (C) 40 to 59 y, and (D) ≥ 60 y. CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Overwt_Obesity, overweight/obesity; TC, total cholesterol; TG, triglycerides.

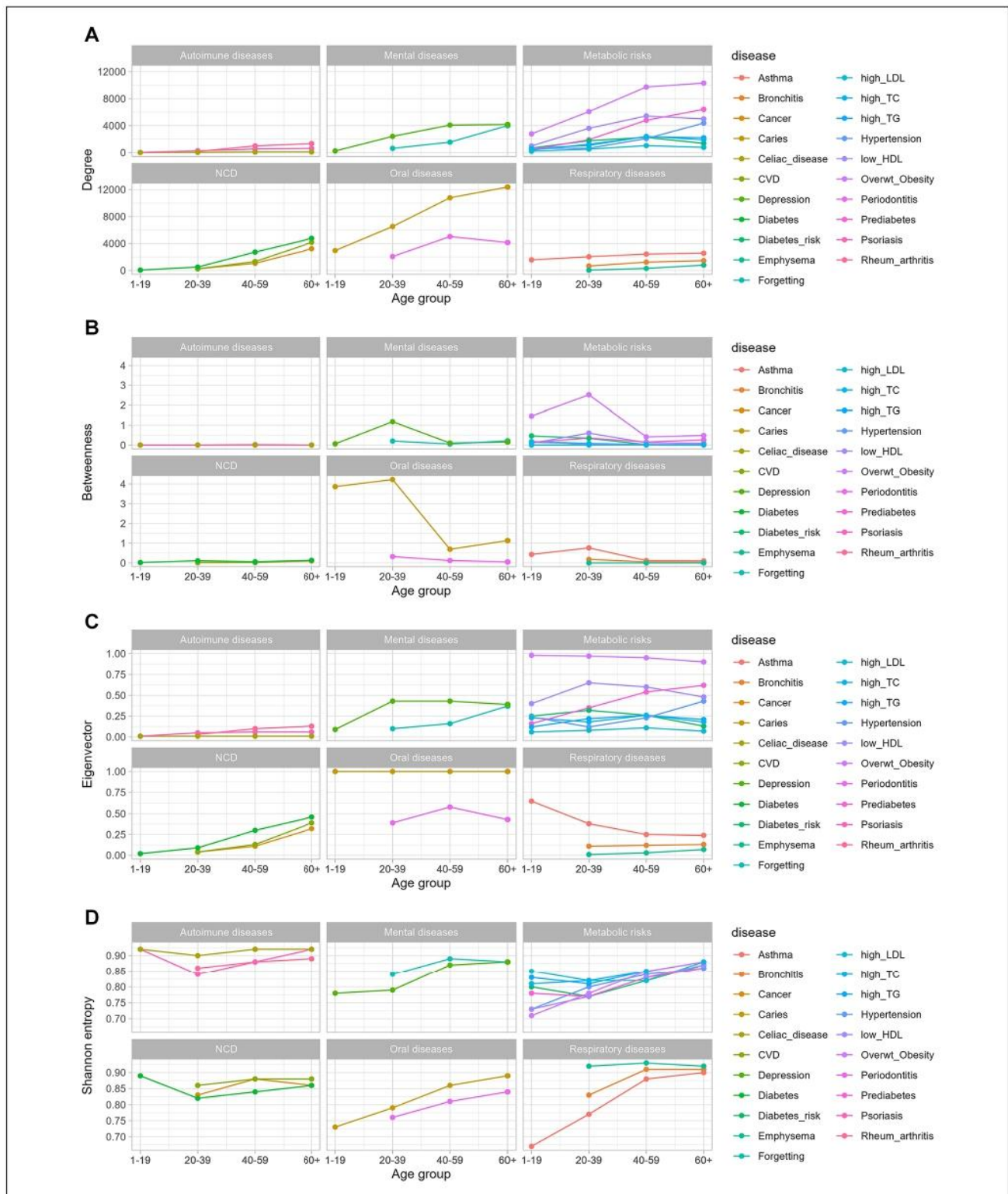


Figure 3. Variation in node-specific measures by age group and type of disease of the US population. National Health and Nutrition Examination Survey, 2011 to 2014. (A) Degree centrality. (B) Betweenness centrality. (C) Eigenvector. (D) Shannon entropy. CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Overwt_Obesity, overweight/obesity; TC, total cholesterol; TG, triglycerides.

reflecting the increasing complexity of the network structure (Fig. 4B). All age groups exhibited high cluster coefficients (varying from 0.85 to 0.98), indicating a high likelihood of diseases forming triangles within the network.

Discussion

This study modeled the complex network of NCDs in the US population from childhood to old age, showing that caries has remained a central element over the decades, with other diseases orbiting around it. Connections between diseases increase with age, adding to the network's complexity. By exploring these patterns, we confirm our hypothesis and suggest potential avenues for interventions considering the interconnected nature of NCDs across life.

Caries emerged as the hub of the NCD network throughout life, representing a central connection node and the most influential factor across all ages. Caries consistently had the highest values for centrality measures: degree, betweenness, and eigenvector. Degree measures the number of connections that a disease has; betweenness measures the number of paths that pass through a disease; and eigenvector centrality measures the overall relevance of a disease in the network structure (Costa et al. 2007). Although caries is the most prevalent NCD worldwide, affecting around 2.7 billion people (Naghavi et al. 2024), our analysis showed that its centrality remains prominent beyond prevalence. Our sensitivity analyses confirmed caries as a hub, even in deciduous teeth, suggesting that modifiable behaviors may connect chronic conditions to caries as a proxy for poor eating habits.

A notable pattern is the relationship between caries and periodontitis, beginning in the age range of 20 to 39 y and intensifying by ages 40 to 59 y. The collapse of the oral system begins within the first 2 decades, with caries appearing in early childhood. By age 20 y, caries is linked with periodontitis, the destruction of tooth-supporting tissues, consistent with studies showing this relationship throughout life (Costa et al. 2023). Around age 20 y, periodontitis also connects with metabolic risk factors, mainly obesity, indicating inflammation as a shared mechanism (Ribeiro et al. 2021; Alves-Costa, de Souza, et al. 2024). A frequent relationship exists between caries and hypertension, diabetes, and cardiovascular diseases in those aged ≥ 60 y.

Overweight/obesity had a strong influence on the network through its degree of connections and mediating role across all ages, along with other metabolic factors such as low HDL-c and prediabetes. Metabolic risks are consistently linked to chronic conditions, including diabetes, cardiovascular disease, and depression (Pryor et al. 2017; WHO 2021). During the first 2 decades, caries, overweight/obesity, and asthma were interconnected. Sensitivity analysis in early childhood (1 to 5 y) confirmed the links among caries, obesity, and asthma, which were associated with other metabolic risk factors, particularly low HDL-c, hypertension, and high cholesterol. Our findings align with literature showing strong relationships between caries and obesity (Manohar et al. 2020) and asthma (Agostini et al. 2019) in children and adolescents. Additionally, epidemiologic evidence supports an obesity-related asthma phenotype in children

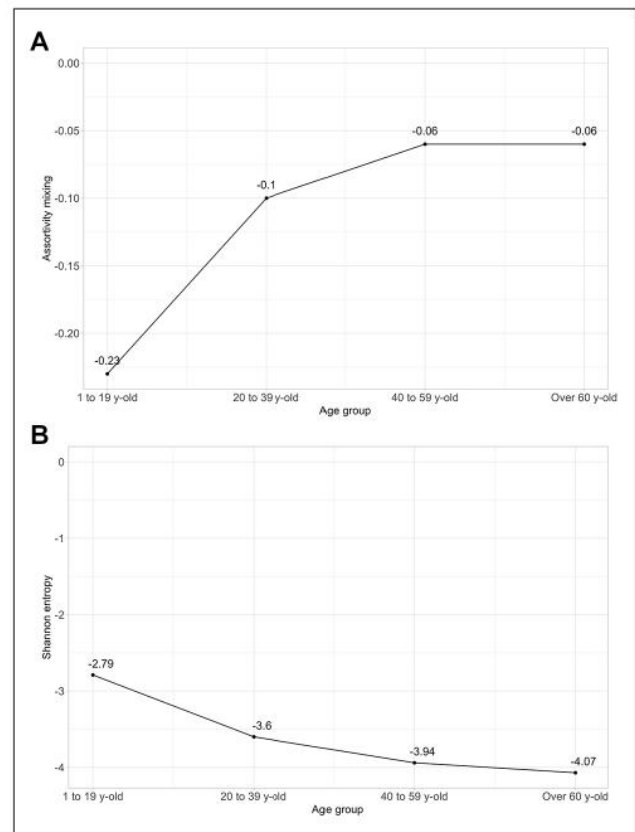


Figure 4. Assortativity mixing and Shannon entropy of complex network noncommunicable diseases by age group in the US population. National Health and Nutrition Examination Survey, 2011 to 2014. (A) Assortativity mixing. (B) Shannon entropy.

(Reyes-Angel et al. 2022). While asthma ranked highly in the network for youth, its influence lessens with age, as its prevalence declines in adulthood (Cao et al. 2022).

Depression played a significant role in the NCD network, particularly noted by its mediating role (betweenness) among 20- to 39-y-olds, closely linked with caries and obesity in adulthood. In older individuals, episodes of forgetting and mental confusion surpass the depression influence. Depression, a mental NCD, frequently coincides with other NCDs (Pryor et al. 2017) and may worsen morbidity, and medications used in treatment may exacerbate psychiatric symptoms, particularly in adulthood (National Institute for Health and Care Excellence 2022). Forgetting and mental confusion, more significant from age 60 y onward, potentially serve as an indicator of cognitive decline and Alzheimer disease (Mogle et al. 2021). Evidence suggests that midlife depression may increase Alzheimer risk, while persistent depression may precede dementia (Kuring et al. 2020).

Among the 4 most deadly NCDs, diabetes showed the most connections, mediation, and relevance from age 40 y onward. By age 60 y, cardiovascular disease and cancer also had increased centrality measures, though they did not surpass diabetes. Diabetes often predicts cardiovascular disease (Pennells et al. 2023), with affected individuals facing 2- to 4-fold higher

risks (Dunlay et al. 2019). Moreover, causal links exist among diabetes, fasting insulin, and cancer (e.g., endometrial, pancreatic, and breast; Pearson-Stuttard et al. 2021). For many cancer survivors, the risk of fatal heart disease escalates over time (Stoltzfus et al. 2020).

Primarily, social determinants of health, such as poverty, are closely linked to getting sicker and contribute to the clustering of NCD. Vulnerable and socially disadvantaged groups often experience greater exposure to harmful products, heightened stress, behavioral risks, and limited health care access (WHO 2021). Additionally, inequalities related to gender, race, and ethnicity worsen health outcomes in the United States (Frankenfeld et al. 2022). Furthermore, high sugar intake, for example, plays a role in caries development and may explain associations between caries and other chronic conditions through mechanisms such as insulin resistance (Lana et al. 2014). Excessive sugar in beverages contributes to diabetes, cardiovascular disease (Meng et al. 2021), obesity, dyslipidemia (Malik and Hu 2022), asthma (Nascimento et al. 2017), depression (Barbosa et al. 2022), and periodontitis (Alves-Costa, Nascimento, et al. 2024). Besides ultraprocessed foods rich in sugar, other shared behavioral risk factors for NCDs include smoking, alcohol, and physical inactivity (WHO 2021).

Our findings suggest a progressive NCD clustering with age, indicating a complex network of interactions influenced by biological, environmental, and behavioral factors. NCD co-occurrence frequency and interaction complexity have increased over the decades, with network complexity metrics such as Shannon entropy indicating heightened structural complexity. This trend aligns with aging's biological trajectory, marked by declining physiologic reserves and increased stressor vulnerability, raising risks for NCDs such as cardiovascular diseases, diabetes, and neurodegenerative disorders (Ogaz-González et al. 2024). Age-related factors predispose individuals to complex, multimorbid conditions, while accumulated risk factors such as sedentary behavior and unhealthy diet increase disease connections (WHO 2021; Ogaz-González et al. 2024). Consequently, aging acts as a catalyst for NCD clustering, highlighting the importance of integrated health strategies that address these conditions across life stages to reduce morbidity burden with aging (Padrón-Monedero 2023).

The study has several limitations, including potential recall bias and the lack of specific medical assessments in young participants, leading to underestimated connections and missing data among those aged 1 to 19 y. Furthermore, data collection occurred from 2011 to 2014, meaning that population health trends, demographics, and NCD prevalence may have shifted over time. Shannon entropy assigns greater weight to frequent events and assumes independence between outcomes (Wiesner and Ladyman 2019), which can limit interpretations within NCD networks where diseases often share risk factors. Additionally, complex networks typically assume a static structure, which, when combined with the cross-sectional design, restricts the ability to capture changes in disease interactions that can evolve throughout an individual's life. The cross-sectional design also prevents assuming causal relationships among NCDs. Despite these challenges, this study uses National Health and Nutrition Examination Survey data to explore NCD

interactions through complex network analysis, providing new insights into chronic disease progression and aging and significantly advancing our understanding of illness dynamics.

Therefore, caries remained a central hub across the life course and was especially connected to overweight/obesity from childhood, indicating their essential roles in disease interactions. Connections among NCDs intensify with age, increasing network complexity. Integrated strategies addressing shared risk factors for caries and obesity can improve childhood health and affect the later development of other NCDs. Public policies promoting healthy food systems, equitable health care, and economic opportunities may alleviate these linked diseases and enhance Americans' health.

Author Contributions

S. Alves-Costa, contributed to conception, design, data analysis and interpretation, drafted and critically revised the manuscript; F.A. Rodrigues, contributed to conception, design, data analysis and interpretation, critically revised the manuscript; A.A. Ferraro, contributed to conception, data to interpretation, critically revised the manuscript; G.G. Nascimento, F.R.M. Leite, contributed to data interpretation, critically revised the manuscript; B.F. Souza, contributed to data analysis and interpretation, critically revised the manuscript; C.C.C. Ribeiro, contributed to conception, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

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Data Availability

The data supporting this study's findings are available from the National Center for Health Statistics at <https://www.cdc.gov/nchs/nhanes/index.htm>.

References

- Agostini BA, Collares KF, dos Santos Costa F, Correa MB, Demarco FF. 2019. The role of asthma in caries occurrence—meta-analysis and meta-regression. *J Asthma*. 56(8):841–852. doi:10.1080/02770903.2018.1493602

- Alves-Costa S, de Souza BF, Rodrigues FA, Ferraro AA, Nascimento GG, Leite FRM, Ladeira LLC, Batista RFL, Thomaz EBAF, Alves CMC, et al. 2024. High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the complex network of non-communicable diseases in adolescents. *Diabetol Metab Syndr*. 16(1):235. doi:10.1186/s13098-024-01469-8
- Alves-Costa S, Nascimento GG, Peres MA, Li H, Costa SA, Ribeiro CCC, Leite FRM. 2024. Sugar-sweetened beverage consumption and periodontitis among adults: a population-based cross-sectional study. *J Clin Periodontol*. 51(6):712–721. doi:10.1111/jcpe.13961
- Ballerini C, Njamnshi AK, Juliano SL, Kalaria RN, Furlan R, Akinyemi RO. 2022. Non-communicable neurological disorders and neuroinflammation. *Front Immunol*. 13:834424. doi:10.3389/fimmu.2022.834424
- Barbosa JMA, Ribeiro CCC, Batista RFL, Brondani MA, Simões VMF, Bettiol H, Barbieri MA, de Aguiar Cameiro Coelho SJDD, da Silva AAM. 2022. Behavioral risk factors for noncommunicable diseases associated with depression and suicide risk in adolescence. *Cad Saude Publica*. 38(2):e00055621. doi:10.1590/0102-311X00055621
- Cao Y, Chen S, Chen X, Zou W, Liu Z, Wu Y, Hu S. 2022. Global trends in the incidence and mortality of asthma from 1990 to 2019: an age-period-cohort analysis using the global burden of disease study 2019. *Front Public Health*. 10:1036674. doi:10.3389/fpubh.2022.1036674
- Costa LDF, Rodrigues FA, Travieso G, Villas Boas PR. 2007. Characterization of complex networks: a survey of measurements. *Adv Phys*. 56(1):167–242. doi:10.1080/00018730601170527
- Costa SA, Ribeiro CCC, Leite FRM, Peres MA, de Fátima Carvalho Souza S, Nascimento GG. 2023. Chronic oral diseases burden: the confluence of caries and periodontitis throughout life. *J Clin Periodontol*. 50(4):452–462. doi:10.1111/jcpe.13761
- Demmer RT, Jacobs DR, Desvarieux M. 2008. Periodontal disease and incident type 2 diabetes: results from the First National Health and Nutrition Examination Survey and its epidemiologic follow-up study. *Diabetes Care*. 31(7):1373–1379. doi:10.2337/dc08-0026
- Dunlay SM, Givertz MM, Aguilar D, Allen LA, Chan M, Desai AS, Deswal A, Dickson VV, Kosioborod MN, Lekavich CL, et al. 2019. Type 2 diabetes mellitus and heart failure: a scientific statement from the American Heart Association and the Heart Failure Society of America: this statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. *Circulation*. 140(7):e294–e324. doi:10.1161/CIR.0000000000000691
- Frankenfeld CL, Hakes JK, Leslie TF. 2022. All-cause mortality and residential racial and ethnic segregation and composition as experienced differently by individual-level race, ethnicity, and gender: mortality disparities in American communities data. *Ann Epidemiol*. 65:38–45. doi:10.1016/j.annepidem.2021.10.008
- Geifman N, Cohen R, Rubin E. 2013. Redefining meaningful age groups in the context of disease. *Age (Dordr)*. 35(6):2357–2366. doi:10.1007/s11357-013-9510-6
- Groenwold RHH, Dekkers OM. 2023. Is it a risk factor, a predictor, or even both? The multiple faces of multivariable regression analysis. *Eur J Endocrinol*. 188(1):E1–E4. doi:10.1093/ajendo/lvac012
- Higa S, Nozawa K, Karasawa Y, Shirai C, Matsuyama S, Yamamoto Y, Laurent T, Asami Y. 2022. The use of a network analysis to identify associations and temporal patterns among non-communicable diseases in Japan based on a large medical claims database. *Drugs Real World Outcomes*. 9(3):463–476. doi:10.1007/s40801-022-00310-w
- Kuan V, Denaxas S, Patalay P, Nitsch D, Mathur R, Gonzalez-Izquierdo A, Sofat R, Partridge L, Roberts A, Wong ICK, et al. 2023. Identifying and visualising multimorbidity and comorbidity patterns in patients in the English National Health Service: a population-based study. *Lancet Digit Health*. 5(1):e16–e27. doi:10.1016/S2589-7500(22)00187-X
- Kuring JK, Mathias JL, Ward L. 2020. Risk of dementia in persons who have previously experienced clinically-significant depression, anxiety, or PTSD: a systematic review and meta-analysis. *J Affect Disord*. 274:247–261. doi:10.1016/j.jad.2020.05.020
- Lana A, Rodríguez-Artalejo F, López-García E. 2014. Consumption of sugar-sweetened beverages is positively related to insulin resistance and higher plasma leptin concentrations in men and nonoverweight women. *J Nutr*. 144(7):1099–1105. doi:10.3945/jn.114.195230
- Lima GQT, Brondani MA, da Silva AAM, do Carmo CDS, da Silva RA, Ribeiro CCC. 2018. Serum levels of proinflammatory cytokines are high in early childhood caries. *Cytokine*. 111:490–495. doi:10.1016/j.cyto.2018.05.031
- Liu J, Zong X, Vogtmann E, Cao C, James AS, Chan AT, Rimm EB, Hayes RB, Colditz GA, Michaud DS, et al. 2022. Tooth count, untreated caries and mortality in US adults: a population-based cohort study. *Int J Epidemiol*. 51(4):1291–1303. doi:10.1093/ije/dyac072
- Malik VS, Hu FB. 2022. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. *Nat Rev Endocrinol*. 18(4):205–218. doi:10.1038/s41574-021-00627-6
- Manohar N, Hayen A, Fahey P, Arora A. 2020. Obesity and dental caries in early childhood: a systematic review and meta-analyses. *Obes Rev*. 21(3):e12960. doi:10.1111/obr.12960
- Meng Y, Li S, Khan J, Dai Z, Li C, Hu X, Shen Q, Xue Y. 2021. Sugar- and artificially sweetened beverages consumption linked to type 2 diabetes, cardiovascular diseases, and all-cause mortality: a systematic review and dose-response meta-analysis of prospective cohort studies. *Nutrients*. 13(8):2636. doi:10.3390/nu13082636
- Mogle J, Hill NL, Turner JR. 2021. Individual differences and features of self-reported memory lapses as risk factors for Alzheimer disease among adults aged 50 years and older: protocol for a coordinated analysis across two longitudinal data sets. *JMIR Res Protoc*. 10(5):e25233. doi:10.2196/25233
- Naghavi M, Ong KL, Aali A, Ababneh HS, Abate YH, Abbafati C, Abbasgholizadeh R, Abbasian M, Abbasi-Kangevari M, Abbastabar H, et al. 2024. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 403(10440):2100–2132. doi:10.1016/S0140-6736(24)00367-2
- Nascimento JXPT, Ribeiro CCC, Batista RFL, de Brito Alves MTSS, Simões VMF, Padilha LL, Cardoso VC, Vianna EO, Bettiol H, Barbieri MA, et al. 2017. The first 1000 days of life factors associated with “childhood asthma symptoms”: Brisa Cohort, Brazil. *Sci Rep*. 7(1):16028. doi:10.1038/s41598-017-16295-4
- National Center for Chronic Disease Prevention and Health Promotion. 2022. About chronic diseases. Atlanta (GA): Centers for Disease Control and Prevention; [accessed 2024 Feb 7]. <https://www.cdc.gov/chronic-disease/about/>
- National Institute for Health and Care Excellence. 2022. Depression in adults: treatment and management (NG222). London: National Institute for Health and Care Excellence; [accessed 2024 Feb 5]. <https://www.nice.org.uk/guidance/ng222>
- Ogaz-González R, Corpeleijn E, García-Chanes RE, Gutiérrez-Robledo LM, Escamilla-Santiago RA, López-Cervantes M. 2024. Assessing the relationship between multimorbidity, NCD configurations, frailty phenotypes, and mortality risk in older adults. *BMC Geriatr*. 24(1):355. doi:10.1186/s12877-024-04948-9
- Padrón-Monedero A. 2023. A pathological convergence theory for non-communicable diseases. *Aging Med (Milton)*. 6(4):328–337. doi:10.1002/agm2.12273
- Pearson-Stuttard J, Papadimitriou N, Markozannes G, Cividini S, Kakourou A, Gill D, Rizos EC, Monori G, Ward HA, Kyrgiou M, et al. 2021. Type 2 diabetes and cancer: an umbrella review of observational and Mendelian randomization studies. *Cancer Epidemiol Biomarkers Prev*. 30(6):1218–1228. doi:10.1158/1055-9965.EPI-20-1245
- Pennells L, Kaptoge S, Østergaard HB, Read SH, Carinci F, Franch-Nadal J, Petitjean C, Taylor O, Hageman SHJ, Xu Z, et al. 2023. SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. *Eur Heart J*. 44(28):2544–2556. doi:10.1093/eurheartj/ehad260
- Pryor L, Da Silva MA, Melchior M. 2017. Mental health and global strategies to reduce NCDs and premature mortality. *Lancet Public Health*. 2(8):e350–e351. doi:10.1016/S2468-2667(17)30140-8
- Puri P, Singh SK. 2022. Exploring the non-communicable disease (NCD) network of multi-morbid individuals in India: a network analysis. *PLOS Glob Public Health*. 2(6):e0000512. doi:10.1371/journal.pgph.0000512
- Reyes-Angel J, Kaviani P, Rastogi D, Forno E. 2022. Obesity-related asthma in children and adolescents. *Lancet Child Adolesc Health*. 6(10):713–724. doi:10.1016/S2352-4642(22)00185-7
- Ribeiro CCC, Carmo CDS, Benatti BB, Casarin RVC, Alves CMC, Nascimento GG, Moreira ARO. 2021. Systemic circulating inflammatory burden and periodontitis in adolescents. *Clin Oral Investig*. 25(10):5855–5865. doi:10.1007/s00784-021-03891-y
- Stoltzfus KC, Zhang Y, Sturgeon K, Sinoway LI, Trifiletti DM, Chinchilli VM, Zaorsky NG. 2020. Fatal heart disease among cancer patients. *Nat Commun*. 11(1):2011. doi:10.1038/s41467-020-15639-5
- Wang Y, Xue H, Esposito L, Joyner MJ, Bar-Yam Y, Huang TT-K. 2014. Applications of complex systems science in obesity and noncommunicable chronic disease research. *Adv Nutr*. 5(5):574–577. doi:10.3945/an.114.006650
- Wiesner K, Ladyman J. 2019. Measuring complexity [preprint]. arXiv:1909.13243. doi:10.48550/arXiv.1909.13243
- World Health Organization. 2021. Noncommunicable diseases. Geneva: World Health Organization; [accessed 2024 Jul 12]. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>

5.3.1 Material Suplementar do Capítulo 3

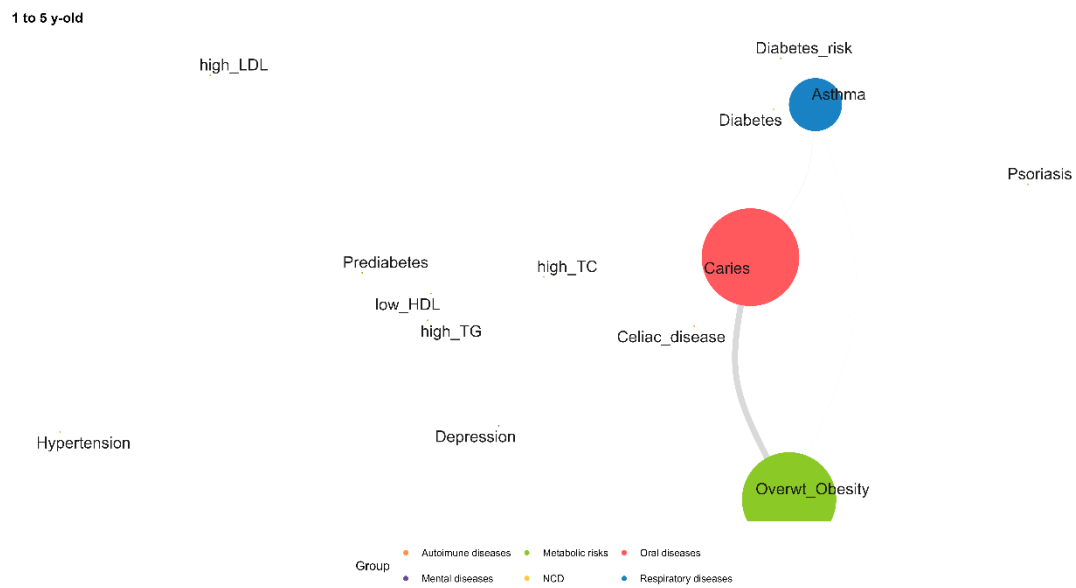
Silas Alves-Costa, Francisco Aparecido Rodrigues, Alexandre Archanjo Ferraro, Gustavo G. Nascimento, Fabio R. M. Leite, Bruno de Souza Feres, Cecilia Claudia Costa Ribeiro

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Appendix Figure 1. Non-communicable diseases complex networks among US children aged 1 to 5. NHANES 2011-2014 (N = 2401).



Note: No data was available for depression, diabetes risk, prediabetes, diabetes, celiac disease, psoriasis, LDL-c, HDL-c, triglycerides (TG), total cholesterol (TC), and hypertension.

Degree: Caries (168), Overweight/Obesity (162), and Asthma (90);

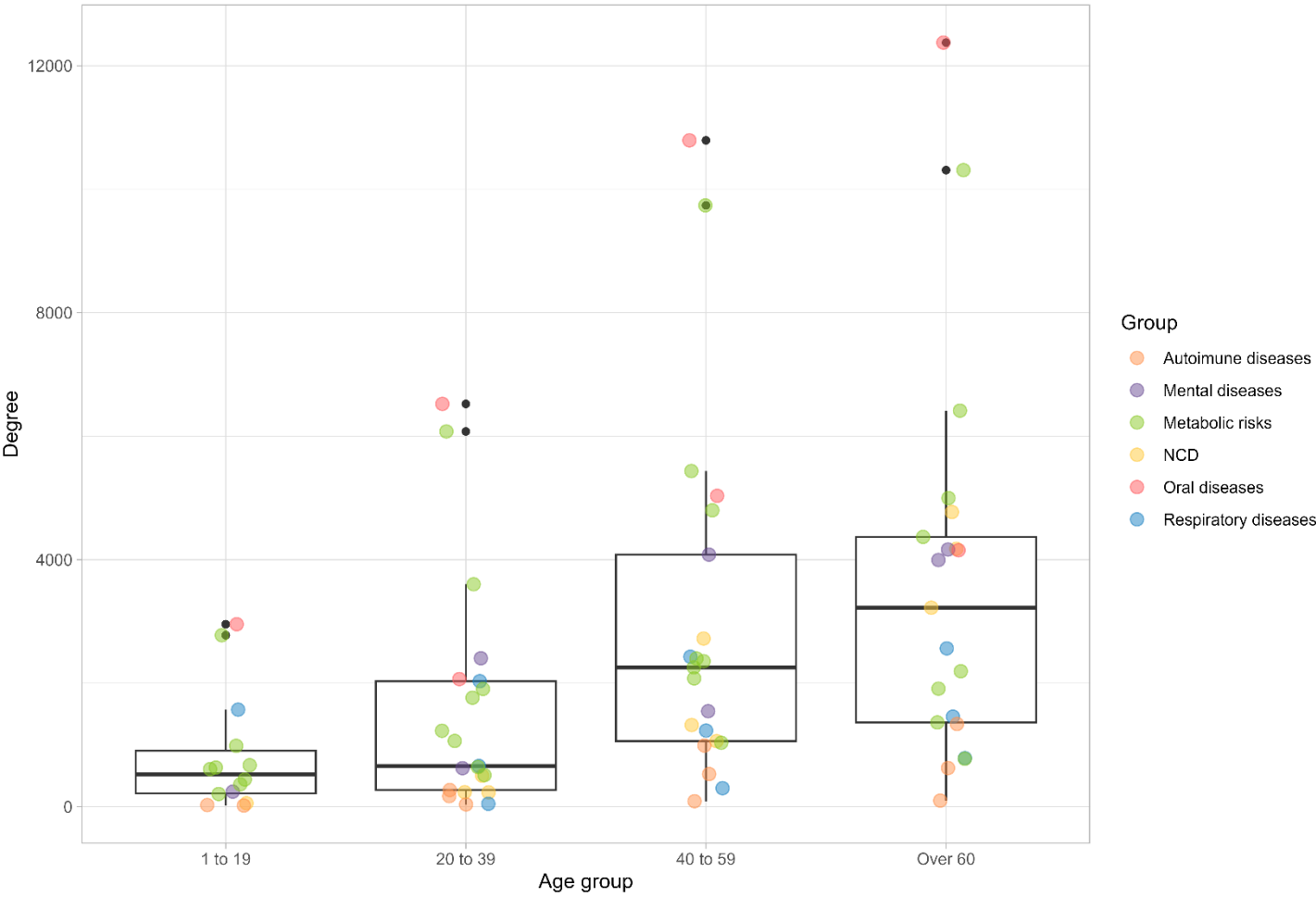
Betweenness: Caries (0.0), Overweight/Obesity (0.0), and Asthma (0.0);

Eigenvector: Caries (1.0), Overweight/Obesity (0.99), and Asthma (0.61);

Local transitivity: Caries (1.0), Overweight/Obesity (1.0), and Asthma (1.0);

Shannon entropy: Caries (0.86), Overweight/Obesity (0.83), and Asthma (1.00).

Appendix Figure 2. Boxplot of the degree distribution by age group in the US population. NHANES 2011-2014.



Appendix Table 1. Characteristics of the US population. NHANES 2011-2014.

Group	Diseases	Overall N (%)	1 to 19 y-old N (%)	20 to 39 y-old N (%)	40 to 59 y-old N (%)	Over 60 y-old N (%)
Autoimmune diseases	Rheumatoid arthritis					
	No	1,550 (8.1)	NA	130 (3.3)	456 (12.0)	964 (26.5)
	Yes	503 (2.6)		36 (0.9)	193 (5.1)	274 (7.5)
	Missing	17,081 (89.3)		3,745 (95.8)	3,137 (82.9)	2,394 (65.9)
	Psoriasis					
	No	12,296 (64.3)	1,298 (16.6)	3,824 (97.8)	3,665 (96.8)	3,509 (96.6)
	Yes	329 (1.7)	11 (0.1)	85 (2.2)	118 (3.1)	115 (3.2)
	Missing	6,509 (34.0)	6,496 (83.2)	2 (0.1)	3 (0.1)	8 (0.2)
	Celiac disease					
	No	16,665 (87.1)	5,393 (69.1)	3,900 (99.7)	3,768 (99.5)	3,604 (99.2)
Mental diseases	Yes	56 (0.3)	9 (0.1)	9 (0.2)	17 (0.4)	21 (0.6)
	Missing	2,413 (12.6)	2,403 (30.8)	2 (0.1)	1 (<0.1)	7 (0.2)
	Depression					
	No	7,763 (40.6)	468 (6.0)	2,567 (65.6)	2,336 (61.7)	2,392 (65.9)
	Yes	2,534 (13.2)	136 (1.7)	747 (19.1)	856 (22.6)	795 (21.9)
	Missing	8,837 (46.2)	7,201 (92.3)	597 (15.3)	594 (15.7)	445 (12.3)
	Forgetting					
	No	10,046 (52.5)	NA	3,761 (96.2)	3,491 (92.2)	2,795 (77.0)
	Yes	1,279 (6.7)		150 (3.8)	295 (7.8)	834 (23.0)
	Missing	7,809 (40.8)		-	-	3 (<0.1)
Metabolic risks						
	HDL-c					
	High	11,831 (61.8)	4,007 (51.3)	2,430 (62.1)	2,220 (58.6)	2,237 (61.6)
	Low	2,782 (14.5)	350 (4.5)	1,120 (28.6)	1,250 (33)	998 (27.5)
	Missing	4,521 (23.6)	3,448 (44.2)	361 (9.2)	316 (8.3)	397 (10.9)
	LDL-c					
	Low	4,543 (23.7)	1,074 (13.8)	1,538 (39.3)	1,463 (38.6)	1449 (39.9)
	High	1,504 (7.9)	67 (0.9)	111 (2.8)	201 (5.3)	144 (4)
	Missing	13,087 (68.4)	6,664 (85.4)	2,262 (57.8)	2,122 (56)	2,039 (56.1)
	Total cholesterol					
	Low	10,247 (53.6)	4,007 (51.3)	3284 (84)	2,935 (77.5)	2,837 (78.1)
	High	4,365 (22.8)	350 (4.5)	266 (6.8)	535 (14.1)	398 (11)
	Missing	4,522 (23.6)	3,448 (44.2)	361 (9.2)	316 (8.3)	397 (10.9)
	Triglycerides					
	Low	4,843 (25.3)	1,014 (13.0)	1,354 (34.6)	1,224 (32.3)	1,212 (33.4)
	High	1,293 (6.8)	130 (1.7)	323 (8.3)	480 (12.7)	399 (11.0)
	Missing	12,998 (67.9)	6,661 (85.3)	2,234 (57.1)	2,082 (55.0)	2,021 (55.6)
	Body mass index					
	Eutrophic	7,067 (36.9)	4,580 (58.7)	1,430 (36.6)	962 (25.4)	957 (26.3)
	Overweight/Obesity	5,637 (29.5)	2,298 (29.4)	2,303 (58.9)	2,667 (70.4)	2,438 (67.1)
	Missing	6,430 (33.6)	927 (11.9)	178 (4.6)	157 (4.1)	237 (6.5)
	Hypertension					
	No	11,876 (62.1)	3,494 (44.8)	3,214 (82.2)	2,773 (73.2)	2,069 (57.0)
	Yes	1,643 (8.6)	335 (4.3)	162 (4.1)	482 (12.7)	990 (27.3)
	Missing	5,615 (29.3)	3,976 (50.9)	535 (13.7)	531 (14.0)	573 (15.8)
	Prediabetes					
	No	11,749 (61.4)	2,152 (27.6)	2,979 (76.2)	1,980 (52.3)	1,190 (32.8)
	Yes	523 (2.7)	204 (2.6)	527 (13.5)	1,162 (30.7)	1,480 (40.7)
	Missing	6,862 (35.9)	5,449 (69.8)	405 (10.4)	644 (17.0)	962 (26.5)
	Diabetes risk					
	No	10,912 (57.0)	2,371 (30.4)	3,295 (84.2)	2,783 (73.5)	2,463 (67.8)
	Yes	1,645 (8.6)	309 (4.0)	527 (13.5)	524 (13.8)	285 (7.8)
	Missing	6,577 (34.4)	5,125 (65.7)	89 (2.3)	479 (12.7)	884 (24.3)
NCD						
	CVD					
	No	10,149 (53.0)	NA	3,852 (98.5)	3,511 (92.7)	2,753 (75.8)
	Yes	1,176 (6.1)		53 (1.4)	266 (7.0)	857 (23.6)

	<i>Missing</i>	7,809 (40.8)		6 (0.2)	9 (0.2)	22 (0.6)
	Diabetes					
	No	17,365 (90.8)	2,347 (30.1)	3,435 (87.8)	2885 (76.2)	2,237 (61.6)
	Yes	1,445 (7.6)	23 (0.3)	121 (3.1)	600 (15.8)	1,023 (28.2)
	<i>Missing</i>	324 (1.7)	5,435 (69.6)	355 (9.1)	301 (8.0)	372 (10.2)
	Cancers					
	No	10,288 (53.8)	NA	3,844 (98.3)	3,546 (93.7)	2,898 (79.8)
	Yes	1,035 (5.4)		66 (1.7)	239 (6.3)	730 (20.1)
	<i>Missing</i>	7,811 (40.8)		1 (<0.1)	1 (<0.1)	4 (0.1)
Respiratory diseases	Asthma					
	No	16,128 (84.3)	6,496 (83.2)	3,243 (82.9)	3,262 (86.2)	3,127 (86.1)
	Yes	2,986 (15.6)	1,298 (16.6)	666 (17.0)	521 (13.8)	501 (13.8)
	<i>Missing</i>	20 (0.1)	11 (0.1)	2 (0.1)	3 (0.1)	4 (0.1)
	Emphysema					
	No	11,121 (58.1)	NA	3,900 (99.7)	3,734 (98.6)	3,487 (96.0)
	Yes	195 (1.0)		9 (0.2)	49 (1.3)	137 (3.8)
	<i>Missing</i>	7,818 (40.9)		2 (0.1)	3 (0.1)	8 (0.2)
	Bronchitis					
	No	10,694 (55.9)	NA	3,759 (96.1)	3,562 (94.1)	3,373 (92.9)
	Yes	617 (3.2)		148 (3.8)	219 (5.8)	250 (6.9)
	<i>Missing</i>	7,823 (40.9)		4 (0.1)	5 (0.1)	9 (0.2)
Oral diseases	Caries					
	No	4,603 (24.1)	3,918 (50.2)	549 (14.0)	112 (3.0)	24 (0.7)
	Yes	12,800 (66.9)	3,372 (43.2)	2,986 (76.3)	3,257 (86.0)	3,185 (87.7)
	<i>Missing</i>	1,731 (9.0)	515 (6.6)	376 (9.6)	417 (11.0)	423 (11.6)
	Periodontitis					
	No	4,786 (25.0)	NA	1,072 (27.4)	1,864 (49.2)	1,850 (50.9)
	Yes	2,877 (15.0)		626 (16.0)	1,290 (34.1)	961 (26.5)
	<i>Missing</i>	11,471 (60.0)		2,213 (56.6)	632 (16.7)	821 (22.6)

Note: NA – Data not collected. CVD – Cardiovascular diseases. NCD - Fatal non-communicable diseases.

Appendix Table 2. Ten more frequent co-occurrences among non-communicable diseases complex networks by age group in the US population. NHANES 2011-2014.

1 to 19 y-old			20 to 39 y-old			40 to 59 y-old			Over 60 y-old		
Disease connection		Freq (%)	Disease connection		Freq (%)	Disease connection		Freq (%)	Disease connection		Freq (%)
Caries	Overwt/Obesity	1174 (20.3)	Caries	Overwt/Obesity	1844 (11.3)	Caries	Overwt/Obesity	2381 (7.7)	Caries	Overwt/Obesity	2258 (5.9)
Caries	Asthma	606 (10.5)	Caries	Low HDL-c	911 (5.6)	Caries	Periodontitis	1237 (4.0)	Caries	Prediabetes	1366 (3.6)
Overwt/Obesity	Asthma	486 (8.4)	Low HDL-c	Overwt/Obesity	888 (5.4)	Caries	Low HDL-c	1124 (3.6)	Overwt/Obesity	Prediabetes	1082 (2.8)
Low HDL-c	Overwt/Obesity	338 (5.8)	Caries	Depression	615 (3.8)	Low HDL-c	Overwt/Obesity	1066 (3.4)	Caries	Periodontitis	948 (2.5)
Caries	Low HDL-c	288 (5.0)	Caries	Periodontitis	542 (3.3)	Caries	Prediabetes	1030 (3.3)	Caries	Low HDL-c	923 (2.4)
Caries	Hypertension	183 (3.2)	Caries	Asthma	529 (3.2)	Periodontitis	Overwt/Obesity	972 (3.1)	Caries	Hypertension	911 (2.4)
Caries	High TC	181 (3.1)	Overwt/Obesity	Depression	494 (3.0)	Overwt/Obesity	Prediabetes	935 (3.0)	Caries	Diabetes	900 (2.4)
Caries	Diabetes risk	178 (3.1)	Periodontitis	Overwt/Obesity	460 (2.8)	Caries	Depression	803 (2.6)	Low HDL-c	Overwt/Obesity	813 (2.1)
Overwt/Obesity	Hypertension	172 (3.0)	Overwt/Obesity	Asthma	438 (2.7)	Overwt/Obesity	Depression	676 (2.2)	Overwt/Obesity	Diabetes	802 (2.1)
Overwt/Obesity	Diabetes risk	162 (2.8)	Caries	Prediabetes	428 (2.6)	Caries	Diabetes	521 (1.7)	Caries	CVD	755 (2.0)

Note: Overwt/Obesity - Overweight/Obesity. TC – Total cholesterol.

Appendix Table 3. Node-specific measures by age group of the US population. NHANES 2011-2014.

Group	Disease	Degree	Betweenness	Eigenvector	Local transitivity	Shannon entropy
Autoimmune diseases	Rheumatoid arthritis					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	172	0.00	0.03	1.00	0.86
	40-59 y-old	991	0.02	0.10	0.99	0.88
	Over 60 y-old	1339	0.00	0.13	1.00	0.89
	Psoriasis					
	1-19 y-old	27	0.00	0.01	1.00	0.92
	20-39 y-old	271	0.00	0.05	1.00	0.84
	40-59 y-old	529	0.00	0.06	1.00	0.88
	Over 60 y-old	627	0.00	0.06	1.00	0.92
	Celiac disease					
	1-19 y-old	19	0.00	0.01	1.00	0.92
	20-39 y-old	37	0.00	0.01	1.00	0.90
	40-59 y-old	89	0.00	0.01	1.00	0.92
	Over 60 y-old	99	0.00	0.01	1.00	0.92
Mental diseases	Depression					
	1-19 y-old	244	0.06	0.09	0.95	0.78
	20-39 y-old	2404	1.18	0.43	0.94	0.79
	40-59 y-old	4082	0.10	0.43	0.99	0.87
	Over 60 y-old	4165	0.15	0.39	0.98	0.88
	Forgetting					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	625	0.20	0.10	0.94	0.84
	40-59 y-old	1547	0.05	0.16	0.99	0.89
	Over 60 y-old	3995	0.21	0.37	0.98	0.88
Metabolic risks	Low HDL-c					
	1-19 y-old	986	0.09	0.40	0.95	0.73
	20-39 y-old	3603	0.60	0.65	0.94	0.77
	40-59 y-old	5436	0.12	0.60	0.99	0.83
	Over 60 y-old	4998	0.09	0.48	0.98	0.87
	High LDL-c					
	1-19 y-old	206	0.00	0.06	1.00	0.85
	20-39 y-old	511	0.00	0.08	1.00	0.82
	40-59 y-old	1036	0.00	0.11	0.99	0.82
	Over 60 y-old	777	0.00	0.07	0.98	0.88
	High TC					
	1-19 y-old	635	0.17	0.23	0.95	0.81
	20-39 y-old	1065	0.08	0.18	0.97	0.82
	40-59 y-old	2400	0.01	0.26	0.99	0.85
	Over 60 y-old	1911	0.03	0.18	0.98	0.88
	High TG					
	1-19 y-old	362	0.14	0.12	0.91	0.83
	20-39 y-old	1230	0.07	0.22	0.97	0.81
	40-59 y-old	2357	0.03	0.26	0.99	0.85
	Over 60 y-old	2194	0.03	0.21	0.98	0.88
	Overweight/Obesity					
	1-19 y-old	2777	1.46	0.98	0.91	0.71
	20-39 y-old	6077	2.52	0.97	0.94	0.78
	40-59 y-old	9738	0.41	0.95	0.99	0.85
	Over 60 y-old	10309	0.48	0.90	0.98	0.88
	Hypertension					
	1-19 y-old	609	0.18	0.24	0.91	0.73
	20-39 y-old	643	0.02	0.12	0.97	0.80
	40-59 y-old	2078	0.01	0.23	0.99	0.84
	Over 60 y-old	4369	0.07	0.43	0.98	0.86
	Prediabetes					

	1-19 y-old	442	0.13	0.16	0.91	0.78
	20-39 y-old	1907	0.35	0.35	0.94	0.77
	40-59 y-old	4800	0.15	0.54	0.99	0.83
	Over 60 y-old	6414	0.26	0.62	0.98	0.86
	Diabetes risk					
	1-19 y-old	672	0.46	0.25	0.91	0.80
	20-39 y-old	1765	0.34	0.32	0.94	0.77
	40-59 y-old	2257	0.02	0.26	0.99	0.82
	Over 60 y-old	1365	0.01	0.13	0.98	0.87
NCD						
	CVD					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	233	0.01	0.04	0.97	0.86
	40-59 y-old	1323	0.02	0.13	0.99	0.88
	Over 60 y-old	4176	0.13	0.39	0.98	0.88
	Diabetes					
	1-19 y-old	56	0.02	0.02	0.95	0.89
	20-39 y-old	502	0.11	0.09	0.94	0.82
	40-59 y-old	2723	0.06	0.30	0.99	0.84
	Over 60 y-old	4772	0.13	0.46	0.98	0.86
	Cancers					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	235	0.03	0.04	0.94	0.83
	40-59 y-old	1062	0.02	0.11	0.99	0.88
	Over 60 y-old	3223	0.10	0.32	0.98	0.86
Respiratory diseases						
	Asthma					
	1-19 y-old	1572	0.43	0.65	0.91	0.67
	20-39 y-old	2033	0.76	0.38	0.94	0.77
	40-59 y-old	2429	0.12	0.25	0.99	0.88
	Over 60 y-old	2564	0.10	0.24	0.98	0.90
	Emphysema					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	47	0.00	0.01	1.00	0.92
	40-59 y-old	300	0.00	0.03	1.00	0.93
	Over 60 y-old	787	0.00	0.07	1.00	0.92
	Bronchitis					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	660	0.18	0.11	0.94	0.83
	40-59 y-old	1233	0.05	0.12	0.99	0.91
	Over 60 y-old	1459	0.03	0.13	0.98	0.91
Oral diseases						
	Caries					
	1-19 y-old	2955	3.86	1.00	0.91	0.73
	20-39 y-old	6523	4.22	1.00	0.94	0.79
	40-59 y-old	10791	0.69	1.00	0.99	0.86
	Over 60 y-old	12374	1.13	1.00	0.98	0.89
	Periodontitis					
	1-19 y-old	NA	NA	NA	NA	NA
	20-39 y-old	2067	0.32	0.39	0.94	0.76
	40-59 y-old	5035	0.12	0.58	0.99	0.81
	Over 60 y-old	4153	0.05	0.43	0.98	0.84

Note: NA – Data not collected. TC – Total cholesterol. TG – Triglycerides. CVD – Cardiovascular diseases.

5.4 Capítulo 4 - Alto teor de açúcares livres, resistência à insulina e baixos indicadores socioeconômicos: os elementos centrais da complexa rede de doenças não transmissíveis em adolescentes

“High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the complex network of non-communicable diseases in adolescents”

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RESEARCH

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High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the complex network of non-communicable diseases in adolescents

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Abstract

Background Noncommunicable diseases (NCDs) predominantly affect adults, but pathophysiological changes begin decades earlier, as a *continuum*, with initial events apparent in adolescence. Hence, early identification and intervention are crucial for the prevention and management of NCDs. We investigated the complex network of socioeconomic, behavioral, and metabolic factors associated with the presence of NCD in Brazilian adolescents.

Methods We conducted a cross-sectional study nested within the São Luís segment of the Ribeirão Preto, Pelotas, and São Luís (RPS) cohort's consortium, focusing on 18–19-year-olds ($n = 2515$). Data were collected prospectively, from which we constructed a complex network with NCD-related factors/indicators as nodes and their co-occurrences as edges. General and sex-based models analyzed: socioeconomic status, behavioral (smoking, alcohol, and other drugs use, unhealthy diet, poor sleep, physical inactivity), and metabolic factors (overweight/obesity, elevated blood pressure, poor lipid profile). We also looked for NCDs in adolescence like asthma, abnormal spirometry, depression, suicide risk, and poor oral health. The network was characterized by degree, betweenness, eigenvector, local transitivity, Shannon entropy, and cluster coefficient.

Results The adolescents had an average age of 18.3 years, 52.3% were female and 47.7% male. 99.8% of them have a diet rich in free sugars, 15% are overweight/obese and 72.3% had an elevated TyG index. High free sugar emerged as the central hub, followed by high TyG index (an early marker of insulin resistance) and low socioeconomic class. In males, low fiber intake and a high triglycerides/HDL ratio highlighted cardiometabolic concerns; in females, sedentary behavior and poor sleep marked metabolic and psychological challenges, along with caries in both sexes.

Conclusions Our findings provide insights into central health challenges during adolescence, such as high free sugars, insulin resistance, and low socioeconomic indicators, suggesting that interventions targeted at these central hubs could have a significant impact on their NCD network.

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Keywords Adolescent, Noncommunicable diseases, Dietary sugar, Insulin resistance, Socioeconomic status, Complex network

Background

Non-communicable diseases (NCDs) are the leading cause of premature deaths globally, affecting individuals under 70 years old, especially in low and middle-income countries [1]. Addressing NCDs is critical to achieving the Agenda for Sustainable Development goals, which include a target to reduce premature mortality from NCDs by one-third by 2030 through prevention and treatment. Key to this effort are high-impact NCD interventions alongside the early identification of risk factors [2].

By the age of 40, many individuals will develop at least one NCD as a lifetime risk, and a third of them will be subsequently diagnosed with multiple NCDs due to shared risk factors [3]. Although NCDs predominantly affect adults, their pathophysiological *continuum* traces back to much earlier in life, with initial events detectable in youth [4]. Detecting early NCD signs, recognizing their determinants and risk factors, and understanding how these conditions cluster are essential for developing effective prevention and control strategies [5]. Adolescence is a sensitive period of human development, during which exposure to risk factors can profoundly impact biological and cognitive systems [6]. Behavioral factors are often established during this life period, potentially leading to metabolic dysfunctions and elevating the risk of developing NCDs later in life [7].

Traditional analyses of behavioral and metabolic conditions often fail to capture the complexity of their relationships at the onset of NCDs [8]. Identifying how and which related factors co-occur can improve diagnostic and intervention strategies at both clinical and population levels [9]. Moreover, public policies developed without considering the interconnected nature of these factors may lead to suboptimal resource allocation and less effective intervention programs [10]. Complex network analysis offers a holistic and comprehensive method to examine these intricate systems, especially in challenging environments with great social and healthcare disparities, allowing for the identification of subtle interactions and hidden patterns [11].

We hypothesize that non-linear relationships among contributing factors form a complex network, leading to NCD clusters already in adolescence. Accordingly, we investigated the complex connections between socioeconomic determinants, behavioral and metabolic factors with NCDs in Brazilian adolescents. This knowledge would shed light on the interconnected nature of these

factors and the NCD signs, ultimately informing more effective prevention and intervention strategies.

Methods

Study design

A population-based cross-sectional study nested within the São Luís, segment of the Ribeirão Preto, Pelotas, and São Luís (RPS) cohort's consortium in Brazil, focusing on 18–19 year-olds. All individuals who participated at the inception of the original cohort were invited to join the second follow-up ($n=687$). To enhance the statistical power of the sample and minimize potential dropouts, the cohort follow-up also included 1133 individuals born in São Luís in 1997, identified through the Brazilian Live Birth Information System (SINASC). Additionally, the sample encompassed 695 volunteers born in 1997 and identified through schools and universities registered in SINASC [12]. Thus, the study's sample comprised 2515 adolescents, with 52.3% female and 47.7% male participants.

Ethical statement

This study was approved by the Ethics and Research Committee of the Federal University of Maranhão University Hospital (IRB #1302489). All participants signed the informed consent.

Data collection

To capture and analyze co-occurrence patterns in complex networks, we transformed variables into dichotomous forms in order to simplify the representation and interpretation of connections between health conditions and contributing factors.

Socioeconomic determinants

Socioeconomic information was collected using an assessment questionnaire. The socioeconomic variables included low educational attainment of the adolescent and the family head (up to elementary school), low family income ($\leq$ USD 270.76, based on the Brazilian national minimum wage in 2016), and low socioeconomic class (C–E classes) based on the Brazilian Economic Classification Criteria (A representing the highest and E the lowest) [13].

Behavioral factors

Current tobacco use and current or former use of other drugs (marijuana, cocaine, heroin, ecstasy, crack, or LSD)

were collected through a confidential self-reported questionnaire. High alcohol consumption was assessed using the Alcohol Use Disorders Identification Test (AUDIT).

Dietary information was collected using a quality-quantity Food Frequency Questionnaire (FFQ), administered by trained nutritionists, which asked about the frequency, portion size, and quantity of food consumed over the past 12 months. The final measures were reported as daily consumption. Dietary variables included high intake of saturated fats ($\geq 10\%$ of total calories), lipids ($\geq 30\%$ of total calories), sodium (≥ 5 g), and free sugars ($\geq 5\%$ of total calories, ideal limit according by the World Health Organization-WHO) [14]. Low fiber intake was defined as < 25 g for females and 38 g for males. Low protein intake was < 0.8 g/kg of body weight, while high protein intake was > 2 g/kg. Sensitivity analysis evaluated high free sugar consumption as 10% (maximum WHO guidelines limits) [14] and 25 g (maximum American Heart Association recommendation) [15].

Sedentary behavior was defined as < 150 min of physical activity per week by the Self-Administered Physical Activity Checklist (SAPAC) questionnaire. Poor sleep quality was based on scores > 5 in the Pittsburgh Sleep Quality Index (PSQI), and excessive daytime sleepiness by scores ≥ 9 on the Epworth Sleepiness Scale (ESS).

Metabolic conditions

We considered overweight/obesity as a body mass index > 25 kg/m² and high body fat percentage $\geq 30\%$ in females and $\geq 25\%$ in males, using a BOD POD and a stadiometer (Altura Exata®). Hypertension was defined by blood pressure $> 130/80$ mmHg and high pulse wave velocity ≥ 90 th percentile of the sample distribution [16]. Additional markers included high levels of total cholesterol (≥ 200 mg/dL), LDL-c (≥ 130 mg/dL), VLDL-c (≥ 30 mg/dL), triglycerides (≥ 150 mg/dL), and low HDL-c (< 40 mg/dL). The triglycerides/HDL-c ratio ≥ 1.75 [17] and the TyG index ≥ 7.94 [18] were utilized as markers of insulin resistance.

NCD in adolescence

Asthma was self-reported based on a previous medical diagnosis. Lung capacity was evaluated using the KoKo PFT Spirometer (Koko® Spirometer), with Forced Expiratory Volume in 1 s (FEV₁) values $< 80\%$ of the predicted value considered abnormal [19].

Depression and suicide risk were assessed using the Mini-International Neuropsychiatric Interview (MINI), diagnosing major and recurrent major depressive episodes. High suicide risk was indicated by a score ≥ 6 .

Oral health was assessed using the number of decayed teeth (DMFT index) and recording severe caries (characterized by visible pulpal involvement and ulceration

caused by dislocated tooth fragments, fistula, or abscess). Periodontitis was classified following the American Academy of Periodontology/European Federation of Periodontology (AAP/EFP) guidelines and dichotomized as none or any periodontitis. The presence of bleeding on probing (BoP) was set if $> 15\%$ of surfaces were affected [20].

Data analysis

We created an undirected graph structure based on a co-occurrence matrix, where nodes represented contributing factors/health conditions and edges represented their co-occurrences. The edge was weighted according to the proportion of co-occurrences between conditions. We built general and sex-based models for analysis.

To describe the network's structure, we calculated four centrality measures specific to each node: degree, betweenness, eigenvector centrality, and local transitivity. The degree of a node (condition) represents its number of connections (edges), indicating its involvement in the network. Betweenness measures how often a node serves as a bridge on the shortest paths between other nodes; a higher betweenness value suggests the node (condition) acts as a mediator or bridge between other conditions, implying shared pathophysiological mechanisms or risk factors. Eigenvector centrality assigns a value to each node based on the centrality of the nodes to which it is connected, thus identifying influential nodes and assigning higher values to conditions connected to many other highly connected diseases. Local transitivity is the ratio of the number of triangles connected to a node to the number of triples centered on that node, indicating the probability that two diseases will co-occur if they are both linked to a third disease [21].

The Shannon entropy specific to each node was measured to evaluate the diversity of each node's connections, with higher values indicating more diverse connections [22]. Shannon entropy for the entire network was also computed to reflect the overall complexity of the network structure [23]. The clustering coefficient was also calculated to assess the likelihood that a node forms a triangle with two other nodes, thus providing insights into the network's clustering characteristics.

Results

Population characteristics are presented in Table 1. Adolescents had an average age of 18.3 years, 52.3% were female and 47.7% male. 99.8% consumed more than 5% of their daily calories from free sugars, regardless of sex ($p=0.178$). Additionally, 72.3% had a TyG index above 7.94. Approximately 70% belonged to socioeconomic classes C, D, or E, with 54.4% being females ($p=0.018$). Furthermore, the education level of the family head,

Table 1 Population characteristics. RPS São Luís (N=2515)

	Overall	Male	Female	p-value
Adolescent education				0.160
High school or more	2486 (98.9)	1177 (47.5)	1301 (52.5)	
Elementary school or less	27 (1.1)	17 (63.0)	10 (37.0)	
Family head education				0.011
High school or more	1919 (76.5)	942 (49.1)	977 (50.9)	
Elementary school or less	588 (23.5)	253 (43.0)	335 (57.0)	
Household income				1.00
> USD 270.76	1214 (54.2)	575 (47.5)	635 (52.5)	
≤ USD 270.76	1026 (45.8)	486 (47.5)	537 (52.5)	
Socioeconomic class				0.018
A/B	654 (29.5)	334 (51.2)	318 (48.8)	
C/D/E	1560 (70.5)	709 (45.6)	845 (54.4)	
Smoking				< 0.001
No	2407 (96.5)	1127 (46.8)	1280 (53.2)	
Yes	88 (3.5)	61 (69.3)	27 (30.7)	
Alcohol use				< 0.001
No	2026 (80.7)	905 (44.8)	1116 (55.2)	
Yes	486 (19.3)	290 (59.7)	196 (40.3)	
Drug use				< 0.001
No	2030 (82.1)	913 (45.0)	1117 (55.0)	
Yes	443 (17.9)	264 (59.6)	179 (40.4)	
Saturated fat consumption ^a				< 0.001
< 10%	1819 (72.8)	935 (51.4)	884 (48.6)	
≥ 10%	680 (27.2)	254 (37.4)	426 (62.6)	
Lipids consumption ^a				< 0.001
< 30%	2249 (90.0)	1102 (49.0)	1147 (51.0)	
≥ 30%	250 (10.0)	87 (34.8)	163 (65.2)	
Free sugar consumption				
< 5% ^a	6 (0.2)	5 (83.3)	1 (16.7)	0.178
≥ 5%	2493 (99.8)	1184 (47.5)	1309 (52.5)	
< 10% ^a	56 (2.2)	29 (51.8)	27 (48.2)	0.616
≥ 10%	2443 (97.8)	1160 (47.5)	1283 (52.5)	
< 25 g ^b	25 (1.0)	14 (56.0)	11 (44.0)	0.524
≥ 25 g	2482 (99.0)	1181 (47.6)	1301 (52.4)	
Sodium consumption				0.230
< 5 g	2415 (96.3)	1145 (47.4)	1270 (52.6)	
≥ 5 g	92 (3.7)	50 (54.3)	42 (45.7)	
Protein consumption ^c				0.950
≥ 0.8 g/kg	1734 (70.5)	833 (48.0)	901 (52.0)	
< 0.8 g/kg	725 (29.5)	350 (48.3)	375 (51.7)	
≤ 2.0 g/kg	2227 (90.6)	1068 (48.0)	1159 (52.0)	0.690
> 2.0 g/kg	232 (9.4)	115 (49.6)	117 (50.4)	
Fiber consumption				< 0.001
≥ 25 g for women; ≥ 38 g for men	1446 (58.0)	558 (38.6)	886 (61.4)	
< 25 g for women; < 38 g for men	1049 (42.0)	634 (60.4)	415 (39.6)	
Body mass index				0.530
Eutrophic	2002 (81.0)	962 (48.1)	1040 (51.9)	
Overweight/Obesity	370 (15.0)	169 (45.7)	201 (54.3)	

Table 1 (continued)

	Overall	Male	Female	p-value
Blood pressure				< 0.001
< 130/80 mgHg	2055 (83.3)	882 (43.0)	1168 (57.0)	
≥ 130/80 mgHg	413 (16.7)	302 (73.1)	111 (26.9)	
pWV ^d				< 0.001
< 90th percentile	1983 (89.0)	920 (46.5)	1058 (53.5)	
≥ 90th percentile	245 (11.0)	153 (62.4)	92 (37.6)	
Body fat				< 0.001
< 30% for women; < 25% for men	1810 (73.5)	1059 (58.7)	745 (41.3)	
≥ 30% for women; ≥ 25% for men	652 (26.5)	121 (18.6)	531 (81.4)	
Total cholesterol				< 0.001
< 200 mg/dL	2071 (90.1)	1034 (50.1)	1029 (49.9)	
≥ 200 mg/dL	228 (9.9)	73 (32.0)	155 (68.0)	
LDL-c				0.001
< 130 mg/dL	2107 (92.0)	1041 (49.4)	1066 (50.6)	
≥ 130 mg/dL	184 (8.0)	67 (36.4)	117 (63.6)	
VLDL-c				0.002
< 30 mg/dL	2089 (90.9)	984 (47.3)	1097 (52.7)	
≥ 30 mg/dL	209 (9.1)	123 (58.9)	86 (41.1)	
Triglycerides				< 0.001
< 150 mg/dL	2088 (91.1)	985 (47.2)	1103 (52.8)	
≥ 150 mg/dL	203 (8.9)	123 (60.6)	80 (39.4)	
HDL-c				< 0.001
≥ 40 mg/dL	1834 (80.0)	782 (42.6)	1052 (57.4)	
< 40 mg/dL	458 (20.0)	326 (71.2)	132 (28.8)	
Triglycerides/ HDL-c				< 0.001
< 1.75	1471 (59.2)	584 (39.8)	882 (60.2)	
≥ 1.75	1014 (40.8)	599 (59.2)	412 (40.8)	
TyG index				0.688
< 7.94	634 (27.7)	307 (48.7)	324 (51.3)	
≥ 7.94	1653 (72.3)	785 (47.6)	864 (52.4)	
Asthma				0.040
No	2209 (88.7)	1035 (46.9)	1174 (53.1)	
Yes	282 (11.3)	151 (53.5)	131 (46.5)	
FEV ₁ ^e				< 0.001
> 80%	1485 (66.1)	758 (51.0)	727 (49.0)	
≤ 80%	762 (33.9)	316 (41.5)	446 (58.5)	
Depression				< 0.001
No	2135 (85.7)	1089 (51.0)	1046 (49.0)	
Yes	356 (14.3)	97 (27.2)	259 (72.8)	
Suicide risk				< 0.001
1–5 score	2368 (94.5)	1155 (48.8)	1213 (51.2)	
≥ 6 score	139 (5.5)	40 (28.8)	99 (71.2)	
Physical activity				< 0.001
≥ 150 min	1377 (55.2)	892 (64.8)	485 (35.2)	
< 150 min	1117 (44.8)	295 (26.4)	822 (73.6)	
Sleep quality				< 0.001
Good	977 (46.3)	527 (53.9)	450 (46.1)	
Poor	1133 (53.7)	471 (41.6)	662 (58.4)	
Sleepiness				< 0.001

Table 1 (continued)

	Overall	Male	Female	p-value
No	1582 (63.2)	808 (51.1)	774 (48.9)	0.565
Yes	920 (36.8)	383 (41.6)	537 (58.4)	
Caries				0.220
No	1054 (44.1)	492 (46.8)	559 (53.2)	
Yes	1336 (55.9)	640 (48.1)	691 (51.9)	0.013
Severe caries				
No	1459 (73.5)	688 (47.3)	766 (52.7)	0.706
Yes	527 (26.5)	265 (50.6)	259 (49.4)	
Periodontitis				0.706
No	1548 (65.0)	710 (46.0)	835 (54.0)	
Yes	832 (35.0)	426 (51.4)	403 (48.6)	
Bleeding on probing ^f				0.706
< 15%	1352 (56.8)	640 (47.5)	708 (52.5)	
≥ 15%	1028 (43.2)	496 (48.3)	530 (51.7)	

The p-value was obtained from the Chi-squared test to observe differences between the sexes at a significance level of 5%. Totals may vary due to missing data for some variables

^a % of total daily calories
^b grams per day
^c Consumption in grams in relation to body weight
^d PWV: Pulse wave velocity
^e FEV₁: Forced expiratory volume in the first second
^f % of sites affected in comparison to the total evaluated

smoking, alcohol and drug use, high consumption of saturated fats and lipids, low fiber intake, metabolic conditions, poorer mental and respiratory health indicators, sedentary behavior, and periodontitis were all associated with the sex of the participant.

Figure 1 illustrates the complex networks, with node-specific measures detailed in Table S1. In all models, the highest degrees were observed for high free sugar consumption, high TyG index, and low socioeconomic class (Fig. 1 and Fig. 2). These were followed by caries, poor sleep, sedentary behavior, and high triglycerides/HDL-c ratio in the overall model (Fig. 2a). This pattern persisted in supplementary analysis defining high sugar consumption as $\geq 10\%$ of daily calories and as ≥ 25 g (see Additional file, Fig. S2). Among males, caries, high triglycerides/HDL-c ratio, low fiber consumption, and high bleeding on probing were the next highest degrees of centrality (Fig. 2b), while among females, sedentarism, caries, poor sleep, and high body fat were observed (Fig. 2c). Similar patterns were observed for betweenness and eigenvector centrality (Fig. 2). Node-related Shannon entropy values ranged between 0.90 and 0.95, and local transitivity values ranged between 0.99 and 1.00. The cluster coefficient was 0.99, and Shannon entropy was -5.3 across all models.

Figure 3 depicts the frequency of connections between each condition. In the overall model (Fig. 3a), the most

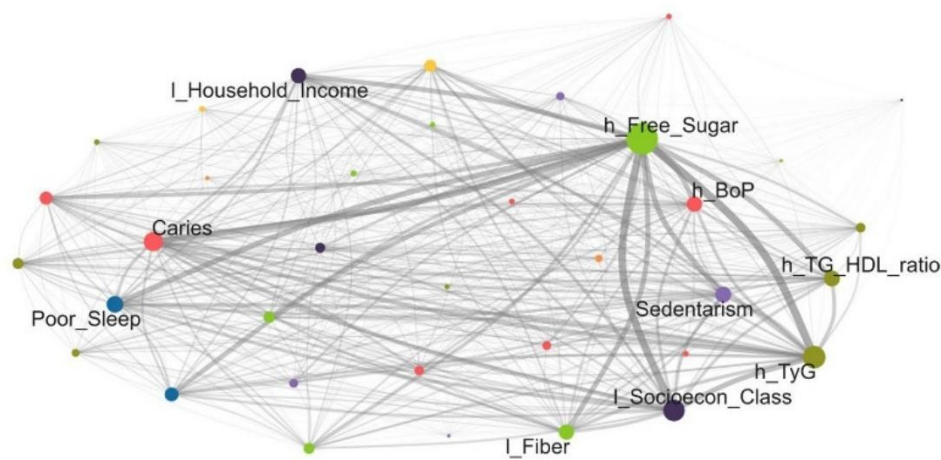
frequent pairs were those linked to high sugar consumption: high TyG index (1.4%), low socioeconomic class (1.3%), and caries (1.2%), and poor sleep (1.0%). Among males (Fig. 3b), the most frequent pairs were those associated with high sugar consumption: high TyG index (1.5%), low socioeconomic class (1.3%), caries (1.2%), low fiber intake (1.2%), and high triglycerides/HDL-c ratio (1.1%). Among females (Fig. 3c), the most frequent pairs were those linked to high sugar consumption: high TyG index (1.4%), low socioeconomic class (1.4%), sedentary behavior (1.3%), caries (1.1%), and poor sleep (1.1%).

Discussion

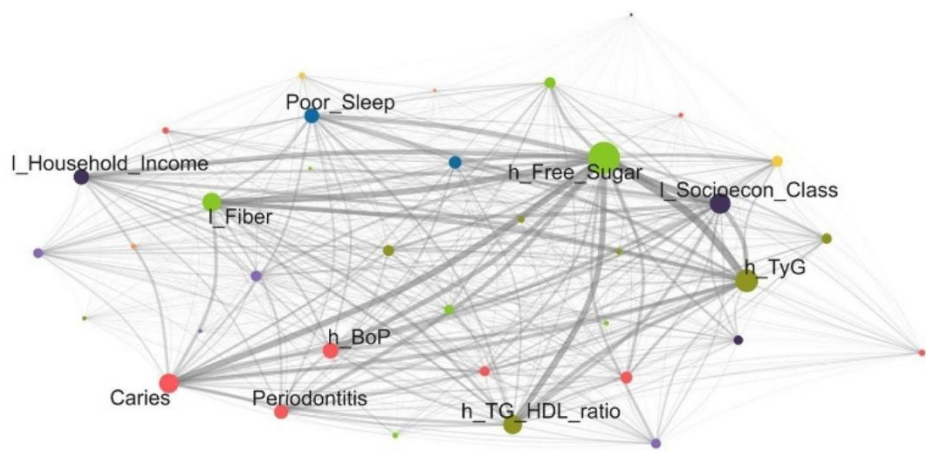
We identified a pattern of interconnection among NCDs in adolescents and their related factors. High free sugar consumption emerged as the central hub, followed by other significant elements such as the high TyG index (an early event in the diabetes *continuum*) and low socioeconomic status. These elements were highly interconnected, regardless of the adolescent's sex. To our knowledge, this is the first study analyzing the non-linear connections between related factors (socioeconomic, behavioral, and metabolic conditions) and NCDs in adolescents.

The prominence of high free sugar consumption consistently emerged across all analyses, highlighting its significant impact on adolescent health. Notably, the pattern persisted even when defining high sugar consumption

a. Overall



b. Male



c. Female

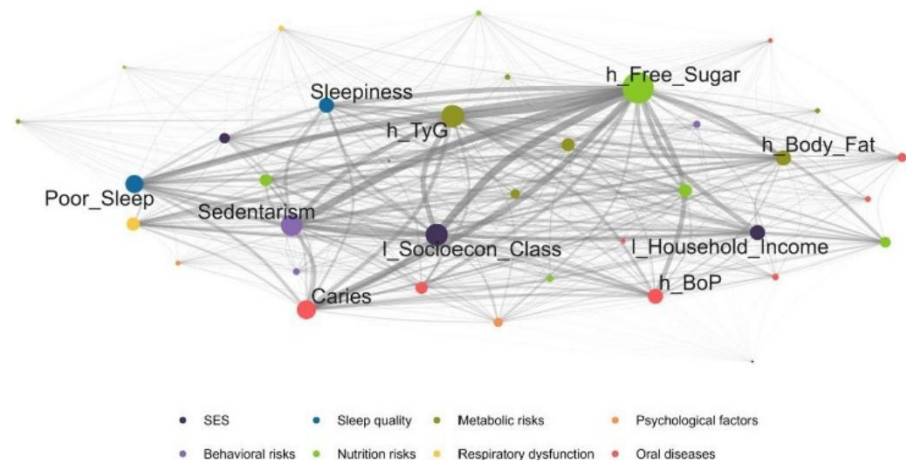


Fig. 1 Complex networks of non-communicable diseases and risks by sex. RPS São Luís (N = 2515). The edges represent the co-occurrences between any two conditions, with thicker edges indicating a higher number of connections. The size of each node reflects its degree, meaning the number of connections it has with other nodes. Larger nodes indicate greater centrality. The figure with all the nodes identified can be found in the Additional file (Fig. S1). I_: Low; h_: High; PWV: pulse wave velocity; BoP: Gingival bleeding on probing

as $\geq 10\%$ of daily calories or ≥ 25 g. As the primary source of discretionary calories in the Western diet, high sugar intake has substantial implications for metabolic health. Excessive sugar consumption leads to *de novo lipogenesis*, resulting in increased fat storage, especially in the liver, and contributes to the development of insulin resistance [24]. Furthermore, sugar intake is associated with chronic low-grade inflammation and oxidative stress, which are key mechanisms in the pathogenesis of NCDs [25]. These processes can lead to a range of metabolic disturbances, including dyslipidemia, hypertension, and endothelial dysfunction, setting the stage for early onset of conditions such as type 2 diabetes and cardiovascular diseases [26]. We observed frequent pairings, such as high sugar consumption with elevated TyG index, a marker of insulin resistance [18], reinforces the metabolic impact of sugar intake on diabetes. Furthermore, the link between low socioeconomic status and high sugar consumption may be due to the greater availability and lower cost of sugary foods, which are more accessible to vulnerable families [27]. Moreover, the connection between sugar consumption and caries corroborates the harmful effects of excess sugar on oral health [28].

The TyG index had a high centrality in the analyzed models, underscoring dyslipidemia and insulin resistance [18], an early event of the diabetes *continuum*. Insulin resistance fosters a lipogenic state, increasing hepatic triglyceride synthesis and reducing lipoprotein lipase activity, resulting in elevated serum triglyceride levels and decreased HDL cholesterol [25]. In adipose tissue, several early steps in insulin signaling to lipolysis and lipogenesis in subcutaneous fat cells occur independently of the liver, contributing to variations in circulating triglycerides and HDL cholesterol [29]. This dyslipidemic state is a well-established risk factor for atherosclerosis, an early sign of the cardiovascular *continuum* [30]. The significance of dyslipidemia is further emphasized by the high eigenvector and betweenness values observed for the triglycerides/HDL ratio in our network analysis, indicating that this relationship is central and highly interconnected with other factors and conditions within the NCD network.

The centrality of low socioeconomic position in the complex networks of NCDs among adolescents highlights the importance of social determinants on health. Adolescents from lower socioeconomic classes were found

to have a higher prevalence of adverse health outcomes, underscoring the association between socioeconomic disadvantage and NCDs [20, 31]. In 2022, approximately 31.6% of the Brazilian population lived in poverty, equating to about 67.8 million people [32]. Notably, the poverty rate is not uniform across Brazil; the Northeast region, where the study was conducted, has nearly 43.5% of its population living in poverty [32]. Theories of inequalities in health, such as the social determinants of health framework, explain how lower socioeconomic status often correlates with reduced access to healthcare, poorer nutrition, higher exposure to environmental hazards, and increased levels of stress, contributing to the development and progression of NCDs [33]. The chronic stress associated with socioeconomic hardship can lead to physiological changes, including increased inflammation and hormonal imbalances, which further exacerbate the risk of NCDs [34]. These findings may be particularly relevant for other settings with similar socioeconomic disparities, but contextual differences such as healthcare infrastructure, social safety nets, and dietary patterns may influence the extent to which these findings are applicable elsewhere.

Our results revealed similarities in the complex networks of males and females, which shared high sugar consumption, high TyG index, and low socioeconomic class as central nodes, underscoring the pervasive impact of these factors on adolescents' health, irrespective of their sex. However, differences were observed beyond these shared elements. In the males' network, the main factors were caries, high triglycerides/HDL-c ratio, and low fiber consumption. Low fiber intake and high triglycerides/HDL-c ratio in males suggest a dietary pattern predisposing them to higher cardiometabolic risk [35]. For females, sedentary behavior and poor sleep emerged alongside caries. Sedentary behavior increases the risk of obesity and metabolic syndrome, while poor sleep quality leads to hormonal imbalances and increased stress levels, both of which are risk factors for NCDs [36, 37].

Poor sleep quality and daytime sleepiness were not strongly related in this study as expected. Adolescents exhibit significant variability in their sleep needs and responses to sleep deprivation [38]. Some adolescents may have a higher tolerance for sleep loss, meaning they can function adequately during the day despite not

(See figure on next page.)

Fig. 2 Complex networks node-specific measurements of non-communicable diseases and risks. RPS São Luís (N = 2515). The size of each node reflects its degree, meaning the number of connections it has with other nodes. Betweenness is a measure that quantifies the importance of a node in a network based on the number of shortest paths that pass through it, as a mediation value. Eigenvector measures a node's influence by considering the importance of the nodes it is connected to. The detailed values of each measurement are detailed in the Additional file (Table S1)

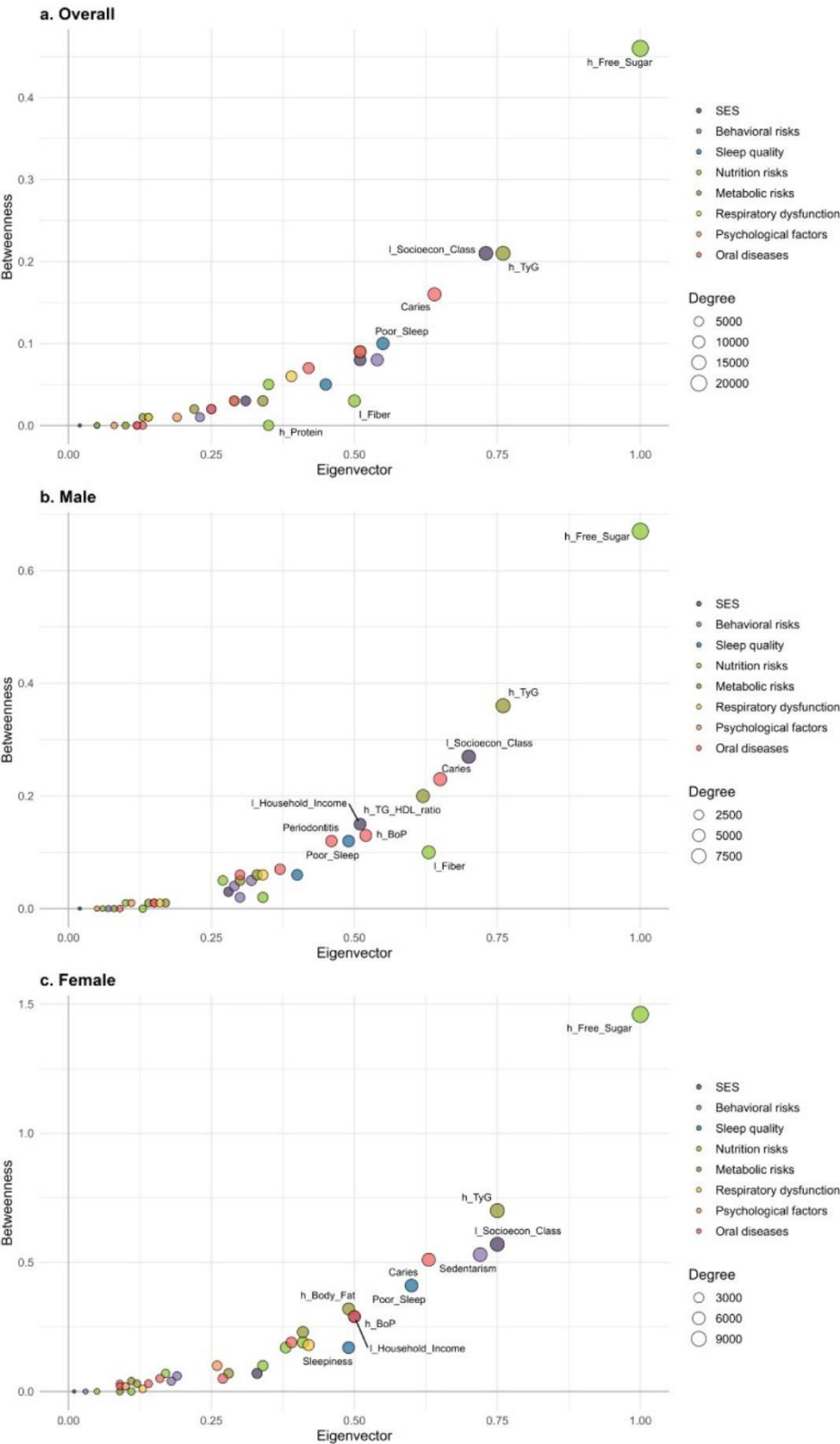


Fig. 2 (See legend on previous page.)

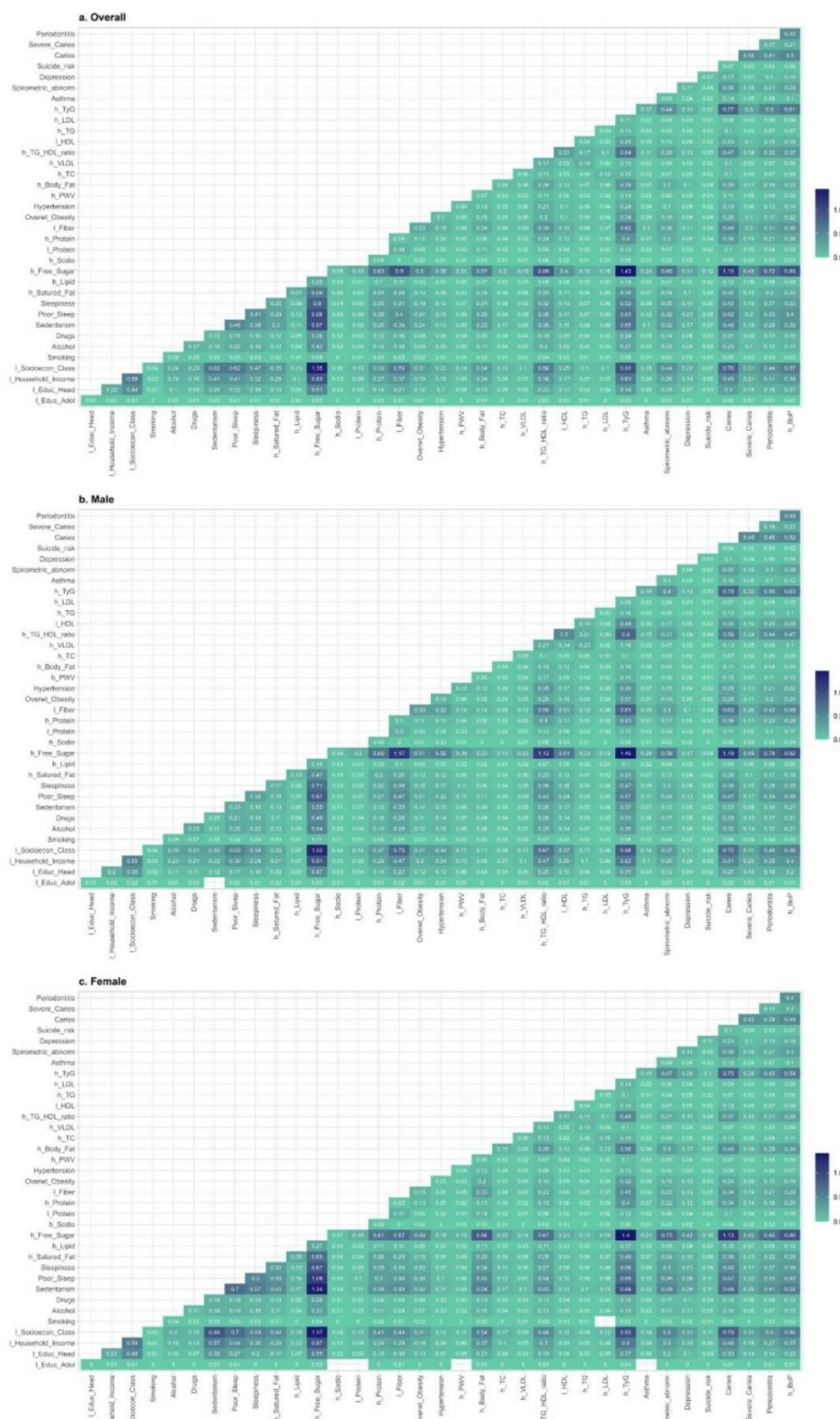


Fig. 3 Percentage of connections between each condition by sex. RPS São Luís (N= 2515). The values correspond to the percentage of co-occurrence between two conditions, representing the thickness of the edges in the networks. The darker, the greater the co-occurrence

getting enough sleep [39, 40]. The same was observed for socioeconomic class and household income. Household income reflects immediate financial resources, while socioeconomic class encompasses a wider range of factors, such as parents' level of education, number of bathrooms, ownership of certain household utensils and access to safe water, among others [13].

As a limitation, we do not intend to infer temporality or causality between risk factors and health outcomes due to the cross-sectional nature of this study. Instead, we assume a complex, intricate network of non-linear relationships between multiple factors and NCDs in adolescence. Socioeconomic indicators and drug use were self-reported, which could introduce reporting bias. To mitigate this, we previously tested the instruments and provided comprehensive training for data collectors to ensure consistent administration and accurate responses. Furthermore, drug assessment was done through a confidential self-reported questionnaire. Dietary information was elicited using food frequency questionnaires, which may be prone to recall bias and measurement errors; to minimize bias, we used a quality–quantity instrument with photographic records and administered the questionnaires by trained nutritionists.

Our study has several strengths that enhance its significance and potential impact. We used validated instruments and standardized procedures, e.g., air displacement plethysmography (BOD POD) to evaluate body composition. Calibrated dentists conducted full-mouth examinations using international indices for caries and periodontitis, ensuring high data quality and reliability. Additionally, a population-based sample provides robust analysis and allows for the generalization of findings to similar urban populations. The novelty of this study lies in the complex network approach to investigating the interconnections among related factors and NCDs in adolescence, offering a broad perspective on the multifaceted nature of NCD onset.

Conclusions

In sum, our findings emphasize the importance of understanding the intricate interconnections among contributing factors and NCDs in adolescents. This study highlights the central roles of high free sugar consumption, high TyG index, and low socioeconomic status in these complex networks. By identifying these dietary patterns and socioeconomic disparities, we emphasize the need for early, multifaceted interventions to effectively mitigate the burden of NCDs that adolescents face.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13098-024-01469-8>.

Supplementary Material 1.

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Author contributions

SAC: Conception, data analysis, data interpretation, and drafting of the work. BSF: Data analysis, data interpretation, and critical review. FAR: Design of the work, data analysis, data interpretation, and critical review. AAF: Conception, data interpretation, critical review. GGN: Data interpretation, critical review. FRML: Data interpretation, critical review. LLCL: Data acquisition, data interpretation, critical review. RFLB: Data acquisition, data interpretation, critical review. EBART: Data acquisition, data interpretation, critical review. CMCA: Data acquisition, data interpretation, critical review. CCCR: Conception, data interpretation, critical review. All authors contributed to the final manuscript.

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Availability of data and materials

The data analyzed during this study is not publicly available, but can be obtained from the RPS São Luis cohort committee upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Ethics and Research Committee of the Federal University of Maranhão University Hospital (IRB #1302489). Written informed consent was obtained from all subjects/patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Naghavi M, Ong KL, Aali A, Ababneh HS, Abate YH, Abbafati C, et al. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the global burden of disease study 2021. *Lancet*. 2024;403:2100–32.
- United Nations. Health—United Nations sustainable development. Sustainable development goals. <https://www.un.org/sustainabledevelopment/health/>. Accessed 15 May 2024
- Licher S, Heshmatollah A, van der Willik KD, Stricker BHCh, Ruiter R, de Roos EW, et al. Lifetime risk and multimorbidity of non-communicable diseases and disease-free life expectancy in the general population: a population-based cohort study. *PLoS Med*. 2019;16: e1002741.
- Dzau VJ, Antman EM, Black HR, Hayes DL, Manson JE, Plutzky J, et al. The cardiovascular disease continuum validated: clinical evidence of improved patient outcomes. *Circulation*. 2006;114:2850–70. <https://doi.org/10.1161/CIRCULATIONAHA.106.655688>.
- Faienza MF, Urbano F, Lassandro G, Valente F, D'Amato G, Portincasa P, et al. The cardiovascular disease (CVD) risk continuum from prenatal life to adulthood: a literature review. *Int J Environ Res Public Health*. 2022;19:8282.
- Barouki R, Gluckman PD, Grandjean P, Hanson M, Heindel JJ. Developmental origins of non-communicable disease: implications for research and public health. *Environ Health*. 2012;11:42. <https://doi.org/10.1186/1476-069X-11-42>.
- National academies of sciences e and m, health and medicine division, Division of behavioral and social sciences and education, Board on children Y and F, Committee on applying lessons of optimal adolescent health to improve behavioral outcomes for youth. Promoting positive adolescent health behaviors and outcomes: Thriving in the 21st Century. Graham R, Kahn NF (Eds.). Washington, D.C.: National Academies Press; 2019. <https://www.ncbi.nlm.nih.gov/books/NBK554988/>. Accessed 15 May 2024
- Padrón-Monedero A. A pathological convergence theory for non-communicable diseases. *Aging Med*. 2023;6:328–37. <https://doi.org/10.1002/agm2.12273>.
- Budreviciute A, Damiati S, Sabir DK, Onder K, Schuller-Goetzburg P, Plakys G, et al. Management and prevention strategies for non-communicable diseases (NCDs) and their risk factors. *Front Public Health*. 2020. <https://doi.org/10.3389/fpubh.2020.574111/full>.
- Banatvala N, Akselrod S, Bovet P, Mendis S. The WHO global action plan for the prevention and control of NCDs 2013–2030. In: Banatvala N, Akselrod S, Bovet P, Mendis S, editors. *Noncommunicable diseases*. London: Routledge; 2023. p. 234–9.
- Vulliard L, Menche J. Complex networks in health and disease. *Syst Med*. Elsevier. 2021. pp. 26–33. <https://linkinghub.elsevier.com/retrieve/pii/B978012801238311640X>
- Confortin SC, Ribeiro MRC, Barros AJD, Menezes AMB, Horta BL, Victora CG, et al. RPS Brazilian Birth Cohorts Consortium. In: R Preto, Pelotas, S Luis (Eds.) *History, objectives and methods*. Cad Saude Publica: Rio de Janeiro. 2021; 37.
- Association of Research Companies. Brazilian economic classification criteria. ABER. 2008. pp. 1–3. <http://www.abep.org/criterio-brasil>. Accessed 26 May 2024.
- Ruanpeng D, Thongprayoon C, Cheungpasitporn W, Harindhanavudhi T. Sugar and artificially sweetened beverages linked to obesity: a systematic review and meta-analysis. *QJM Int J Med*. 2017;110:513–20.
- Vos MB, Kaar JL, Welsh JA, Van Horn LV, Feig DI, Anderson CAM, et al. Added sugars and cardiovascular disease risk in children: a scientific statement from the American heart association. *Circulation*. 2017;135:e1017–34. <https://doi.org/10.1161/CIR.0000000000000439>.
- Zhao M, Mill JG, Yan W-L, Hong YM, Skidmore P, Stoner L, et al. Static cut-points of hypertension and increased arterial stiffness in children and adolescents: the international childhood vascular function evaluation consortium. *J Clin Hypertens*. 2019;21:1335–42.
- Shim YS, Baek JW, Kang MJ, Oh YJ, Yang S, Hwang IT. Reference values for the triglyceride to high-density lipoprotein cholesterol ratio and non-high-density lipoprotein cholesterol in Korean children and adolescents: The Korean national health and nutrition examination surveys 2007–2013. *J Atheroscler Thromb*. 2016;23:1334–44.
- Reckziegel MB, Nepomuceno P, Machado T, Renner JDP, Pohl HH, Nogueira-de-Almeida CA, et al. The triglyceride-glucose index as an indicator of insulin resistance and cardiometabolic risk in Brazilian adolescents. *Arch Endocrinol Metab*. 2023. <https://doi.org/10.20945/2359-3997000000506>.
- Global initiative for chronic obstructive lung disease. Gold spirometry guide. Global initiative for chronic obstructive lung disease (GOLD). 2010. <https://goldcopd.org/gold-spirometry-guide/>. Accessed 16 May 2024.
- Ladeira LLC, Nascimento GG, Leite FRM, Alves-Costa S, Barbosa JMA, Alves CMC, et al. Obesity, insulin resistance, caries, and periodontitis: syndemic framework. *Nutrients*. 2023. 15. <https://pubmed.ncbi.nlm.nih.gov/37630703/>. Accessed 29 Jan 2024.
- da Costa L F, Rodrigues FA, Travieso G, Villas Boas PR. Characterization of complex networks: a survey of measurements. *Adv Phys*. 2007;56:167–242. <https://doi.org/10.1080/00018730601170527>.
- Eagle N, Macy M, Claxton R. Network diversity and economic development. *Science*. 2010;328:1029–31. <https://doi.org/10.1126/science.1186605>.
- Wiesner K, Ladyman J. Measuring complexity. 2019. <http://arxiv.org/abs/1909.13243>
- Softic S, Gupta MK, Wang G-X, Fujisaka S, O'Neill BT, Rao TN, et al. Divergent effects of glucose and fructose on hepatic lipogenesis and insulin signaling. *J Clin Invest*. 2017;127:4059–74.
- Chen Z, Yu R, Xiong Y, Du F, Zhu S. A vicious circle between insulin resistance and inflammation in nonalcoholic fatty liver disease. *Lipids Health Dis*. 2017;16:203.
- Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. *Diabetol Metab Syndr*. 2023;15:60. <https://doi.org/10.1186/s13098-023-01025-w>.
- Mayén A-L, Marques-Vidal P, Paccaud F, Bovet P, Stringhini S. Socioeconomic determinants of dietary patterns in low- and middle-income countries: a systematic review. *Am J Clin Nutr*. 2014;100:1520–31.
- Ladeira LLC, Nascimento GG, Leite FRM, Alves-Costa S, Thomaz EBAF, Alves CMC, et al. Sugar intake above international recommendations and oral disease burden: a population-based study. *Oral Dis*. 2022. <https://doi.org/10.1111/odi.14464>.
- Kerr AG, Andersson DP, Dahlman I, Rydén M, Arner P. Adipose insulin resistance associates with dyslipidemia independent of liver resistance and involves early hormone signaling. *Arterioscler Thromb Vasc Biol*. 2023;43:1054–65.
- Che B, Zhong C, Zhang R, Pu L, Zhao T, Zhang Y, et al. Triglyceride-glucose index and triglyceride to high-density lipoprotein cholesterol ratio as potential cardiovascular disease risk factors: an analysis of UK biobank data. *Cardiovasc Diabetol*. 2023;22:34.
- Barbosa JMA, Ribeiro CCC, Batista RFL, Brondani MA, Simões VMF, Bettiol H, et al. Behavioral risk factors for noncommunicable diseases associated with depression and suicide risk in adolescence. *Rio de Janeiro: Cad Saude Publica*; 2022. p. 38.
- Irene Gomes. Poverty drops to 31.6% of the population in 2022, after reaching 36.7% in 2021. IBGE. 2023. <https://agenciadenoticias.ibge.gov.br/en/agencia-news/2184-news-agency/news/38574-poverty-drops-to-31-6-of-the-population-in-2022-after-reaching-36-7-in-2021>. Accessed 2 Sep 2024.
- Di Cesare M, Khang Y-H, Asaria P, Blakely T, Cowan MJ, Farzadfar F, et al. Inequalities in non-communicable diseases and effective responses. *Lancet*. 2013;381:585–97.
- Parker HW, Abreu AM, Sullivan MC, Vadeloo MK. Allostatic load and mortality: a systematic review and meta-analysis. *Am J Prev Med*. 2022;63:131–40.
- Isasi CR, Parrinello CM, Ayala GX, Delamater AM, Perreira KM, Daviglius ML, et al. Sex differences in cardiometabolic risk factors among hispanic/latino youth. *J Pediatr*. 2016;176:121–127.e1.
- Fatima Y, Doi SAR, Mamun AA. Sleep quality and obesity in young subjects: a meta-analysis. *Obes Rev*. 2016;17:1154–66.
- Pearson N, Braithwaite RE, Biddle SJH, van Sluijs EMF, Atkin AJ. Associations between sedentary behaviour and physical activity in children and adolescents: a meta-analysis. *Obes Rev*. 2014;15:666–75.
- Agostini A, Centofanti S. Normal sleep in children and adolescence. *Child Adolesc Psychiatr Clin N Am*. 2021;30:1–14.

39. Taylor DJ, Jenni OG, Acebo C, Carskadon MA. Sleep tendency during extended wakefulness: insights into adolescent sleep regulation and behavior. *J Sleep Res.* 2005;14:239–44.
40. Jenni OG, Achermann P, Carskadon MA. Homeostatic sleep regulation in adolescents. *Sleep.* 2005;28:1446–54.

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5.4.1 Material Suplementar do Capítulo 4

Title: High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the Complex Network of Non-Communicable Diseases in Adolescents

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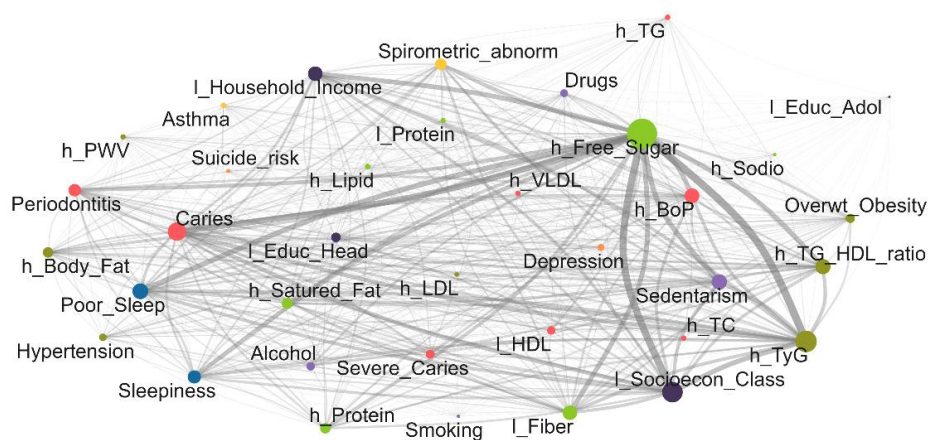
Av. dos Portugueses, 1966

São Luís, MA, Brazil

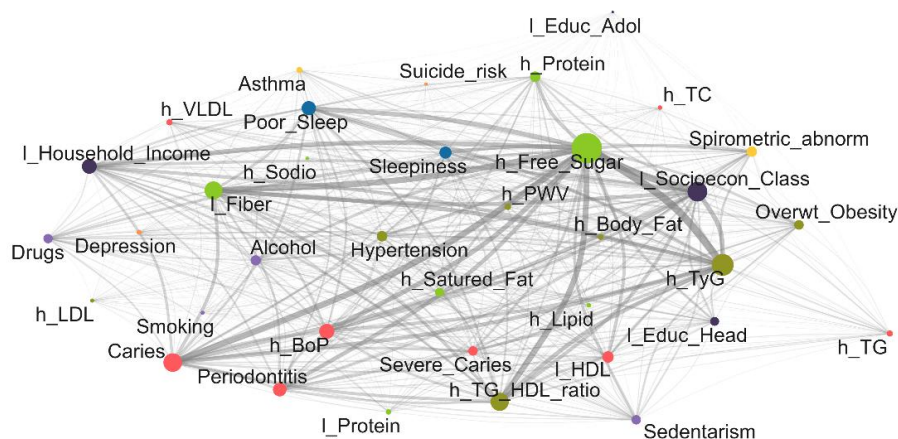
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Fig. S1 Complex networks of non-communicable diseases and risk factors by sex. RPS São Luís (N = 2515).

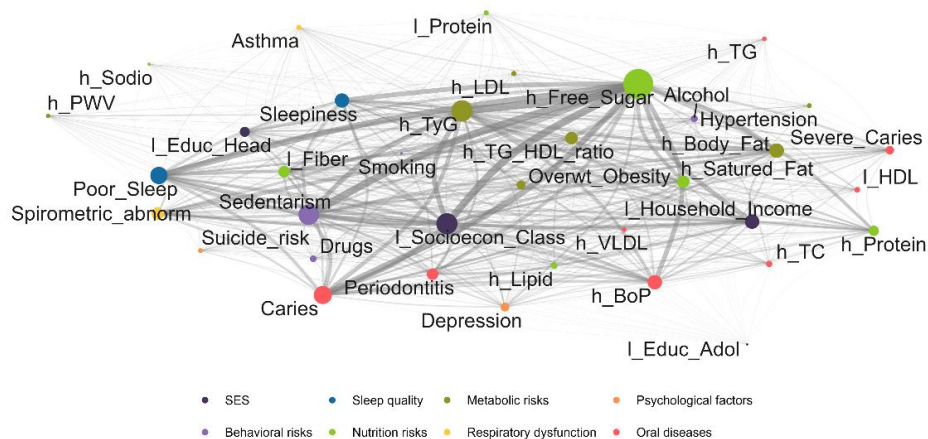
a. Overall



b. Male



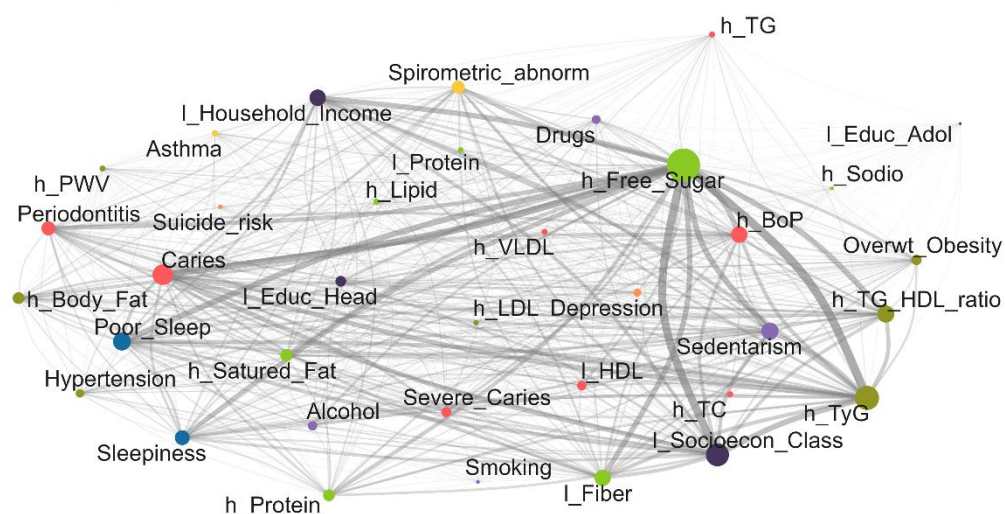
c. Female



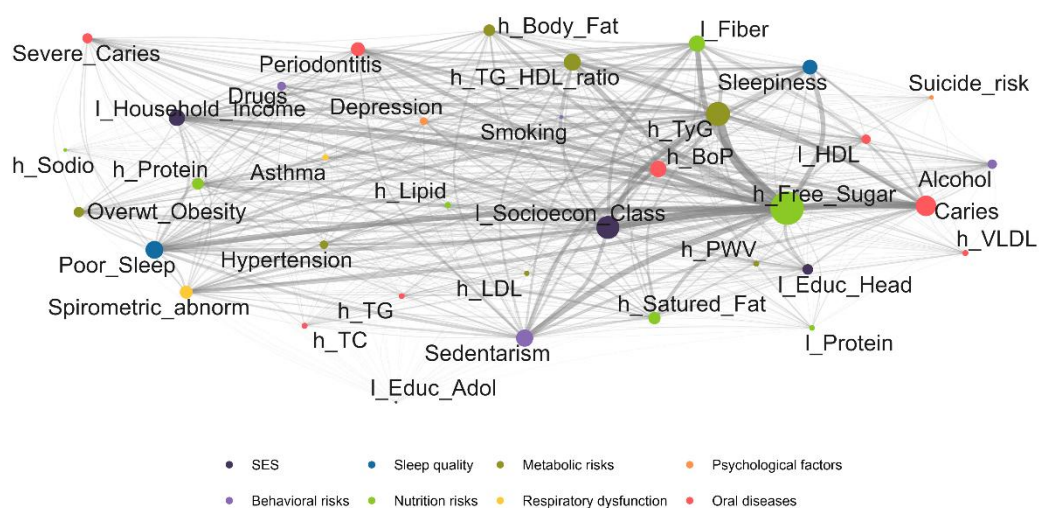
Legend: The edges represent the co-occurrences between any two conditions, with thicker edges indicating a higher number of connections. The size of each node reflects its degree, meaning the number of connections it has with other nodes. Larger nodes indicate greater centrality. l_ : Low; h_ : High; PWV: pulse wave velocity; BoP: Gingival bleeding on probing.

Fig. S2 Complex networks of non-communicable diseases and risk factors with free sugar at different cut-off points. RPS São Luís (N = 2515).

a. High Free Sugar as 10% or more



b. High Free Sugar as 25g or more



Legend: Complex networks of non-communicable diseases and risk factors by sex. RPS São Luís (N = 2515). The edges represent the co-occurrences between any two conditions, with thicker edges indicating a higher number of connections. The size of each node reflects its degree, meaning the number of connections it has with other nodes. Larger nodes indicate greater centrality. l_ : Low; h_ : High; PWV: pulse wave velocity; BoP: Gingival bleeding on probing.

Table S1. Complex networks node-specific measurements of non-communicable diseases and risk factors.
RPS São Luís (N = 2515).

Node	Overall			Male			Female		
	Degree	Betweenness	Eigenvector	Degree	Betweenness	Eigenvector	Degree	Betweenness	Eigenvector
Low adolescent education	329	0.00	0.02	218	0.00	0.02	111	0.00	0.01
Low family head education	5746	0.03	0.31	2465	0.03	0.28	3281	0.07	0.33
Low household income	9612	0.08	0.51	4534	0.15	0.51	5064	0.29	0.50
Low socioeconomic class	14124	0.21	0.73	6307	0.27	0.70	7797	0.57	0.75
Smoking	1005	0.00	0.05	696	0.00	0.07	309	0.00	0.03
Alcohol use	4923	0.02	0.25	2896	0.05	0.32	2027	0.06	0.19
Drugs use	4471	0.01	0.23	2619	0.04	0.29	1852	0.04	0.18
Sedentarism	10165	0.08	0.54	2635	0.02	0.30	7530	0.53	0.72
Poor sleep	10565	0.10	0.55	4341	0.12	0.49	6224	0.41	0.60
Sleepiness	8571	0.05	0.45	3562	0.06	0.40	5009	0.17	0.49
High saturated fat consumption	6771	0.05	0.35	2463	0.05	0.27	4308	0.19	0.41
High lipid consumption	2775	0.01	0.14	934	0.01	0.10	1841	0.07	0.17
High free sugar consumption	21260	0.46	1.00	9977	0.67	1.00	11283	1.46	1.00
High sodium consumption	1016	0.00	0.05	538	0.00	0.06	478	0.00	0.05
Low protein consumption	2335	0.00	0.12	1184	0.00	0.13	1151	0.00	0.11
High protein consumption	6423	0.00	0.35	3024	0.02	0.34	3399	0.10	0.34
Low fiber consumption	9509	0.03	0.50	5639	0.10	0.63	3870	0.17	0.38
Overweight/Obesity	5537	0.03	0.29	2705	0.05	0.30	2832	0.07	0.28
Hypertension	4205	0.02	0.22	3003	0.06	0.33	1202	0.04	0.11
High PWV ^a	2507	0.01	0.13	1533	0.01	0.17	974	0.00	0.09
High body fat	6473	0.03	0.34	1340	0.01	0.14	5133	0.32	0.49
High total cholesterol	2564	0.00	0.13	858	0.00	0.09	1706	0.05	0.16
High VLDL-c	2595	0.00	0.12	1488	0.01	0.15	1107	0.03	0.09
High triglycerides/HDL-c	10080	0.09	0.51	5736	0.20	0.62	4336	0.23	0.41
Low HDL-c	4833	0.02	0.25	3337	0.07	0.37	1496	0.03	0.14
High triglycerides	2515	0.00	0.12	1487	0.01	0.15	1028	0.02	0.09
High LDL-c	2050	0.00	0.10	747	0.00	0.08	1303	0.03	0.12
High TyG index	14865	0.21	0.76	7022	0.36	0.76	7830	0.70	0.75
Asthma	2732	0.01	0.14	1424	0.01	0.16	1308	0.01	0.13
Spirometry abnormal	7282	0.06	0.39	3030	0.06	0.34	4252	0.18	0.42
Depression	3779	0.01	0.19	1026	0.01	0.11	2753	0.10	0.26
Suicide risk	1580	0.00	0.08	450	0.00	0.05	1130	0.02	0.10
Caries	12438	0.16	0.64	5893	0.23	0.65	6528	0.51	0.63
Severe caries	5336	0.03	0.29	2661	0.06	0.30	2660	0.05	0.27
Periodontitis	7967	0.07	0.42	4074	0.12	0.46	3881	0.19	0.39
High BoP ^b	9704	0.09	0.51	4636	0.13	0.52	5057	0.29	0.50

Legend: ^a PWV: pulse wave velocity; ^b BoP: Gingival bleeding on probing.

5.5 Capítulo 5 - Decodificando a complexidade das conexões entre fatores relacionados à saúde nos primeiros mil dias de vida: análise de rede

“Decoding the Complexity of Health-Related Factors Connections around the First Thousand Days of Life: Network Analysis”

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Decoding the Complexity of Health-Related Factors Connections around the First Thousand Days of Life: Network Analysis

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Word Counting: 2,999 words

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Key points

Question: What are the interconnections among metabolic, behavioral, and socioeconomic factors during pregnancy and early childhood that influence adverse birth outcomes and early NCDs?

Findings: In this cohort study of 1,383 mother-child dyads from São Luís, Brazil, complex network analysis revealed that frequent consumption of ultra-processed foods and sugary drinks during pregnancy, low socioeconomic status, and maternal dental caries were key risk factors. Clusters of these factors were linked to cesarean delivery, childhood obesity, asthma, and allergies.

Meaning: Early interventions targeting these interconnected prenatal and early life risk factors may help break the transgenerational cycle of NCDs.

Abstract

Importance: Non-communicable diseases (NCDs) are a global health challenge, with emerging evidence linking their origins to exposures during the first 1000 days of life.

Objective: To investigate the intricate interconnections among socioeconomic, behavioral, and metabolic risk factors during pregnancy and early childhood and their influence on adverse birth outcomes and early NCDs.

Design, Setting, and Participants: Cohort study using data from the BRISA Prenatal Cohort in São Luís, Brazil. The study included 1,383 mother-child dyads with data collected via structured questionnaires, medical records, and clinical assessments during pregnancy, at birth, and at age 2.

Exposures: Maternal dietary patterns (frequent consumption of ultra-processed foods and sugary drinks), low socioeconomic status, and maternal NCDs, among other metabolic and behavioral factors.

Main Outcomes and Measures: Identification of hubs of risk factors associated with adverse birth outcomes and early childhood NCDs (obesity, caries, asthma, and allergies) using complex network analysis, the Jaccard index, centrality metrics, and the Louvain algorithm.

Results: Frequent consumption of ultra-processed foods (7.74) and sugary drinks (7.41) during pregnancy, low socioeconomic status (7.45), and maternal dental caries (6.66) emerged as the most interconnected risk factors. Early exposure to added sugars (6.22), cesarean delivery (6.18), allergies (5.58), and non-exclusive breastfeeding for six months (5.53) were also prominent. The network analysis revealed clusters of risk factors linked to adverse birth outcomes, childhood obesity, asthma, and allergies, highlighting the transgenerational maintenance of NCD risk factors.

Conclusions and Relevance: Our findings highlight the complex interplay of maternal dietary, metabolic, and socioeconomic factors in the early origins of NCDs, underscoring the need for early interventions to break the transgenerational cycle of these diseases.

Introduction

Non-communicable diseases (NCDs) represent a significant public health burden, accounting for most of the global morbidity and mortality.¹ Evidence suggests that their origins lie in early life, particularly within the first 1000 days—from conception until a child's second birthday.² This developmental window shapes long-term health trajectories.³

Research has identified links between exposures during gestation and adverse birth outcomes affecting child health.² However, the interplay among these factors remains unclear. We provide evidence linking maternal metabolic and behavioral risks in the first 1000 days to adverse infant health outcomes. Pre-gestational obesity has been linked to increased asthma risk in children,⁴ while hypertension during pregnancy raises the likelihood of allergies.⁵ High sugary drink intake is associated with periodontitis⁶ and gestational hypertension,⁷ and negative offspring outcomes. For example, maternal sugary drink consumption during pregnancy correlates with higher asthma risk in children by age two. Our findings also emphasize the intergenerational persistence of risk factors. Maternal obesity and sugar consumption can lead to childhood overweight and increased sugar intake, reinforcing future risk.⁸ Additionally, sugar consumption before age two is associated with caries, gingivitis,⁹ asthma,¹⁰ and allergic conditions such as rhinitis, atopic dermatitis, and food allergies.¹¹

Prior studies often analyze these factors in isolation, not addressing their complex interactions. Understanding how socioeconomic, behavioral, and metabolic exposures interconnect during early life is crucial for comprehensive strategies to prevent childhood NCDs. We decoded the intricate connections around the first 1000 days of life by analyzing the relationships among exposures during the pre-gestational and gestational periods and their influence on adverse birth outcomes and early NCDs in childhood.

Methods

Study design

The Research Ethics Committee of the University Hospital of the Federal University of Maranhão, Brazil (#14771 / 2008–30) approved this study. Written informed consent was obtained. For those under 18 years of age, an adult also signed the consent form. We

followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

We utilized data from “The Etiological Factors of Preterm Birth and Consequences of Perinatal Factors on Children's Health: BRISA Prenatal Cohort,” conducted in São Luís, Brazil. São Luís, the capital of Maranhão in the Northeastern region of the country, had a population of 1,014,837 and a Human Development Index (HDI) of 0.768 as of 2010.

Participants were pregnant women from public and private prenatal care services. As comprehensive registries of pregnant women were unavailable, the sample size was based on prevalence estimates of key explanatory variables (10% to 50%), with a 5% margin of error and 80% statistical power, resulting in a target of 1,500 participants. Eligibility required an obstetric ultrasound before the 20th gestational week to confirm gestational age. Women with multiple pregnancies were excluded due to higher preterm birth risk. The final sample included 1,383 mother-child dyads. Further details of the cohort are described elsewhere.¹²

Data collection

To analyze connection patterns in complex networks, we transformed variables into dichotomous forms to simplify the interpretation of links between health conditions and risk factors.

During the 22nd–25th week of pregnancy, a questionnaire was administered, and a dental examination was performed as baseline assessments. Maternal age was categorized as advanced for those aged 35 or older and as early for those under 20. Participants answered whether they had ever been diagnosed with hypertension or diabetes or if they had undergone cesarean sections prior to their current pregnancy (yes/no). They were asked about their pre-gestational weight, which, combined with measured height, was used to calculate their pre-gestational BMI, with $>25 \text{ kg/m}^2$ being considered overweight/obese.

Socioeconomic variables included low educational attainment (up to elementary), low family income ($\leq$ USD 290.00, based on the Brazilian national minimum wage in 2010), and low socioeconomic class (C-E classes) based on the Brazilian Economic Classification Criteria (A representing the highest and E the lowest).¹³ The head of the family occupation was dichotomized into unskilled vs. semi-skilled/skilled.

Alcohol consumption during pregnancy was self-reported based on weekly intake of beer, wine, and spirits. Smoking during pregnancy was also self-reported. Weekly consumption of sugary drinks was identified when pregnant women reported drinking soft drinks. Ultra-processed food consumption was considered weekly if they reported eating any of the following more than once a week: hamburgers, cheeseburgers, or sandwiches; sausages, hot dogs, salami, ham, bologna, or other processed meats; bacon or sausage; french fries or packaged snacks; ice cream; or baked goods such as cookies, pastries, cakes, pies, or puff pastries.

Dental examinations were performed by six calibrated dentists. Caries lesions were assessed using the DMFT index (number of Decayed, Missing due to caries, and Filled Teeth).¹⁴ A periodontal examination was also performed and analyzed according to the 2018 American Association of Periodontitis and European Federation of Periodontitis consensus.¹⁵ Further, it was dichotomized into healthy vs. any periodontitis.

The first follow-up occurred 48 hours after delivery, during which medical records were collected. Based on medical diagnosis, self-reported anemia, diabetes, and hypertension during pregnancy were dichotomized as yes/no. Children delivered via caesarean section were identified, along with those classified as macrosomic (≥ 4 kg). Gestational age was determined using two criteria: the date of the last menstrual period or an ultrasound performed before 20 weeks of gestation. If the gestational age based on the last menstrual period differed by ≤ 10 days from the age estimated by ultrasound, the last menstrual period was used to calculate gestational age. However, if the difference exceeded 10 days, the ultrasound estimate was used.¹⁶ Preterm births were defined as those occurring before 37 weeks of gestation.

The second follow-up occurred when the child was 2 years old. Mothers were asked, “Up to what age was your baby exclusively breastfed, excluding tea, water, other milk, drinks, and foods?” to identify those not exclusively breastfed during the first six months. Early cessation (before one year) was also assessed through the question, “Did the baby receive breast milk yesterday? If not, until what age was the baby breastfed?” Dietary intake was evaluated using 24-hour recalls by trained nutritionists, detailing all foods and drinks consumed, including brand, preparation, portion size, and volume, aided by a photo album. Data were analyzed using Virtual Nutri Plus® to estimate energy, nutrient intake, and daily added sugar consumption. Harmful intake was defined as >0 g/day.¹⁷

Children's height and weight were measured to calculate BMI z-scores, with overweight/obesity defined as ≥ 1 z-score.¹⁸ Asthma was identified through maternal report of a medical diagnosis, multiple wheezing episodes, or emergency visits. Allergies were defined by maternal reports of atopic dermatitis, rhinitis, or eosinophil count in the third tertile. Intraoral exams identified caries, including non-cavitated lesions, using the dmft index.¹⁴

Analytical approach

Missing data was imputed using the Multiple Imputation by Chained Equations (MICE) method with logistic regression as the imputation model. This preserved the binary structure of the data by imputing values directly as 0 (absence) or 1 (presence), based on predicted probabilities.¹⁹

An undirected network was constructed from a similarity matrix, where nodes represented risk factors or health conditions, and edges represented their relationships.²⁰ Edge weights were calculated using the Jaccard index, which quantifies co-occurrence similarity as:²¹

$$J(A, B) = \frac{|A \cap B|}{|A \cup B|}$$

where A and B represent two sets of attributes, $|A \cap B|$ is the number of attributes, and $|A \cup B|$ is the total number of attributes in either set. Values range from 0 (no overlap) to 1 (perfect overlap), with higher values indicating stronger relationships (represented by thicker edges).

To characterize the network, we computed five centrality metrics for each node. Degree represents the sum of edge weights connected to a node, indicating its overall participation in the network. Eigenvector centrality captures a node's importance based on its connections to other highly connected nodes. Closeness centrality reflects how efficiently a node can reach all others, calculated as the inverse of the average shortest path length. Betweenness quantifies how often a node lies on the shortest paths between others, highlighting its role as a mediator or bridge. Finally, local transitivity measures the proportion of closed triangles around a node, indicating the likelihood that its neighbors are also connected.²²

Community detection was performed using the Louvain algorithm, which optimizes modularity (Q) to identify groups of nodes with dense internal connections and sparse external ones. Modularity is defined as:²³

$$Q = \frac{1}{2m} \sum_{ij} \left[A_{ij} - \frac{k_i k_j}{2m} \right] \delta(c_i, c_j)$$

where A_{ij} is the edge weight between nodes i and j ; k_i and k_j are their degrees, m is the total weight of all edges, and $\delta(c_i, c_j)$ is 1 if nodes belong to the same community, 0 otherwise. The algorithm iteratively merges communities to maximize Q .²³

Additionally, the Shannon entropy for each node was calculated to assess the diversity of its connections, where higher values represent greater diversity.²⁴ Shannon entropy for the entire network was also computed, measuring the network's overall complexity.²⁵ Finally, the clustering coefficient was calculated to determine the probability that a node forms triangles, offering insight into local clustering behavior.²² All analyses were performed in R and RStudio.

Results

Figure 1 and **Supplementary Table S1** show the prevalence of conditions before and after imputation. Before pregnancy, 19.38% of women were overweight/obese, and 19.52% had a prior cesarean. During pregnancy, 85.39% consumed sugary drinks weekly, 66.16% were from socioeconomic class C–E, and 92.41% consumed ultra-processed foods weekly. Among children, 41.21% were born via cesarean, 5.21% had macrosomia, and 4.27% were preterm. Additionally, 36.23% were not exclusively breastfed for six months, 30.08% were overweight/obese at age two, 28.05% had allergies, and 24.73% had asthma. Post-imputation distributions remained similar to the original data.

Figure 2 illustrates the complex network, with node-specific measures detailed in **Supplementary Table S2**. In the overall network, the nodes with the highest degree were weekly consumption of ultra-processed foods (7.74) and sugary drinks (7.41) during pregnancy, maternal low socioeconomic status (7.45), and dental caries (6.66), representing the sum of the weights of their connected edges. These were followed by early exposure of the child to added sugars (6.22), cesarean section (6.18), allergies (5.58) at 2 years of age, and non-exclusive breastfeeding during the first six months (5.53). Additional factors included periodontitis (5.41) and anemia (5.01) during pregnancy and overweight/obesity (5.04) in childhood.

Figure 3 displays the node-specific eigenvector and closeness centrality values. Regarding the pre-gestational period, overweight/obesity exhibited the highest

eigenvector values (0.51), reflecting its connections with other highly central and influential conditions. Behavioral risks during pregnancy, such as the consumption of ultra-processed foods (1.00) and sugary drinks (0.96), followed by low socioeconomic status (0.96), dental caries (0.85), and periodontitis (0.69), had the highest eigenvector values. Cesarean delivery (0.76) was the most important adverse birth outcome. At 2 years of age, the most prominent nodes were the consumption of added sugars (0.79), allergies (0.71), non-exclusive breastfeeding in the first 6 months (0.69), overweight/obesity (0.63), and asthma (0.55). The closeness centrality values exhibited similar patterns.

Node-related Shannon entropy ranged from 0.82 to 0.98, with local transitivity values above 0.99. The network's global clustering coefficient was 0.99, and overall Shannon entropy was 1.26, indicating high connectivity and complexity. Louvain algorithm identified three distinct clusters (**Supplementary Figure S1**). Community 1 (gray) included pre-gestational overweight/obesity, hypertension, and diabetes. Community 2 (orange) featured early maternal age, unskilled family head labor, low income, low education, and child dental caries. Community 3 (yellow) involved ultra-processed food and sugary drink consumption, low socioeconomic status, anemia, and caries during pregnancy. Gestational hypertension showed highest betweenness centrality (52).

Supplementary Figure S2 depicts the strength of connections between various conditions, as measured by the Jaccard index. The strongest links were observed between sugary drinks and ultra-processed food consumption (0.83), followed by low socioeconomic status with ultra-processed foods (0.79) and with sugary drinks (0.72) during pregnancy. Additional connections included those between ultra-processed foods and sugary drinks with caries during pregnancy (0.62 and 0.58, respectively).

The connections with adverse birth outcomes are explored in **Figure 4**. Sugary drinks and low socioeconomic indicators during pregnancy were strongly connected to all connected adverse birth outcomes. Ultra-processed foods and dental caries during pregnancy were the nodes most strongly connected with the cesarean section. Pre-gestational overweight/obesity and diabetes during pregnancy were linked to macrosomia and appeared to influence cesarean delivery, childhood overweight/obesity, and allergies. Hypertension during pregnancy, advanced maternal age, ultra-processed food consumption, and periodontitis during pregnancy were closely connected with preterm

birth, which, in turn, was related to breastfeeding for less than 1-year, early exposure to added sugars, and asthma at 2 years of age.

Figure 5 presents the strength of the edges connecting nodes neighboring early NCDs at 2 years of age within the network. Behavioral risks, such as the weekly consumption of ultra-processed foods and sugary drinks during pregnancy, along with low socioeconomic status, anemia and caries during pregnancy, as well as early exposure to added sugars by age 2, formed strong connections with all NCDs observed in childhood. The child's birth via cesarean section, the lack of exclusive breastfeeding during the first six months of life, and periodontitis were particularly linked with allergies, overweight/obesity, and asthma at 2 years of age.

Discussion

We analyzed the complex network within the BRISA Prenatal Cohort, mapping central nodes from pre-pregnancy through the child's second year. Key nodes and connections were identified, including behavioral risk factors like consumption of ultra-processed foods and sugary drinks during pregnancy and low socioeconomic status, which emerged as central hubs. Maternal dental caries and early exposure to added sugars were also prominent. Cesarean delivery, allergies, overweight/obesity at age two, non-exclusive breastfeeding, and periodontitis during pregnancy ranked among the ten most influential factors. Our findings highlight that an unhealthy maternal diet, pre-existing conditions, and socioeconomic disadvantages contribute to adverse birth outcomes and early onset of NCDs. Notably, ultra-processed food and sugary drink consumption was linked to increased risk of cesarean delivery, macrosomia, preterm birth, and childhood NCDs, including allergies, obesity, asthma, and caries. Early exposure to added sugars and limited breastfeeding were strongly associated with NCDs by age two.

Our findings underscore the impact of an unhealthy diet, particularly one high in added sugars, during the first 1,000 days of life. Frequent consumption of ultra-processed foods and sugary drinks during pregnancy is a key driver of interconnected chronic conditions. Ultra-processed foods contribute significantly to added sugar intake, 46.1% in Brazil²⁶ and 89.7% in the US²⁷. Excessive maternal sugar consumption has been linked to gestational hypertension,⁷ diabetes, preeclampsia, and preterm birth.²⁸ Maternal dental caries, a strong node in our network, likely reflects prolonged exposure to high-sugar diets, affecting maternal health and shaping long-term dietary patterns in offspring.²⁹ This

cycle is reinforced by early added sugar exposure^{9,29} and reduced breastfeeding,³⁰ both associated with childhood allergies,¹¹ overweight/obesity,⁹ asthma,⁴ and dental caries.⁹

Among pre-pregnancy factors, overweight/obesity was the most prominent node. While not a major hub, it plays an important role in maternal and child health outcomes and is a known risk for hypertensive disorders, cesarean delivery, and maternal mortality.^{31,32} It also disrupts metabolic and hormonal balance, increasing the risk of gestational diabetes.³¹

Cesarean section ranked highly in degree, eigenvector, and closeness centrality, indicating strong influence and susceptibility to multiple interconnected factors. Its high centrality may reflect healthcare practices, sociocultural trends, including the increased medicalization of childbirth and the overuse of elective cesarean sections,³³ and associations with neonatal respiratory distress, delayed breastfeeding initiation, maternal complications, and dysbiosis.³⁴

In the second year of life, early exposure to added sugars was the most central node among childhood conditions and the fifth most influential overall. This highlights its role in shaping interconnected health outcomes in early childhood and beyond. The American Heart Association advises against added sugar before age two, as early exposure affects cardiovascular risk,¹⁷ metabolic pathways, immunity,¹¹ and microbiomes,³⁵ contributing to obesity, dental caries, allergies, and asthma.

Maternal factors were closely tied to adverse birth outcomes like cesarean section, macrosomia, and preterm birth, influenced by sugary drink intake and low socioeconomic status. This suggests that an unhealthy diet and socioeconomic disadvantage are overarching risk factors. Sugary drinks may contribute to insulin resistance³⁶ and obesity,⁹ increasing the likelihood of these complications.³⁷ Ultra-processed foods and maternal dental caries were linked to cesarean delivery,³⁸ while pre-gestational obesity and diabetes were associated with macrosomia.³⁹ Hypertension, older maternal age, and periodontitis during pregnancy were linked to preterm birth.³⁷ Preterm birth, in turn, was connected to shorter breastfeeding duration, early sugar exposure, and asthma, suggesting that its effects extend beyond birth.

Network analysis revealed key factors influencing childhood NCDs, including allergies, overweight/obesity, asthma, and caries. Behavioral risks like consuming ultra-processed foods and sugary drinks during pregnancy, low socioeconomic status, anemia,

and maternal dental caries were associated with all childhood NCDs. An unhealthy maternal diet may shape intergenerational habits, increasing early exposure to added sugars and ultra-processed products,⁴⁰ potentially affecting metabolism, immune function, and microbiome development. Cesarean delivery, reduced exclusive breastfeeding, and maternal periodontitis were linked to asthma, obesity, and allergies, likely due to immune and microbial disruption.⁴¹ Maternal periodontitis may also reflect systemic inflammation⁴² and unhealthy behaviors.⁶

Socioeconomic disparities were a central hub, magnifying risk factor transmission across generations. Families in lower socioeconomic strata often rely on low-cost, energy-dense foods and face barriers to healthcare and breastfeeding support.⁴³ These disparities reinforce a cycle of unhealthy behaviors and chronic stress, perpetuating the NCDs across generations.

Limitations include reliance on self-reported data for behaviors such as diet, alcohol, and smoking, which may introduce recall bias. Structured questionnaires and 24-hour dietary recalls by trained nutritionists were used to mitigate this. The use of dichotomous variables may oversimplify complex conditions, but the Jaccard index enabled nuanced co-occurrence analysis. While the study's focus on São Luís limits generalizability, findings align with global research. Though causal inference is limited, this network analysis offers a dynamic systems perspective of the first thousand days.

Conclusions

Our findings highlight the complex interplay of maternal health, unhealthy diet, and socioeconomic factors in shaping adverse birth outcomes and early childhood NCDs. Central hubs—such as sugary drink and ultra-processed food intake, low socioeconomic status, and maternal conditions like caries, anemia, and periodontitis—were pivotal in childhood NCD development. The intergenerational transmission of unhealthy dietary habits, along with systemic socioeconomic disparities, perpetuates metabolic and immune dysregulation starting in utero and continuing into early childhood. Understanding these interactions is essential for designing interventions to reduce NCD risk from early life stages.

Author Contributions:

Silas Alves-Costa contributed to the conception and design of the study, data analysis and interpretation and drafting the manuscript. *Francisco Aparecido Rodrigues* contributed to the design and implementation of the network analysis, interpretation of findings, and critical revision of the manuscript. *Luiza Lober de Souza Piva* contributed to the design and implementation of the network analysis, interpretation of findings, and critical revision of the manuscript. *Rosângela Fernandes Lucena Batista* contributed to data collection, coordination of the BRISA cohort, and critical revision of the manuscript. *Claudia Maria Coelho Alves* contributed to data interpretation and critical revision of the manuscript. *Erika Bárbara Abreu Fonseca Thomaz* contributed to data interpretation and critical revision of the manuscript. *Fábio Renato M. Leite* contributed to methodological review, data interpretation, and drafting the manuscript. *Alexandre Archanjo Ferraro* contributed to data interpretation and critical revision of the manuscript. *Bruno Feres de Souza* contributed to the design and implementation of the network analysis, interpretation of findings, and critical revision of the manuscript. *Cecilia Claudia Costa Ribeiro* contributed to design conception, data analysis and interpretation, and drafting and revision of the manuscript.

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Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: Data will be available upon request to the BRISA cohort management committee (pesquisacoortes.slz@ufma.br).

References

1. Naghavi M, Ong KL, Aali A, et al. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet*. 2024;403(10440):2100-2132. doi:10.1016/S0140-6736(24)00367-2
2. Baird J, Jacob C, Barker M, et al. Developmental Origins of Health and Disease: A Lifecourse Approach to the Prevention of Non-Communicable Diseases. *Healthcare*. 2017;5(1):14. doi:10.3390/healthcare5010014
3. Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of lifetime health around the time of conception: causes and consequences. *The Lancet*. 2018;391(10132):1842-1852. doi:10.1016/S0140-6736(18)30312-X
4. Nascimento JXPT, Ribeiro CCC, Batista RFL, et al. The First 1000 Days of Life Factors Associated with “Childhood Asthma Symptoms”: Brisa Cohort, Brazil. *Sci Rep*. 2017;7(1):16028. doi:10.1038/s41598-017-16295-4
5. Muniz AKOA, Ribeiro CCC, Vianna EO, et al. Factors associated with allergy traits around the 2nd year of life: a brazilian cohort study. *BMC Pediatr*. 2022;22(1):703. doi:10.1186/s12887-022-03772-7
6. Menezes CC, Ribeiro CCC, Alves CMC, et al. Soft drink consumption and periodontal status in pregnant women. *J Periodontol*. 2019;90(2):159-166. doi:10.1002/JPER.16-0388
7. Barbosa JMA, Silva AAM da, Kac G, et al. Is soft drink consumption associated with gestational hypertension? Results from the BRISA cohort. *Brazilian Journal of Medical and Biological Research*. 2021;54(1):1-9. doi:10.1590/1414-431x202010162
8. Pinto DAS, Nascimento JXPT, Padilha LL, et al. High sugar content and body mass index: modelling pathways around the first 1000 d of life, BRISA cohort. *Public Health Nutr*. 2021;24(15):4997-5005. doi:10.1017/S136898002000525X
9. Araújo SMP, Nascimento GG, Ladeira LLC, et al. Chronic oral disease burden at the first 1000 days: Intergenerational risk factors, BRISA cohort. *Oral Dis*. Published online June 9, 2024. doi:10.1111/odi.15010
10. Padilha LL, Vianna EO, Vale ATM, Nascimento JXPT, Silva AAM, Ribeiro CCC. Pathways in the association between sugar sweetened beverages and child asthma traits in the 2nd year of life: Findings from the BRISA cohort. Genuneit J, ed. *Pediatric Allergy and Immunology*. 2020;31(5):480-488. doi:10.1111/pai.13243
11. Muniz AKOA, Vianna EO, Padilha LL, et al. Sugar-Sweetened Beverages and Allergy Traits at Second Year of Life: BRISA Cohort Study. *Nutrients*. 2023;15(14):3218. doi:10.3390/nu15143218
12. da Silva AAM, Simões VMF, Barbieri MA, et al. A protocol to identify non-classical risk factors for preterm births: the Brazilian Ribeirão Preto and São Luís prenatal cohort (BRISA). *Reprod Health*. 2014;11(1):79. doi:10.1186/1742-4755-11-79
13. Association of Research Companies. Brazilian Economic Classification Criteria. *ABEP*. Published online 2008:1-3. Accessed May 26, 2024. <http://www.abep.org/criterio-brasil>
14. World Health Organization. *Oral Health Surveys: Basic Methods*. 5th ed. (World Health Organization, ed.); 2013. Accessed February 12, 2022. <https://www.who.int/publications/i/item/9789241548649>

15. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *J Periodontol.* 2018;89(S1):S159-S172. doi:10.1002/JPER.18-0006
16. Verburg BO, Steegers EAP, De Ridder M, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound in Obstetrics & Gynecology.* 2008;31(4):388-396. doi:10.1002/uog.5225
17. Vos MB, Kaar JL, Welsh JA, et al. Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. *Circulation.* 2017;135(19):e1017-e1034. doi:10.1161/CIR.0000000000000439
18. World Health Organization. *WHO Expert Committee on Physical Status: The Use and Interpretation of Anthropometry.*; 1995. Accessed August 7, 2022. <https://apps.who.int/iris/handle/10665/37003>
19. Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw.* 2011;45(3). doi:10.18637/jss.v045.i03
20. Comin CH, Peron T, Silva FN, Amancio DR, Rodrigues FA, Costa L da F. Complex systems: Features, similarity and connectivity. *Phys Rep.* 2020;861:1-41. doi:10.1016/j.physrep.2020.03.002
21. Fletcher S, Islam MZ. Comparing sets of patterns with the Jaccard index. *Australasian Journal of Information Systems.* 2018;22. doi:10.3127/ajis.v22i0.1538
22. Costa L da F, Rodrigues FA, Travieso G, Villas Boas PR. Characterization of complex networks: A survey of measurements. *Adv Phys.* 2007;56(1):167-242. doi:10.1080/00018730601170527
23. Blondel VD, Guillaume JL, Lambiotte R, Lefebvre E. Fast unfolding of communities in large networks. *Journal of Statistical Mechanics: Theory and Experiment.* 2008;2008(10):P10008. doi:10.1088/1742-5468/2008/10/P10008
24. Eagle N, Macy M, Claxton R. Network Diversity and Economic Development. *Science (1979).* 2010;328(5981):1029-1031. doi:10.1126/science.1186605
25. Wiesner K, Ladyman J. Measuring complexity. Published online 2019. <https://doi.org/10.48550/arXiv.1909.13243>
26. Louzada ML da C, Ricardo CZ, Steele EM, Levy RB, Cannon G, Monteiro CA. The share of ultra-processed foods determines the overall nutritional quality of diets in Brazil. *Public Health Nutr.* 2018;21(1):94-102. doi:10.1017/S1368980017001434
27. Martínez Steele E, Baraldi LG, Louzada ML da C, Moubarac JC, Mozaffarian D, Monteiro CA. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. *BMJ Open.* 2016;6(3):e009892. doi:10.1136/bmjopen-2015-009892
28. Goran MI, Plows JF, Ventura EE. Effects of consuming sugars and alternative sweeteners during pregnancy on maternal and child health: evidence for a secondhand sugar effect. *Proceedings of the Nutrition Society.* 2019;78(3):262-271. doi:10.1017/S002966511800263X
29. Araújo SMP, da Silva GQTL, Costa EL, Nunes AMM, Ribeiro CCC. Pathways in the association between added sugar consumption, obesity in mother-child dyads, and chronic oral disease burden in early childhood. *Eur J Oral Sci.* 2022;130(2). doi:10.1111/eos.12847

30. FELDENS CA, ALVAREZ L, ACEVEDO AM, et al. Early-life sugar consumption and breastfeeding practices: a multicenter initiative in Latin America. *Braz Oral Res.* 2023;37. doi:10.1590/1807-3107bor-2023.vol37.0104
31. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ.* Published online February 8, 2017;j1. doi:10.1136/bmj.j1
32. Papachatz E, Dimitriou G, Dimitropoulos K, Vantarakis A. Pre-pregnancy obesity: Maternal, neonatal and childhood outcomes. *J Neonatal Perinatal Med.* 2013;6(3):203-216. doi:10.3233/NPM-1370313
33. Angolile CM, Max BL, Mushemba J, Mashauri HL. Global increased cesarean section rates and public health implications: A call to action. *Health Sci Rep.* 2023;6(5). doi:10.1002/hsr2.1274
34. National Health Service. Caesarean section: risks. National Health Service. 2023. Accessed February 5, 2025. <https://www.nhs.uk/conditions/caesarean-section/risks/>
35. Nyvad B, Takahashi N. Integrated hypothesis of dental caries and periodontal diseases. *J Oral Microbiol.* 2020;12(1):1710953. doi:10.1080/20002297.2019.1710953
36. Aeberli I, Gerber PA, Hochuli M, et al. Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. *Am J Clin Nutr.* 2011;94(2):479-485. doi:10.3945/ajcn.111.013540
37. Dong B, Yu H, Wei Q, et al. The effect of pre-pregnancy body mass index and excessive gestational weight gain on the risk of gestational diabetes in advanced maternal age. *Oncotarget.* 2017;8(35):58364-58371. doi:10.18632/oncotarget.17651
38. International Weight Management in Pregnancy (i-WIP) Collaborative Group. Effect of diet and physical activity based interventions in pregnancy on gestational weight gain and pregnancy outcomes: meta-analysis of individual participant data from randomised trials. *BMJ.* Published online July 19, 2017;j3119. doi:10.1136/bmj.j3119
39. Englund-Ögge L, Brantsæter AL, Juodakis J, et al. Associations between maternal dietary patterns and infant birth weight, small and large for gestational age in the Norwegian Mother and Child Cohort Study. *Eur J Clin Nutr.* 2019;73(9):1270-1282. doi:10.1038/s41430-018-0356-y
40. Mahmood L, Flores-Barrantes P, Moreno LA, Manios Y, Gonzalez-Gil EM. The Influence of Parental Dietary Behaviors and Practices on Children's Eating Habits. *Nutrients.* 2021;13(4):1138. doi:10.3390/nu13041138
41. DuPont HL, Salge MMH. The Importance of a Healthy Microbiome in Pregnancy and Infancy and Microbiota Treatment to Reverse Dysbiosis for Improved Health. *Antibiotics (Basel).* 2023;12(11). doi:10.3390/antibiotics12111617
42. Pitiphat W, Joshipura KJ, Rich-Edwards JW, Williams PL, Douglass CW, Gillman MW. Periodontitis and Plasma C-Reactive Protein During Pregnancy. *J Periodontol.* 2006;77(5):821-825. doi:10.1902/jop.2006.050193
43. Katre A, Raddatz B. Low-Income Families' Direct Participation in Food-Systems Innovation to Promote Healthy Food Behaviors. *Nutrients.* 2023;15(5). doi:10.3390/nu15051271

FIGURES

Figure 1. Distribution of population characteristics. BRISA São Luís (N = 1,383).

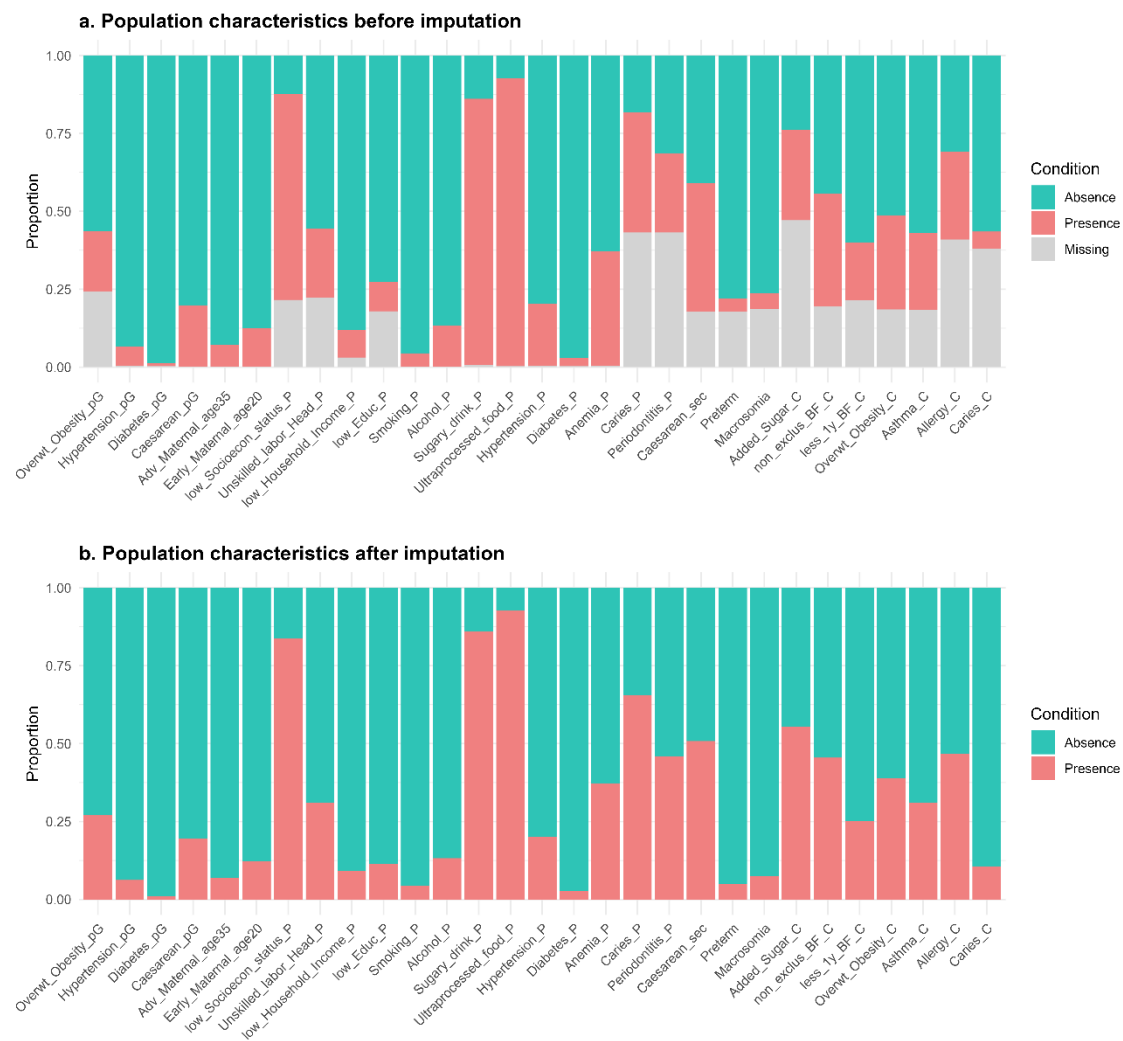
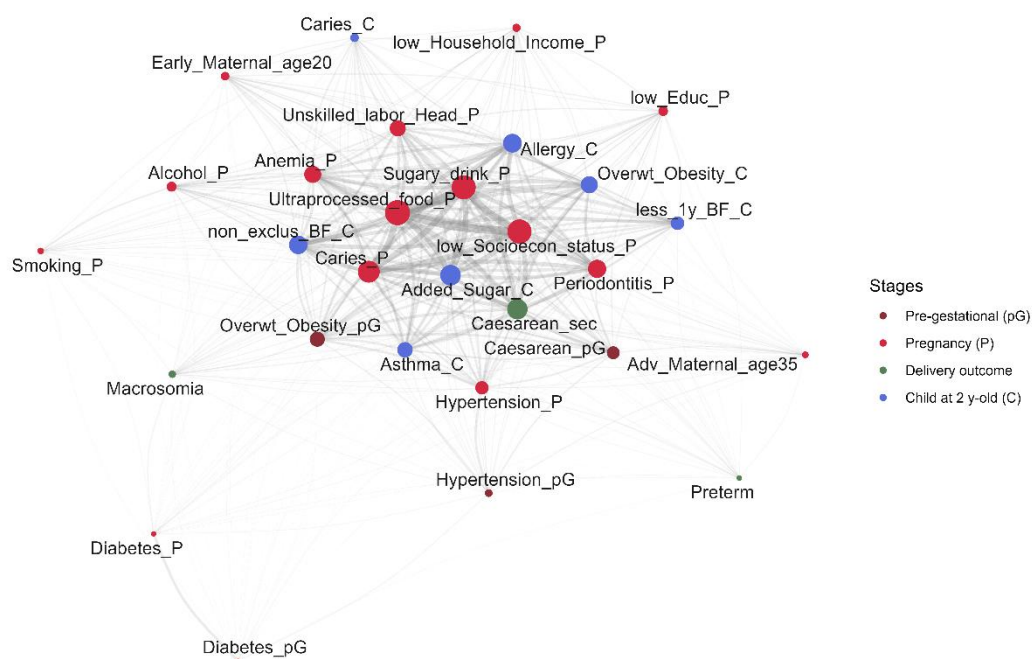
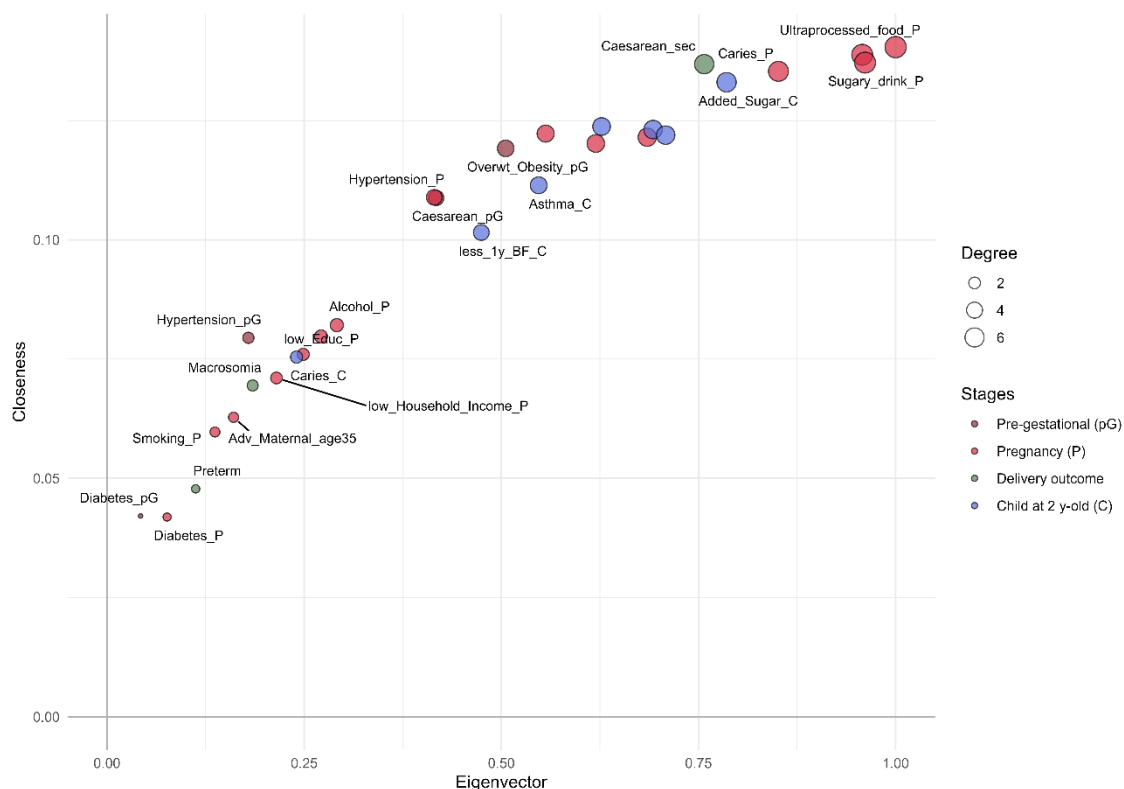


Figure 2. Complex networks of non-communicable diseases in the first 1000 days of life. BRISA São Luís (N = 1,383).



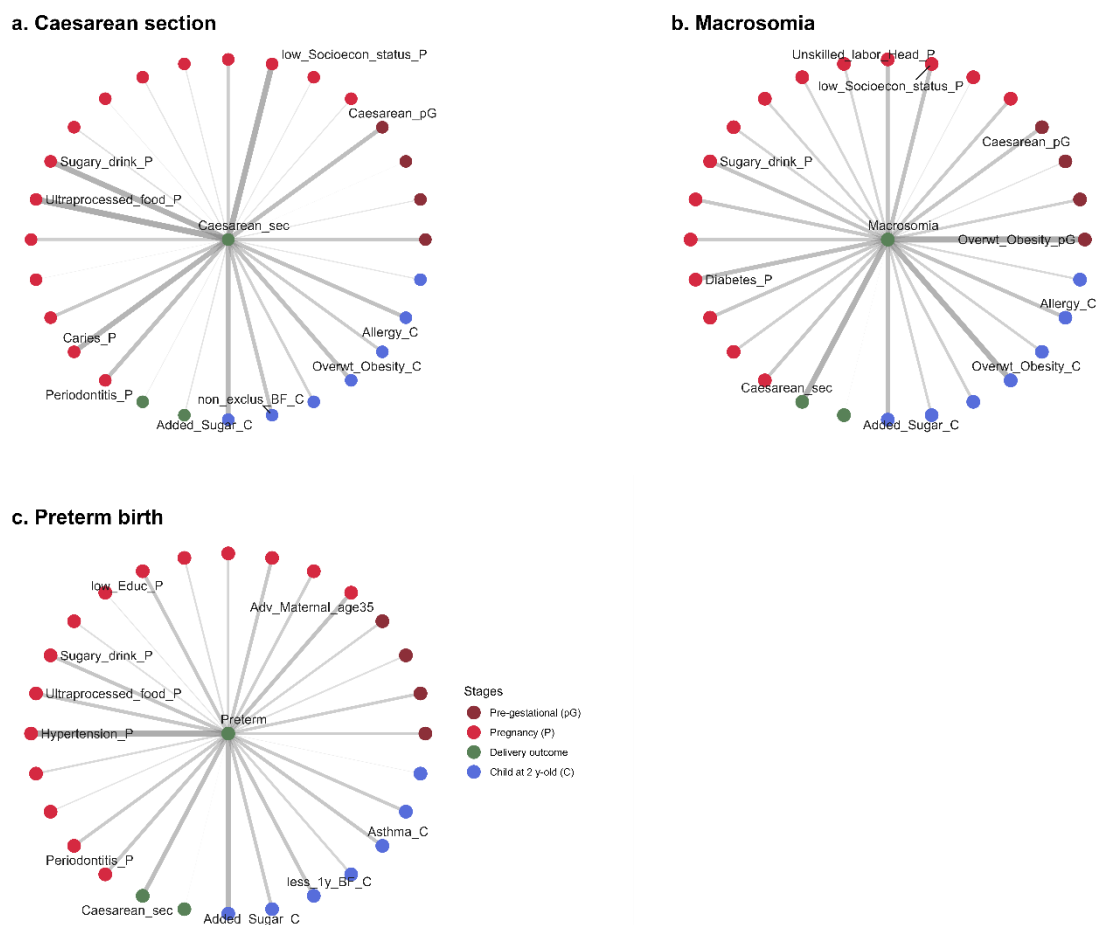
Footnote: The edges represent the co-occurrences between any two conditions, with thicker edges indicating the Jaccard index. The size of each node reflects its degree, meaning the sum of the weights of its connections with other nodes. Larger nodes indicate greater centrality in terms of degree.

Figure 3. Complex networks node-specific measurements of non-communicable diseases and risk factors. BRISA São Luís (N = 1,383).



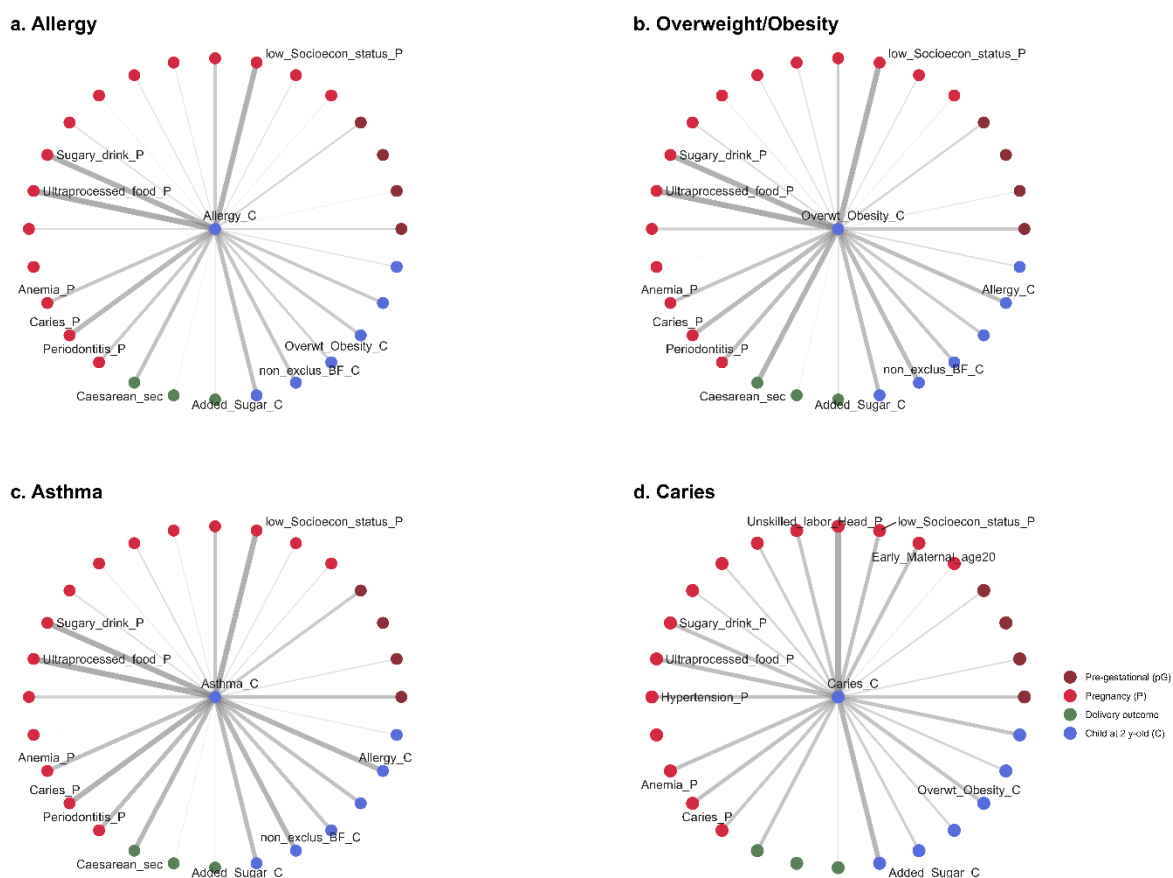
Footnote: The size of each node reflects its degree, meaning the sum of the weights of its connections with other nodes. Eigenvector measures a node's influence by considering the importance of the nodes to which it is connected. Closeness centrality quantifies how efficiently a node can access all other nodes in the network through the shortest paths. The detailed values of each measurement are provided in Supplemental Table S2.

Figure 4. Strength of edges linking nodes neighboring the adverse birth outcome. BRISA São Luís (N = 1,383).



Footnote: Network visualization showing the strength of connections to child-related factors. Each node represents a risk factor or health condition, and edge thickness indicates connection weight based on the Jaccard similarity index.

Figure 5. Strength of edges linking nodes neighboring the NCDs in childhood. BRISA São Luís (N = 1,383).



Footnote: Network visualization showing the strength of connections to child-related factors. Each node represents a risk factor or health condition, and edge thickness indicates connection weight based on the Jaccard similarity index.

5.5.1 Material Suplementar do Capítulo 5

Title: Decoding the Complexity of Health-Related Factors Connections around the First Thousand Days of Life: Network Analysis

Authors: Silas Alves-Costa, Francisco Aparecido Rodrigues, Luiza Lober de Souza Piva, Fábio Renato M. Leite, Rosângela Fernandes Lucena Batista, Erika Bárbara Abreu Fonseca Thomaz, Claudia Maria Coelho Alves, Alexandre Archanjo Ferraro, Bruno Feres de Souza, Cecilia Claudia Costa Ribeiro

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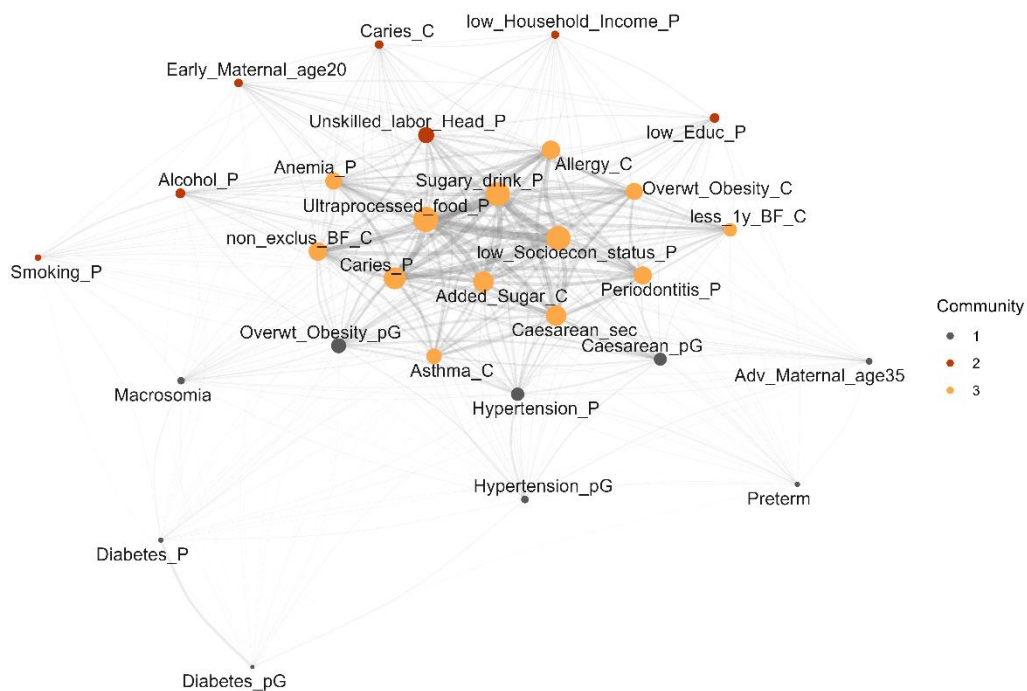
Table S1. Population characteristics. BRISA São Luís (N = 1,383).

	Absence (n, %)	Presence (n, %)	Missing (n, %)
Pre-gestational period (pG)			
Overweight/obesity	779 (56.33)	268 (19.38)	336 (24.30)
Hypertension	1293 (93.49)	84 (6.07)	6 (0.43)
Diabetes	1365 (98.70)	14 (1.01)	4 (0.29)
Caesarean	1111 (80.33)	270 (19.52)	2 (0.14)
Pregnancy (P)			
Advanced maternal age	1285 (92.91)	95 (6.87)	3 (0.22)
Early maternal age	1211 (87.56)	169 (12.22)	3 (0.22)
Low socioeconomic class	169 (12.22)	915 (66.16)	299 (21.62)
Unskilled labor of the head	767 (55.46)	308 (22.27)	308 (22.27)
Low household income	1218 (88.07)	122 (8.82)	43 (3.11)
Low educational level	1004 (72.60)	131 (9.47)	248 (17.93)
Smoking	1321 (95.52)	59 (4.27)	3 (0.22)
Alcohol use	1199 (86.70)	181 (13.09)	3 (0.22)
Sugary drink weekly	192 (13.88)	1181 (85.39)	10 (0.72)
Ultra-processed foods weekly	101 (7.30)	1278 (92.41)	4 (0.29)
Hypertension	1101 (79.61)	277 (20.03)	5 (0.36)
Diabetes	1342 (97.04)	37 (2.68)	4 (0.29)
Anemia	868 (62.76)	508 (36.73)	7 (0.51)
Caries	253 (18.29)	532 (38.47)	598 (43.24)
Periodontitis	433 (31.31)	352 (25.45)	598 (43.24)
Delivery outcome			
Caesarean section	566 (40.93)	570 (41.21)	247 (17.86)
Preterm birth	1077 (77.87)	59 (4.27)	247 (17.86)
Macrosomia	1054 (76.21)	72 (5.21)	257 (18.58)
Child at 2 years old			
Early exposure to added sugars	330 (23.86)	401 (28.99)	652 (47.14)
Non-exclusive breastfeeding up to 6mo	614 (44.40)	501 (36.23)	268 (19.38)
Less than 1y of breastfeeding	828 (59.87)	259 (18.73)	296 (21.40)
Overweight/obesity	711 (51.41)	416 (30.08)	256 (18.51)
Asthma	787 (56.91)	342 (24.73)	254 (18.37)
Allergy	428 (30.95)	388 (28.05)	567 (41.00)
Caries	781 (56.47)	77 (5.57)	525 (37.96)

Table S2. Complex networks node-specific measurements of non-communicable diseases and risk factors. BRISA São Luís (N = 1,383).

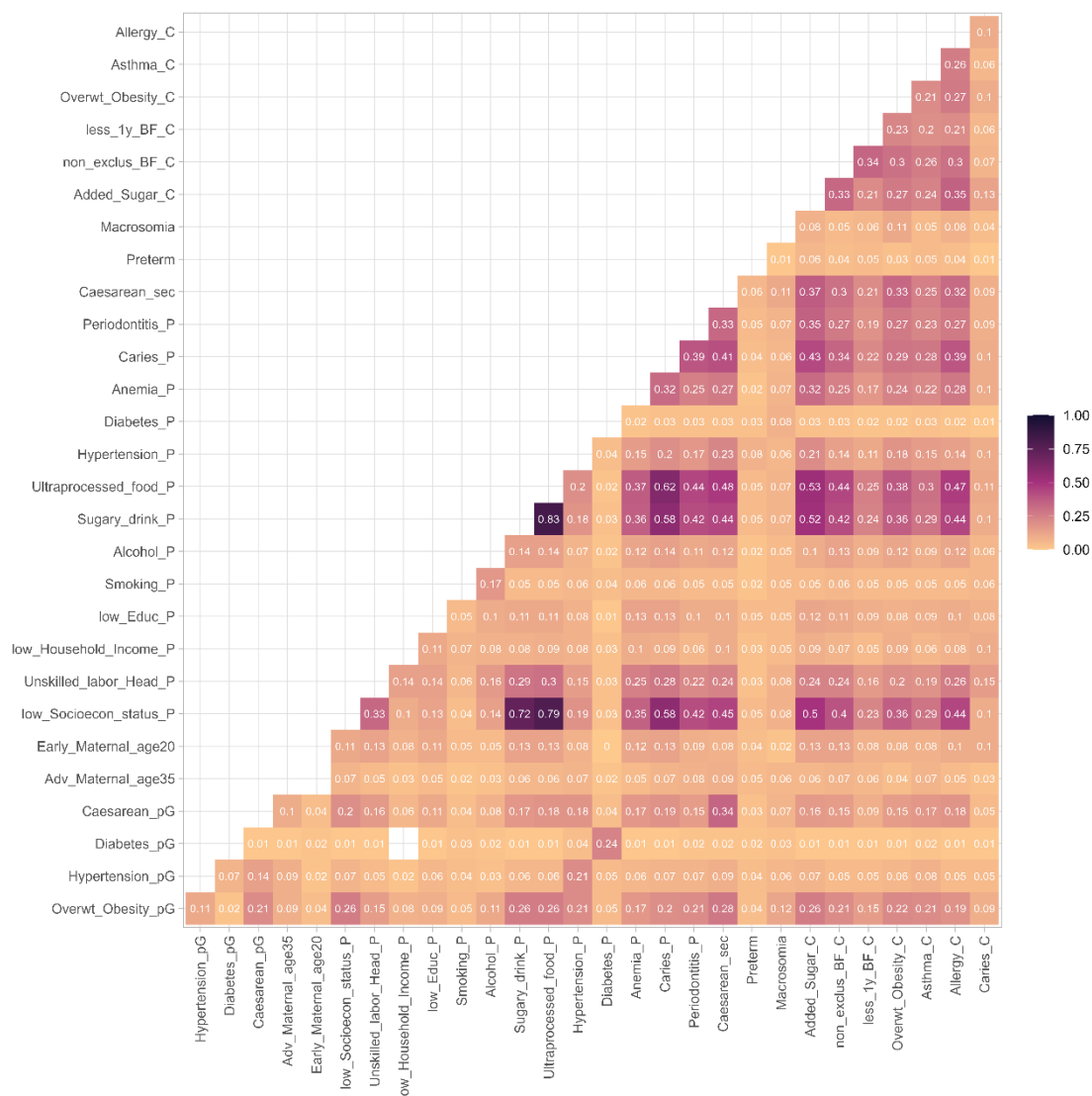
	Degree	Eigenvector	Betweenness	Closeness
Pre-gestational (pG)				
Overweight/obesity	4.34	0.51	13.00	0.12
Hypertension	1.86	0.18	25.00	0.08
Diabetes	0.71	0.04	2.00	0.04
Caesarean	3.63	0.42	3.00	0.11
Pregnancy (P)				
Advanced maternal age (<35 y-old)	1.53	0.16	0.00	0.06
Early maternal age (>20 y-old)	2.14	0.25	0.00	0.08
Low socioeconomic status	7.45	0.96	4.00	0.14
Unskilled labor of the head	4.69	0.56	12.00	0.12
Low household income	2.02	0.21	0.00	0.07
Low educational level	2.51	0.27	0.00	0.08
Smoking	1.45	0.14	0.00	0.06
Alcohol use	2.61	0.29	19.00	0.08
Sugary drink weekly	7.41	0.96	0.00	0.14
Ultra-processed foods weekly	7.74	1.00	19.00	0.14
Hypertension	3.75	0.41	52.00	0.11
Diabetes	1.04	0.08	2.00	0.04
Anemia	5.01	0.62	0.00	0.12
Caries	6.66	0.85	2.00	0.14
Periodontitis	5.41	0.69	0.00	0.12
Delivery outcome				
Caesarean section	6.18	0.76	47.00	0.14
Preterm birth	1.08	0.11	0.00	0.05
Macrosomia	1.78	0.18	13.00	0.07
Child at 2 years old				
Early exposure to added sugars	6.22	0.79	13.00	0.13
Non-exclusive breastfeeding up to 6mo	5.53	0.69	3.00	0.12
Less than 1y of breastfeeding	3.86	0.47	0.00	0.10
Overweight/obesity	5.04	0.63	3.00	0.12
Asthma	4.48	0.55	0.00	0.11
Allergy	5.58	0.71	0.00	0.12
Caries	2.17	0.24	0.00	0.08

Figure S1. Network community detection of non-communicable diseases in the first 1000 days of life. BRISA São Luís (N = 1,383).



Footnote: Network visualization displaying the communities detected using the Louvain algorithm. Nodes represent risk factors or health conditions, and edges represent their weighted connections based on the Jaccard similarity index. Colors indicate the distinct communities identified, where nodes within the same community are more densely connected.

Figure S2. Matrix of adjacency between conditions based on the Jaccard index. BRISA São Luís (N = 1,383).



Footnote: The values correspond to the Jaccard index between two conditions, representing the thickness of the edges in the networks. The darker the index, the greater the similarity.

5.6 Capítulo 6 - Carga global, regional e nacional do consumo elevado de bebidas ricas em açúcares de adição, 1990-2021, com projeções até 2050: uma análise sistemática para o *Global Burden of Disease Study 2021*

“Global, regional, and national burden of high sugar-sweetened beverages consumption, 1990-2021, with projections up to 2050: a systematic analysis for the Global Burden of Disease Study 2021”

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Journal Impact Factor: 6.9 (2024)

Original Research Article

Global, regional, and national burden of high sugar-sweetened beverages consumption, 1990–2021, with projections up to 2050: a systematic analysis for the Global Burden of Disease Study 2021

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ABSTRACT

Background: Sugar-sweetened beverages (SSBs) have emerged as a critical driver of noncommunicable diseases (NCDs), such as obesity, diabetes, cardiovascular, and kidney diseases.

Objectives: To provide a comprehensive analysis of the global, regional, and national burden of high SSB consumption between 1990 and 2021, with projections up to 2050, and to estimate the burden of NCDs attributed to SSBs.

Methods: This study analyzed data from the Global Burden of Disease Study 2021. A diet high in SSBs was defined as any beverage containing ≥ 50 kcal/226.8 g serving, including carbonated beverages, sodas, energy drinks, and fruit drinks, but excluding 100% fruit and vegetable juices. The summary exposure value (SEV) represents the population-level risk exposure to this excessive consumption. The burden of SSB consumption attributed to NCDs, as well as specifically cardiovascular disease, diabetes, and kidney disease, was assessed through death rates (per 100,000 people), years lived with disability, years of life lost, and disability-adjusted life years. Analyses included total and annual percentage changes. Future SEV forecasts were generated using ensemble models considering the sociodemographic index.

Results: In 2021, the global SEV of high SSB consumption was 30.56% (95% uncertainty intervals: 22.83, 41.22), with the highest rates in high-income and Latin America and Caribbean super-regions. SSB consumption increased with the sociodemographic index. The global age-standardized rate (per 100,000 people) of deaths from NCDs attributable to SSB consumption was 0.89 (0.40, 1.38), and the disability-adjusted life year was 41.39 (19.52, 63.92) in 2021. Projection indicates a 9.54% (9.08%, 10.00%) increase in global SSB consumption by 2050, with the highest rise expected in the South Asia super-region.

Conclusions: SSB consumption has increased since 1990 and is projected to rise further by 2050, contributing substantially to the global NCD burden. These trends underscore the urgent need for targeted public health interventions aimed at reducing SSB consumption worldwide.

Keywords: sugar-sweetened beverages, noncommunicable diseases, public health, global burden of disease, forecasts, cardiovascular diseases, diabetes

Introduction

The rising prevalence of sugar-sweetened beverage (SSB) consumption has become a major public health challenge worldwide [1]. Sweetened with mono- or disaccharides such as sucrose, high-fructose corn syrup, and fruit juice concentrates, these beverages have been linked to greater risks of obesity, type 2 diabetes, cardiovascular,

kidney, and oral diseases [1–3]. Consequently, SSBs contribute to premature mortality, impacting healthcare systems globally [4,5]. Moreover, the consumption of SSBs worsens health disparities, particularly impacting vulnerable segments of society across countries [6].

The economic costs associated with SSB consumption are staggering. In the United States, obesity-related noncommunicable diseases (NCDs) cost an estimated \$209.7 billion annually [7], whereas in

Abbreviations: DALY, disability-adjusted life year; GBD, Global Burden of Disease; NCD, noncommunicable diseases; SDI, sociodemographic index; SEV, summary exposure value; SSB, sugar-sweetened beverage; YLD, years lived with disability; YLL, years of life lost.

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the European Union, NCDs account for $\geq 25\%$ of healthcare spending [8]. Over 100 countries have adopted policy measures, including taxation and public health messaging, to reduce SSB consumption [9]. A proposed national tax of United States dollars 0.01/oz on SSBs in the United States could potentially save United States dollars 45 billion in lifetime healthcare costs by lowering medical expenses associated with NCDs, emphasizing the importance of targeting SSB consumption as part of public policy [10].

Accurately measuring the impact of SSB consumption is essential for shaping effective health policies, especially amid shifting global dietary patterns and regional disparities in intake. In low- and middle-income countries, rapid population growth is occurring alongside a rise in the double burden of malnutrition, where underweight and obesity coexist, placing increasing strain on health systems [11]. Understanding current SSB consumption and projecting future trends is therefore critical for anticipating the attributed burden and designing context-specific interventions that mitigate its health and economic impacts.

In light of these challenges, our study aims to comprehensively analyze the global, regional, and national burden of high SSB consumption from 1990 to 2021, with projections extending to 2050. Using the most recent estimates from the Global Burden of Disease (GBD) study 2021, this study assesses excessive SSB consumption over the past three decades, forecasts future trends, and estimates the burden of NCDs attributable to SSB consumption. These results have the potential to aid decision-makers in developing targeted interventions to mitigate the burden of disease due to SSB.

Methods

Data source

This study utilized estimates from the GBD 2021 study, coordinated by the Institute for Health Metrics and Evaluation at the University of Washington. GBD is a comprehensive, publicly available database that provides estimates for 369 diseases and injuries, as well as 88 risk factors across 204 countries and 811 subnational locations from 1990 to 2021. The GBD project compiles data through systematic reviews, targeted searches, and contributions from country collaborators and the WHO. As GBD generates complete country-year estimates by incorporating covariates and regional data to address missing inputs, our dataset contained no missing values, and no additional imputation was necessary. Further methodological details are available in the GBD capstone manuscript [12].

The risk factor analysis draws on data from >54,000 unique sources to produce epidemiological estimates based on 631 risk-outcome pairs, using a data-driven framework that enables age-, sex-, location-, and year-specific modeling at global, regional, and national levels [13]. In the case of high SSB consumption, the burden is modeled through 2 primary risk-outcome pairs: cardiovascular disease and diabetes mellitus combined with chronic kidney disease. This manuscript follows the guidelines for accurate and transparent health estimates reporting statement [14].

Diet high in SSBs

According to GBD, a diet high in SSBs is defined as any intake (in grams per day) of beverages with ≥ 50 kcal/226.8 g (8 oz) serving, including carbonated beverages, sodas, energy drinks, and fruit drinks, but excluding 100% fruit and vegetable juices [13]. The GBD study compiles and harmonizes dietary data from a wide range of existing

sources. These sources employ diverse dietary assessment tools, most commonly 24-h dietary recalls and food frequency questionnaires, which are adjusted and crosswalked using the meta-regression Bayesian regularized trimmed framework to ensure comparability across settings and instruments. Supplemental Figure 1 provides details on the data inputs, processing methods, and modeling techniques used as outlined in the main GBD manuscript [13].

Data presentation

The summary exposure value (SEV) represents the population-level risk exposure to a particular health risk, in this case, a diet high in SSBs. SEV is expressed on a scale from 0 to 100, where 100 indicates that the entire population is at the maximum possible risk of disease due to high SSB consumption, and 0 indicates minimal or no risk. SEVs for a diet high in SSBs from 1990 to 2021 were analyzed globally, for 204 countries, and across the 7 GBD super-regions: Central Europe, Eastern Europe, and Central Asia; High-income; Latin America and Caribbean; North Africa and Middle East; South Asia; Southeast Asia, East Asia, and Oceania; and Sub-Saharan Africa. In the GBD framework, super-regions are broad groupings of countries that share similar epidemiological profiles and levels of socioeconomic development. Each super-region comprises multiple regions (21 in total), which represent smaller and more culturally or geographically cohesive clusters. The analysis includes age-standardized SEV estimates and estimates stratified by 5-y age groups, ranging from 25 to 95 y or older [13].

To further contextualize these findings, estimates of high SSB were reported by the sociodemographic index (SDI). SDI is a composite measure that combines lag-adjusted income per capita, mean years of education, and total fertility rates for individuals under 25 y of age. SDI values range from 0 to 1, with higher values reflecting higher levels of development [12]. To explore the relationship between high SSB consumption and SDI, we used Locally Weighted Scatterplot Smoothing regression [15] at the country level to provide insights into how socioeconomic factors influence SSB consumption patterns and their associated health risks.

Burden of NCD attributed to SSBs in 2021

The GBD study also provides estimates of the disease burden attributed to the consumption of SSBs for NCD. These estimates encompass the impact on all NCDs aggregated (level 1), as well as separately for specific conditions (level 2), such as cardiovascular diseases, diabetes, and kidney diseases. The measures quantify the rate per 100,000 population for various health metrics, including deaths, years lived with disability (YLD), years of life lost (YLL), and disability-adjusted life years (DALY) directly attributable to SSB consumption. Detailed methods for these estimates are available elsewhere [13].

Forecasting the SEV of a diet high in SSB to 2050

Forecasting the SEV of a diet high in SSB ≤ 2050 was provided by GBD. The detailed methods are described elsewhere [16]. Briefly, the forecasts were generated using an ensemble modeling framework that combined 6 annualized rate-of-change models with 6 meta-regression Bayesian regularized trimmed spline models, each driven by the SDI. Within each model family, different recency-weighting schemes were applied, ranging from equal weighting of all past years to exponential weighting of the most recent data points. This structure allowed the models to capture both long-term historical trends and recent shifts in exposure. Forecasts

were generated independently for each location-sex-age-year combination. The final SEV estimates represent the mean values across 500 posterior draws, with 95% uncertainty intervals (UIs) computed accordingly.

Following the GBD risk factors hierarchy, SSB was classified as a level 3 risk, alongside 41 other disaggregated single risks, such as unsafe water source, a diet low in milk, and high LDL cholesterol levels [13]. Level 3 risk indicates a substantial impact on public health, suggesting that SSBs contribute significantly to morbidity and mortality on a population scale. Based on the SEV in 1990, 2021, and 2050, all level 3 risks were ranked.

To describe temporal variations in SSB consumption, we calculated both total percent change and annual percent change for two time periods: 1990–2021 and 2021–2050. Total percent change estimates were derived by comparing prevalence values at the beginning and end of each period, accounting for UIs and SEs to construct 95% confidence intervals for the percentage change. For annual percent change, Prais–Winsten regressions were applied to each country-specific time series, using calendar year as a continuous predictor and log-transformed SSB values as the outcome, which allowed estimation of smoothed annual variation while correcting for autocorrelated residuals. Results were classified based on the direction and statistical significance of the trend. All analyses and visualizations were performed using R (v4.2.1) and RStudio (v2024.04.2+76).

Ethics statement

The GBD protocol was approved by the institutional review board of the University of Washington, and all data collection procedures adhered to institutional guidelines and relevant regulatory standards. As no primary data were collected and no individual-level identifiers were used, additional ethical approval was not required for this secondary data analysis.

TABLE 1

Global and super-region burden of high sugar-sweetened beverages consumption from 1990 to 2021, with projections to 2050 in terms of summary exposure value.

Location	SEV 1990	1990–2021 APC (%)	1990–2021 TPC (%)	SEV 2021	2021–2050 APC (%)	2021–2050 TPC (%)	SEV 2050
Global	29.97 (22.97, 42.54)	0.14 (–0.07, 0.36)	1.96 (1.51, 2.40)	30.56 (22.83, 41.22)	0.75 (0.73, 0.78)	9.54 (9.08, 10.00)	33.56 (25.31, 46.35)
Central Europe, Eastern Europe, and Central Asia	28.09 (19.70, 40.97)	1.40 (0.97, 1.84)	20.64 (20.12, 21.17)	33.88 (24.95, 45.31)	1.04 (0.99, 1.09)	13.40 (12.96, 13.84)	38.65 (28.53, 50.54)
High-income	40.75 (30.21, 53.43)	2.01 (1.70, 2.31)	30.68 (30.29, 31.07)	53.26 (42.47, 64.36)	0.97 (0.94, 1.01)	12.49 (12.20, 12.78)	60.19 (49.15, 71.23)
Latin America and the Caribbean	35.30 (26.48, 48.55)	1.61 (1.46, 1.76)	24.00 (23.55, 24.45)	43.78 (33.34, 56.20)	1.22 (1.20, 1.24)	15.86 (15.49, 16.24)	50.96 (39.99, 63.54)
North Africa and the Middle East	24.41 (16.89, 37.00)	1.86 (1.74, 1.99)	28.17 (27.57, 28.76)	31.29 (22.43, 43.34)	0.97 (0.91, 1.02)	12.43 (11.92, 12.94)	35.39 (25.43, 49.45)
South Asia	18.05 (12.28, 29.07)	1.02 (0.52, 1.53)	14.69 (14.03, 15.36)	20.70 (13.63, 30.94)	2.10 (2.08, 2.12)	28.77 (28.09, 29.45)	26.90 (17.74, 40.12)
Southeast Asia, East Asia, and Oceania	31.16 (21.43, 50.74)	–1.60 (–2.14, –1.06)	–19.55 (–20.13, –18.98)	25.07 (17.49, 38.27)	0.78 (0.70, 0.86)	9.92 (9.30, 10.54)	27.58 (18.96, 42.08)
Sub-Saharan Africa	30.53 (22.42, 46.07)	–1.34 (–1.80, –0.87)	–16.58 (–17.10, –16.07)	25.46 (18.28, 39.18)	–0.15 (–0.18, –0.11)	–1.77 (–2.35, –1.19)	24.98 (17.60, 38.65)

SEV values for 1990, 2021, and 2050 represent aggregate estimates provided by the GBD 2021 for each super-region. APC (%): estimated using Prais–Winsten regression, reflects the mean yearly change in SEV. TPC (%): calculated as the relative difference between 2 time points. Changes were interpreted as increasing or decreasing when the confidence interval did not include 0; otherwise, the trend was considered stable. All analyses were based on GBD-modeled aggregate data; therefore, no individual-level sample size applies.

Abbreviations: APC, annual percent change; GBD, global burden of disease; SEV, summary exposure value; TPC, total percent change.

Results

SSB consumption in 2021

In 2021, the global SEV of high SSB consumption was 30.56%; 95% UI: 22.83%, 41.22% (Table 1 and Figure 1). The age-standardized SEV varied across super-regions, with the highest rate observed in high-income countries at 53.26% (42.47%, 64.36%), followed by Latin America and the Caribbean at 43.78% (33.34%, 56.20%), whereas the South Asia super-region had the lowest rate at 20.70% (13.63%, 30.94%) (Table 1). At the country level, Monaco, Argentina, and Ireland showed the highest SEV rates, at 87.85% (78.77%, 95.63%), 73.89% (59.84%, 84.33%), and 68.94% (54.07%, 81.55%), respectively; whereas Vietnam, Morocco, and Ukraine had the lowest rates, at 16.21% (9.98%, 28.24%), 16.72% (8.87%, 27.77%), and 16.86% (10.27%, 28.34%), respectively (Supplemental Table 1). In 29 countries (14.21% of all countries analyzed), the SEV exceeded 50%, with most of these countries belonging to the high-income super-region. Of note, Mexico in the Latin America and Caribbean super-region and Guam in the Southeast Asia, East Asia, and Oceania super-region also exceeded the threshold (Supplemental Table 1). Moreover, a positive association between SSBs and SDI was seen, indicating that the higher the socioeconomic level of the country, the higher the consumption of SSBs (Figure 2).

Older adults (60–95 y) had higher exposure to SSBs compared to middle-aged (45–59 y) and younger adults (25–44 y), irrespective of the super-region (Figure 3). There were no significant differences in exposure to SSB regarding sex. (Supplemental Figure 2).

Burden of NCDs attributed to high SSBs in 2021

In 2021, the global age-standardized death rate for NCDs attributed to high SSB consumption was 0.89 (0.40, 1.38) per 100,000 people, the YLD rate 21.49 (10.48, 35.37), the YLL rate

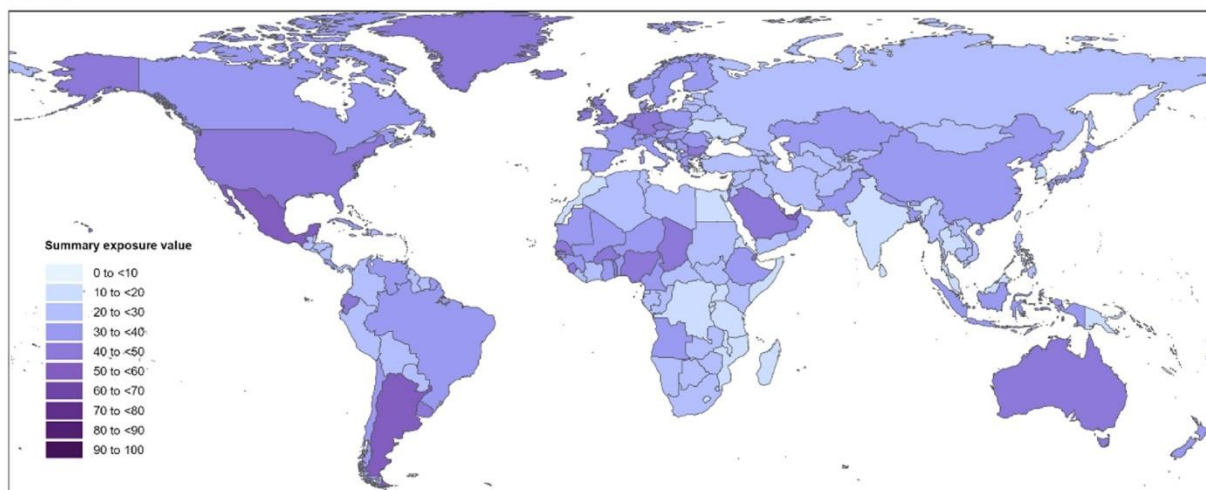
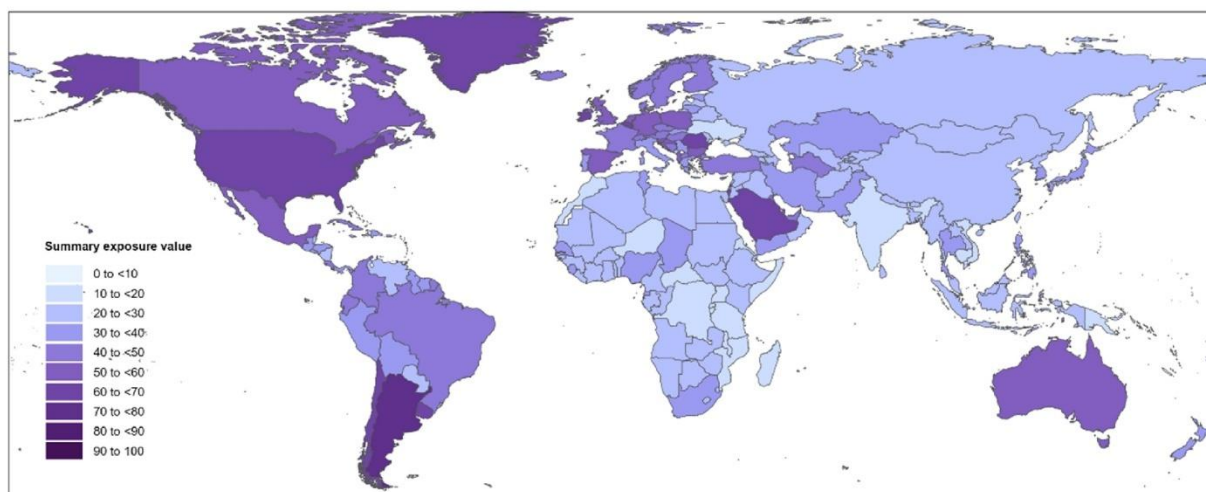
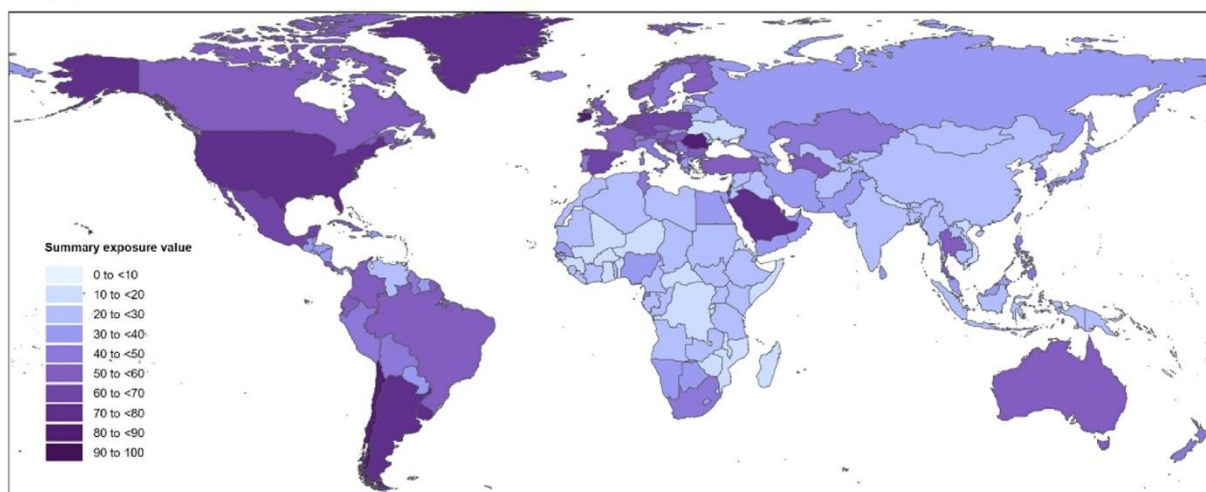
A. 1990**B. 2021****C. 2050**

FIGURE 1. Age-standardized burden of high sugar-sweetened beverages (SSB) from 1990 to 2050. Maps represent the Summary Exposure Value (SEV) for high sugar-sweetened beverage (SSB) consumption by country in 1990, 2021, and 2050. Data were obtained from the Global Burden of Disease (GBD) 2021 study, which provides modeled estimates of population-level exposure to risk factors using standardized methods across countries and years. Values for 1990 (A) and 2021 (B) reflect historical modeled estimates. Projections for 2050 (C) were generated using an ensemble forecasting framework that combines multiple rate-of-change and spline-based models, weighted by the Socio-demographic Index (SDI), to capture both historical trends and recent shifts.

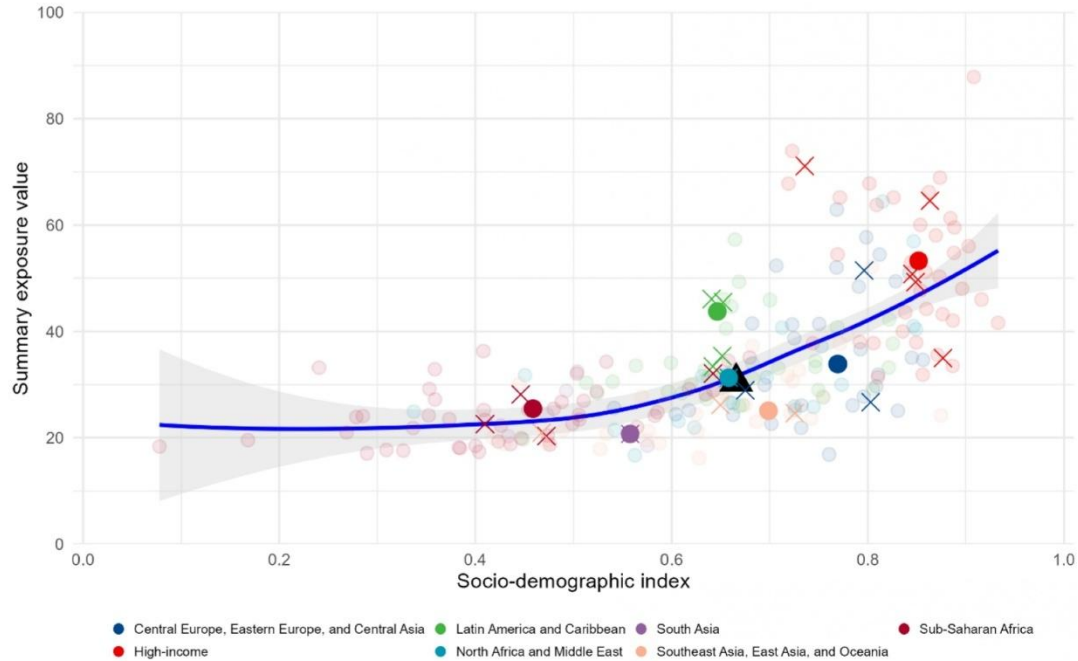


FIGURE 2. Association between the socio-demographic index and summary exposure value of high sugar-sweetened beverage consumption by country in 2021. GBD: Global Burden of Disease. The black triangle represents the global estimate. Each color corresponds to one of the seven GBD super-regions, with filled circles indicating these super-regions. The smaller, lighter-colored circles represent individual countries, while the × symbol denotes GBD regions. The blue line illustrates the Locally Weighted Scatterplot Smoothing estimate of the age-standardized summary exposure value based on the socio-demographic index across all countries, with the gray shading around it showing the 95% confidence interval. All data were obtained from the GBD 2021 study.

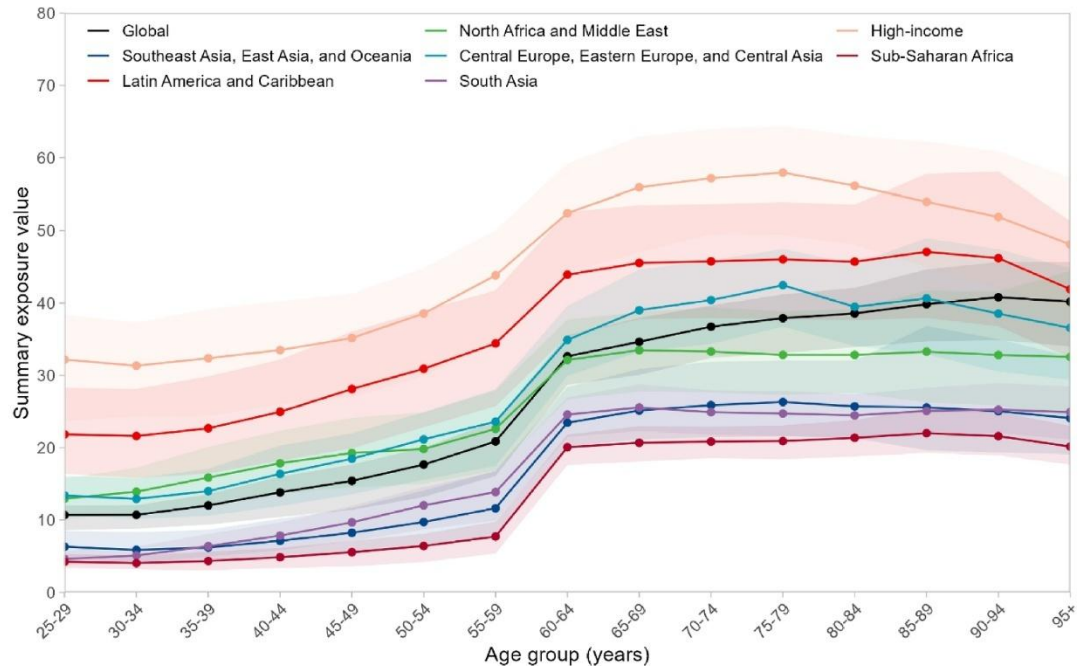


FIGURE 3. Burden of high sugar-sweetened beverages by age and GBD super-region in 2021. GBD: Global Burden of Disease; SEV: Summary Exposure Value. Figure shows age-specific SEV estimates for high sugar-sweetened beverage (SSB) consumption across GBD super-regions in 2021. Estimates were obtained from the GBD 2021 study, which models population-level exposure using standardized methods across age, location, and year.

19.89 (8.63, 30.75), and the DALY rate 41.39 (19.52, 63.92) (Table 2). The Latin America and Caribbean super-region had the highest death and DALY rates, at 2.43 (1.19, 3.66) and 101.40 (48.36, 151.21), respectively. In contrast, the Southeast Asia, East Asia, and Oceania super-region had the lowest rates, with 0.43

(0.18, 0.66) deaths and 20.24 (9.31, 32.27) DALYs per 100,000 people (Table 2).

Regarding cardiovascular diseases attributable to a diet high in SSBs, the global age-standardized death rate was 0.17 (0.02, 0.31), and the DALY was 41.39 (19.52, 63.92). Central Europe, Eastern Europe,

TABLE 2
Global and super-region burden of noncommunicable diseases attributed to a diet high in sugar-sweetened beverages in 2021.

Location	Deaths (per 100,000)		YLDs (per 100,000)		YLLs (per 100,000)		DALYs (per 100,000)	
	NCD	Cardiovascular diseases	Diabetes and kidney diseases	NCD	Cardiovascular diseases	Diabetes and kidney diseases	NCD	Cardiovascular diseases
Global	0.89 (0.40, 1.38)	0.17 (0.02, 0.31)	0.72 (0.37, 1.06)	21.49 (10.48, 35.37)	0.44 (0.17, 0.76)	21.05 (10.31, 34.63)	19.89 (8.63, 30.75)	3.71 (0.18, 7.08)
Central Europe, Eastern Europe, and Central Asia	0.98 (0.39, 1.55)	0.38 (0.07, 0.68)	0.60 (0.31, 0.88)	21.49 (10.10, 34.93)	0.65 (0.25, 1.11)	20.84 (9.85, 33.91)	20.51 (7.69, 32.77)	7.53 (0.90, 14.03)
High-income	0.94 (0.42, 1.44)	0.17 (0.02, 0.32)	0.77 (0.40, 1.12)	43.36 (21.12, 70.78)	0.89 (0.36, 1.52)	42.47 (20.73, 69.34)	20.85 (8.88, 32.01)	3.95 (-0.01, 7.87)
Latin America and Caribbean	2.43 (1.19, 3.66)	0.20 (0.02, 0.37)	2.24 (1.17, 3.30)	42.24 (20.44, 67.89)	0.35 (0.10, 0.64)	41.89 (20.35, 67.37)	59.16 (29.00, 88.09)	4.88 (-0.12, 9.59)
North Africa and Middle East	1.37 (0.58, 2.16)	0.28 (0.03, 0.54)	1.09 (0.55, 1.64)	29.80 (13.93, 49.74)	0.47 (0.16, 0.82)	29.33 (13.77, 49.09)	30.94 (11.87, 49.23)	6.80 (0.20, 13.62)
South Asia	0.76 (0.32, 1.17)	0.13 (0.00, 0.25)	0.63 (0.32, 0.94)	11.60 (5.54, 19.03)	0.16 (0.05, 0.29)	11.44 (5.46, 18.75)	17.57 (6.94, 27.41)	3.37 (-0.22, 6.87)
Southeast Asia, East Asia, and Oceania	0.43 (0.18, 0.66)	0.11 (0.02, 0.21)	0.31 (0.15, 0.47)	10.61 (5.30, 17.75)	0.32 (0.13, 0.55)	10.29 (5.17, 17.28)	9.63 (3.96, 14.98)	2.37 (0.29, 4.50)
Sub-Saharan Africa	0.92 (0.45, 1.37)	0.07 (0.01, 0.13)	0.85 (0.44, 1.24)	7.41 (3.50, 12.24)	0.14 (0.05, 0.25)	7.27 (3.44, 11.97)	20.42 (9.93, 30.54)	1.55 (0.11, 2.96)

Burden estimates are based on aggregate data provided by the GBD 2021 study, which models outcomes at the population level. The attribution of disease burden to sugar-sweetened beverage (SSB) consumption follows a comparative risk assessment framework, linking SSB intake to health outcomes through established risk-outcome pairs. These estimates incorporate exposure data, relative risks from the literature, and theoretical minimum risk levels to quantify the proportion of disease burden attributable to high SSB consumption.

Abbreviations: DALY, disability-adjusted life years; GBD, global burden of disease; NCD, noncommunicable disease; YLD, years lived with disability; YLL, years of life lost.

and Central Asia had the highest death rate at 0.38 (0.07, 0.68) and the highest DALY rate at 8.19 (1.14, 15.09). Sub-Saharan Africa reported the lowest death and DALY rates, of 0.02 (0.45, 1.37) and 1.69 (0.16, 3.19), respectively (Table 2). For diabetes and kidney disease, the global death rate was 0.72 (0.37, 1.06), and the DALY rate was 37.24 (18.74, 56.15). The Latin America and Caribbean super-region again had the highest death (2.24; 95% UI: 1.17, 3.30) and DALY (96.17; 95% UI: 48.24, 142.52) rates, whereas Southeast Asia, East Asia, and Oceania showed the lowest death and DALY rates of 0.31 (0.15, 0.47) and 17.55 (8.85, 27.41), respectively (Table 2). Detailed regional and country-level information can be found in Supplemental Table 2.

Trends in SSB consumption: 1990 to 2021, and forecasts to 2050

From 1990 to 2021, global SSB exposure has risen by a total of +1.96% (1.51%, 2.40%) (Table 1 and Figure 4). The largest increases were observed in the high-income (+30.68%; 95% UI: 30.29%, 31.07%) and North Africa and Middle East (+28.17%; 95% UI: 27.57%, 28.76%) super-regions, whereas declines were noted in Southeast Asia, East Asia, and Oceania (−19.55%; 95% UI: −20.13%, −18.98%), as well as Sub-Saharan Africa (−16.58%; 95% UI: −17.1%, −16.07%) (Table 1 and Figure 4). At the national level, Romania experienced the largest increase (+107.00%; 95% UI: 106.35%, 107.66%), followed by Thailand (+95.07%; 95% UI: 94.08%, 96.07%). Only Cyprus (−9.83%; 95% UI: −10.32%, −9.35%) and Iceland (−6.64%; 95% UI: −7.13%, −6.16%) showed declines in the high-income super-region. The most significant reductions in Southeast Asia, East Asia, and Oceania were observed in Vietnam (−40.25%; 95% UI: −40.90%, −39.60%) and China (−24.99%; 95% UI: −25.58%, −24.41%) (Supplemental Table 1).

Projections from 2021 to 2050 suggest that age-standardized exposure to high SSB consumption will increase by 9.54% (9.08%, 10.00%), with an mean annual growth rate of +0.75% (0.73%, 0.78%), resulting in a SEV of 33.56% (25.31%, 46.35%) by 2050

(Table 1 and Figure 4). Only the Sub-Saharan Africa super-region is expected to experience a decline, with an estimated SEV of −1.77% (−2.35%, −1.19%). The largest increases are estimated in South Asia (+28.77%; 95% UI: 28.09%, 29.45%) and Latin America and the Caribbean (+15.86%; 95% UI: 15.49%, 16.24%), whereas the high-income super-region will remain stable, maintaining values well above other regions (Table 1 and Figure 4). At the country level, Malaysia (+47.31%; 95% UI: 46.45%, 48.18%), Thailand (+46.35%; 95% UI: 45.73%, 46.96%), and India (+40.98%; 95% UI: 40.16%, 41.80%) are projected to experience the greatest increases, whereas Burkina Faso (−24.07%; 95% UI: −24.82%, −23.33%), Niger (−22.95%; 95% UI: −23.74%, −22.16%), and Guinea (−22.16%; 95% UI: −22.90%, −21.41%) will experience the largest declines (Supplemental Table 1). By 2050, a diet high in SSBs is expected to become the sixteenth most significant level 3 risk, rising 6 positions in the global ranking compared to 1990 (Figure 5).

Discussion

The findings highlight that the rising consumption of SSBs poses a serious global health challenge, with a notable increase over the past three decades. By 2021, over 30% of the global population was exposed to excessive SSB intake, with higher rates observed in regions with greater socioeconomic development, including high-income super-regions, especially among older adults. This elevated exposure contributes significantly to the burden of NCDs, as reflected in rates of deaths, YLDs, YLLs, and DALYs. Projections indicate that by 2050, SSB consumption will continue increasing, emerging as one of the most impactful level-3 risk factors for NCDs.

Our findings align with previous literature [17], showing that high-income countries are the most exposed to SSBs due to the convergence of socioeconomic factors, a lack of stringent regulatory approaches, and aggressive marketing strategies [18,19]. A positive association was observed between SSB exposure and the SDI, which

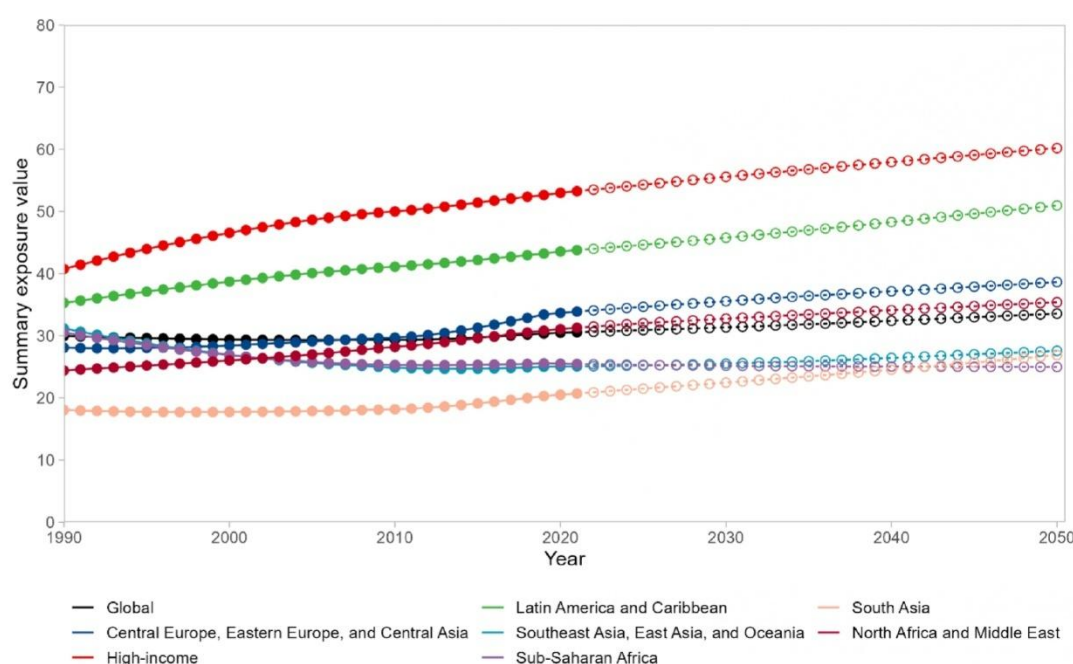


FIGURE 4. Burden of high sugar-sweetened beverages by GBD super-region from 1990 to 2050. GBD: Global Burden of Disease; SEV: Summary Exposure Value. Figure shows age-standardized annual SEV estimates for high sugar-sweetened beverage (SSB) consumption in each GBD super-region from 1990 to 2050. Solid lines represent historical estimates (1990–2021), and dotted lines represent projections (2021–2050), all obtained from the GBD 2021 study.

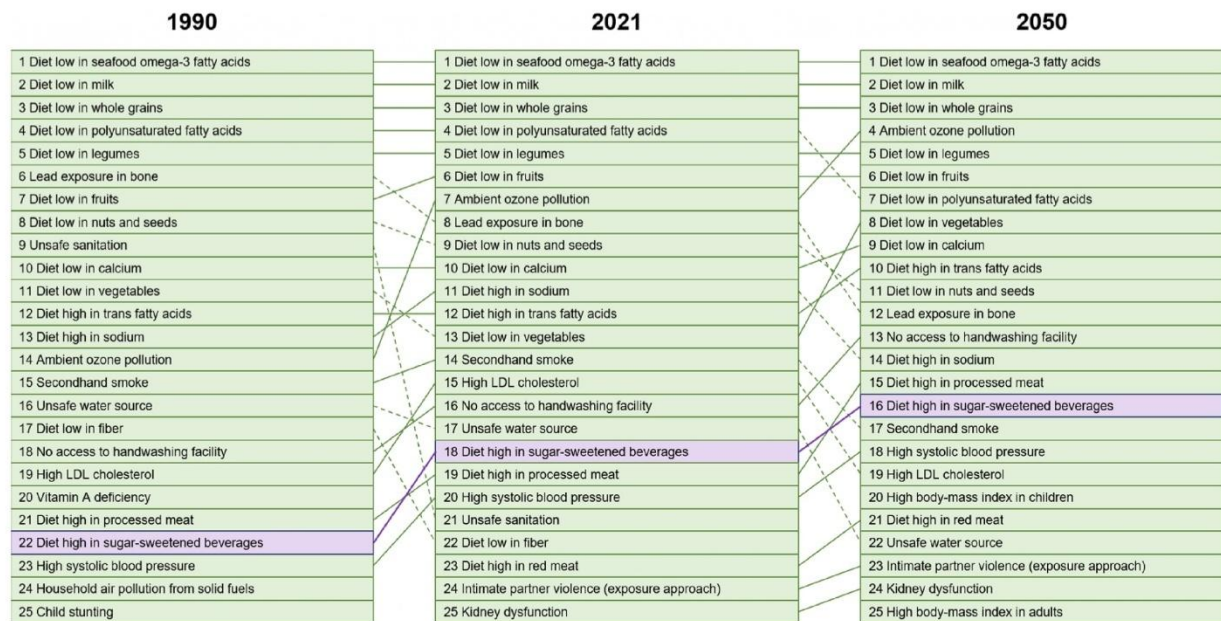


FIGURE 5. Ranking of the burden of Level 3 risks in terms of summary exposure value worldwide from 1990 to 2050. GBD: Global Burden of Disease; SEV: Summary Exposure Value. Figure shows the global ranking of Level 3 risk factors based on SEV estimates for the years 1990, 2021, and 2050. All data were obtained from the GBD 2021 study.

may further explain the widespread availability of these beverages in regions with higher SDI scores, typically characterized by greater socioeconomic development. For instance, Monaco's lack of a national fiscal policy on SSBs, potentially influenced by its tax treaty with France [20], may explain the persistently high exposure (87.85%) observed among its population. The observed relationship may also reflect differing social dynamics across countries. In high-income settings, SSB consumption is often higher among marginalized urban populations [21], whereas in many low- and middle-income countries, these beverages are still viewed as aspirational and more commonly consumed by wealthier groups [22]. This socioeconomic gradient helps explain both the higher national levels in affluent countries and the limited diffusion in lower-SDI contexts.

Another notable disparity lies in the sugar content of SSBs, which can vary considerably across countries. Beverages sold in the Middle East and other lower-income regions often contain higher sugar concentrations than those available in high-income markets. For instance, the median sugar content is ~11 g/100 mL in Saudi Arabia [23], compared to 9–10 g/100 mL in Germany and Switzerland, and even lower levels (4–7 g/100 mL) in countries such as Austria, Australia, and the United Kingdom, where reformulation policies have been implemented [24,25]. In countries like Ecuador, Vietnam, Thailand, and India, the sugar content can reach 13–14 g/100 mL in the absence of effective regulatory measures [26]. These differences in national regulatory policies may contribute to a higher disease burden in lower-income countries.

The burden attributable to high SSB consumption in the GBD is modeled through two primary risk-outcome pairs: cardiovascular disease and diabetes mellitus combined with chronic kidney disease. The association between SSB intake and these conditions is well established [1,2]. Our findings showed that the greatest share of the burden falls on diabetes mellitus combined with chronic kidney disease, both globally and across super-regions, consistent with prior research identifying SSBs as a key contributor to metabolic

dysregulation and insulin resistance [1]. However, a contradiction emerges when examining the disproportionate burden due to NCDs in low- and middle-income countries. In 2021, the global age-standardized mortality rate for NCDs attributed to SSBs was 0.89/100,000, but regions such as Central Latin America (3.58), Southern Sub-Saharan Africa (3.26), Oceania (2.18), Southern Latin America (2.08), and Tropical Latin America (1.75) had much higher rates, despite not being the primary consumers of SSBs. This disparity raises critical questions about the underlying factors contributing to this unequal burden. One reason could be that high-income countries have better access to healthcare and treatment for SSB-related comorbidities, increasing life expectancy even though the population is more exposed to SSBs [27]. Another possible explanation may lie in the marketing tactics of multinational companies, which have been accused of promoting lower-quality products with higher sugar content in countries of the Global South [28,29], potentially exacerbating the burden of NCDs among these populations. Additionally, the consumption of SSBs may indicate a broader unhealthy dietary pattern, as SSB consumers often have diets higher in added sugars and of poorer overall quality [30].

Although a higher SSB consumption would be expected among young adults and youth, our results revealed that exposure was greater among older adults and the elderly, which was corroborated by a previous study [17]. This pattern may be driven by a preference for liquid foods among individuals with chewing difficulties [31] and by the notable consumption of sweetened tea and coffee among older populations [32]. This elevated exposure is particularly concerning given the cumulative burden of NCDs typically observed in this age group.

Although high-income countries have already reached a high plateau of SSB consumption, emerging economies are expected to observe an increase by 2050. This predicted rise is likely to propel high SSB consumption into the sixteenth position in the ranking of the most frequent level-3 risk exposures in the future. This shift could be

attributed to various factors. In South Asia and Latin America, economic growth, urbanization, and shifting dietary patterns drive increased SSB consumption [5,33]. Transnational corporations exacerbate this trend with aggressive marketing and pricing strategies aimed at expanding their markets [33,34]. Additionally, rising affluence and a growing middle class likely contribute to greater exposure to SSBs in these countries [35].

The projected decline in SSB consumption in the Sub-Saharan Africa super-region contrasts with trends in other regions. More restrictive economic constraints and lower overall access to SSBs in these countries may be related to the projected consumption reduction. Additionally, almost all countries in this super-region have some type of commercial policy to curb SSB consumption [9]. For example, South Africa implemented a 10% tax on SSBs in 2018 as part of broader public health initiatives [36], resulting in a 29% reduction in their purchase and a 51% decrease in the amount of sugar consumed from these beverages [37].

The study has some limitations that need to be acknowledged. Selection bias may affect the GBD estimates, particularly as certain regions or populations, especially those in low-income or marginalized areas, may be underrepresented in the data collection [38]. This lack of representation can restrict the generalizability of the results, particularly for countries that did not contribute data, resulting in model-driven estimates with broad UIs [12,13]. Using SDI at the national level may mask within-country social inequalities, which can lead to underestimation of estimates in countries with high internal socioeconomic heterogeneity. Additionally, the GBD does not estimate the nonfatal disease burden attributable to SSBs, such as dental caries, which are known to be a significant health issue. The modeling starts at age 25, missing earlier exposure periods when SSB consumption begins and causes damage, thus overlooking a critical opportunity to inform policies targeting children and adolescents. Moreover, SSBs account for only a fraction of total dietary sugar intake, as other sources such as processed foods and desserts also contribute substantially to the development of NCDs. In the GBD framework, SSB exposure is defined based on beverage consumption (in grams per day) and energy density (≥ 50 kcal/226.8 g serving) as part of overall dietary intake; however, this approach does not account for daily frequency thresholds, which may underestimate both the true exposure and the attributed disease burden. Data on artificially sweetened beverages are not currently available in the GBD study and, therefore, are not modeled separately or in conjunction with SSBs; this gap is relevant, as these products have been increasingly associated with a range of chronic health conditions [39]. Furthermore, the Institute for Health Metrics and Evaluation's approach may not fully capture the complex relationships with macro- and micronutrients, for example, unhealthy fats and sodium, which can also drive the onset of NCDs. Lastly, the forecasting methods used by GBD to predict SSB consumption did not account for confounding factors beyond the SDI [16], such as public health interventions or changes in taxation policies, which could significantly impact future consumption trends [36, 40].

The findings of this study have significant public health implications, particularly in the context of the global drive to achieve the Sustainable Development Goals (SDGs) by 2030. Excessive consumption of SSBs is not only a key modifiable risk factor for NCDs such as cardiovascular diseases and diabetes but also poses challenges to efforts aimed at reducing premature mortality from NCDs (SDG 3.4) [9,41]. The substantial increase in SSB consumption, combined with forecasts predicting further growth in SSB intake, highlights the

urgency for implementing comprehensive public health interventions. These results reinforce the WHO's recommendations for reducing free sugar intake to $<10\%$ of total daily energy intake [42], as well as calls for stronger regulations on SSB marketing and sales [43]. Policies such as taxation on SSBs, as implemented in countries like South Africa, the United Kingdom, and Mexico, should be prioritized globally to mitigate the future burden of NCDs [9]. In this context, addressing the sociodemographic disparities in SSB consumption is critical to achieving equity in health outcomes and aligning with SDG targets of reducing inequalities (SDG 10) while promoting healthier diets and sustainable consumption patterns (SDG 12) [41]. It is also important to shed light on the effects of socioeconomic inequalities on health, as low- and middle-income countries, despite lower SSB consumption, face a significant burden of related health issues, raising speculation about the potential income-modifying effects on the harmful consequences of sugar consumption.

In conclusion, this study highlights the growing global health challenge posed by high SSB consumption, with $>30\%$ of the population exposed in 2021. Significant regional disparities are observed, with higher rates in high-income and Latin America and Caribbean super-regions, whereas South Asia reports the lowest rates. Despite some regional declines, global SSB consumption increases steadily over the past three decades, and projections suggest further increases by 2050. This rise in SSB consumption is directly linked to a substantial burden of NCDs. Reducing SSB consumption worldwide requires a multi-pronged approach focused on the general consumption of ultra-processed foods, including taxation, marketing restrictions, improving access to healthy alternatives, and consumer education. Without efforts on these fronts, the global burden of high SSB consumption will continue to escalate, putting further pressure on health systems globally.

Author contributions

The authors' responsibilities were as follows – SA-C, CCCR: designed research; SA-C: conducted research; SA-C, GGN, BFdS: performed statistical analysis; SA-C, GGN, FRML, FNH: analyzed data; SA-C, CCCR: wrote the paper; SA-C: had primary responsibility for the final content; and all authors: read and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

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Data availability

Data described in the manuscript will be made publicly and freely available without restriction at <https://vizhub.healthdata.org/gbd-results/> and <https://vizhub.healthdata.org/gbd-foresight/>.

Appendix A. Supplementary data

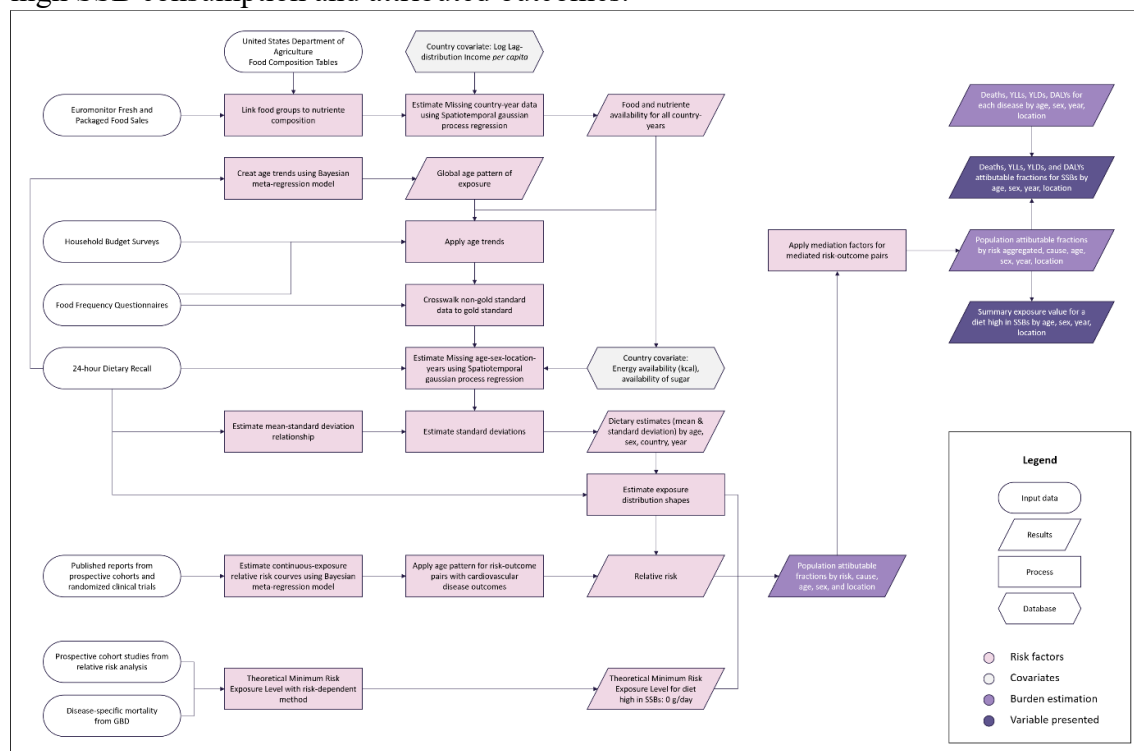
Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajcnut.2025.07.033>.

References

- [1] V.S. Malik, F.B. Hu, The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases, *Nat. Rev. Endocrinol.* 18 (4) (2022) 205–218.
- [2] V.S. Malik, B.M. Popkin, G.A. Bray, J.P. Després, W.C. Willett, F.B. Hu, Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis, *Diabetes Care* 33 (11) (2010) 2477–2483.
- [3] G.Y. Heo, H.B. Koh, J.T. Park, S.H. Han, T.H. Yoo, S.W. Kang, et al., Sweetened beverage intake and incident chronic kidney disease in the UK Biobank study, *JAMA Netw. Open* 7 (2) (2024) e2356885.
- [4] V.S. Malik, Y. Li, A. Pan, L. De Koning, E. Schernhammer, W.C. Willett, et al., Long-term consumption of sugar-sweetened and artificially sweetened beverages and risk of mortality in US adults, *Circulation* 139 (18) (2019) 2113–2125.
- [5] L. Lara-Castor, R. Micha, F. Cudhea, V. Miller, P. Shi, J. Zhang, et al., Sugar-sweetened beverage intakes among adults between 1990 and 2018 in 185 countries, *Nat. Commun.* 14 (1) (2023) 5957.
- [6] A. Roesler, N. Rojas, J. Falbe, Sugar-sweetened beverage consumption, perceptions, and disparities by race, ethnicity, and socioeconomic status in children and adolescents, *J. Nutr. Educ. Behav.* 53 (7) (2021) 553–563.
- [7] C.M. Apovian, The clinical and economic consequences of obesity, *Am. J. Manag. Care* 19 (2013) s219–s228.
- [8] D. Vandenbergh, J. Albrecht, The financial burden of non-communicable diseases in the European Union: a systematic review, *Eur. J. Public Health* 30 (4) (2020) 833–839.
- [9] WHO, Global report on the use of sugar-sweetened beverage taxes, 2023, World Health Organization, Geneva, 2023.
- [10] P. Wilde, Y. Huang, S. Sy, S. Abrahams-Gessel, T.V. Jardim, R. Paarlberg, et al., Cost-effectiveness of a US national sugar-sweetened beverage tax with a multistakeholder approach: who pays and who benefits, *Am. J. Public Health* 109 (2) (2019) 276–284.
- [11] J.C. Wells, A.L. Sawaya, R. Wibaek, M. Mwangome, M.S. Poullas, C. S. Yajnik, et al., The double burden of malnutrition: aetiological pathways and consequences for health, *Lancet* 395 (10217) (2020) 75–88.
- [12] A.E. Schumacher, H.H. Kyu, A. Aali, C. Abbafati, J. Abbas, R. Abbasgholizadeh, Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950–2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021, *Lancet* 403 (10440) (2024) 1989–2056.
- [13] M. Brauer, G.A. Roth, A.Y. Aravkin, P. Zheng, K.H. Abate, Y.H. Abate, et al., Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021, *Lancet* 403 (10440) (2024) 2162–2203.
- [14] G.A. Stevens, L. Alkema, R.E. Black, J.T. Boerma, G.S. Collins, M. Ezzati, et al., Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement, *Lancet* 388 (10062) (2016) e19–e23.
- [15] K. Nordhausen, S. Taskinen, Locally Weighted Scatterplot Smoother, in: B. S. Daya Sagar, Q. Cheng, J. McKinley, F. Agterberg (Eds.), *Encyclopedia of Mathematical Geosciences*, Springer, Encyclopedia of Earth Sciences Series, 2021, pp. 1–4.
- [16] M. Zhou, H. Shen, Forecasting the global burden of disease to 2050, *Lancet* 403 (10440) (2024) 1961–1963.
- [17] H. Sun, Y. Liu, Y. Xu, X. Gong, C. Zhai, W. Hu, et al., Global disease burden attributed to high sugar-sweetened beverages in 204 countries and territories from 1990 to 2019, *Prev. Med. (Baltim)* 175 (2023) 107690.
- [18] M. Claudy, G. Doyle, L. Marriott, N. Campbell, G. O'Malley, Are sugar-sweetened beverage taxes effective? Reviewing the Evidence Through a Marketing Systems Lens, SAGE Publications, Los Angeles CA, 2020, pp. 403–418 [cited September 17, 2024]. Available from: <https://journals.sagepub.com/doi/abs/10.1177/0743915620965153>.
- [19] A. Itria, S.S. Borges, A.E. Rinaldi, L.B. Nucci, C.C. Enes, Taxing sugar-sweetened beverages as a policy to reduce overweight and obesity in countries of different income classifications: a systematic review, *Public Health Nutr* 24 (16) (2021) 5550–5560.
- [20] A.M. Thow, H.L. Rippin, G. Mulcahy, K. Duffey, K. Wickramasinghe, Sugar-sweetened beverage taxes in Europe: learning for the future, *Eur. J. Public Health* 32 (2) (2022) 273–280.
- [21] E. Carrillo-Alvarez, R. Rifa-Ros, B. Salinas-Roca, L. Costa-Tutusa, M. Lamas, M. Rodriguez-Monforte, Diet-related health inequalities in high-income countries: A scoping review of observational studies, *Adv. Nutr.* 16 (6) (2025) 100439.
- [22] L. Machin, M. Cabrera, M.R. Curutchet, J. Martínez, A. Giménez, G. Ares, Consumer perception of the healthfulness of ultra-processed products featuring different front-of-pack nutrition labeling schemes, *J. Nutr. Educ. Behav.* 49 (4) (2017) 330–338.e1.
- [23] L. Almutairi, N. Alammari, A.S. Alqahtani, Descriptive Analysis Study of the Total sugar content of pre-packaged beverages available in Saudi Arabia, 2024 [cited July 8, 2025] Available from: <https://www.researchsquare.com.https://doi.org/10.21203/rs.3.rs-3996135/v1>.
- [24] M. Davey, Sugar increase in Fanta and Sprite prompts calls for new tax on Australia's food and drinks industry, *The Guardian* (2024).
- [25] C. Macdonald, Soft drink industry beats EU sugar reduction targets – but challenges remain, *Global insights*, 2021.
- [26] Action on Sugar, International sugar-sweetened soft drink survey 2015 – All Data, London, 2015.
- [27] G.Y. Maslennikova, R.G. Oganov, Prevention of noncommunicable diseases as an opportunity to increase life expectancy and healthy longevity, *Cardiovasc. Ther. Prev.* 18 (2) (2019) 5–12.
- [28] K.S. Reddy, Back make in India with testing in India, *J. Epidemiol. Foundation of India* 2 (2024) 40–41.
- [29] J. Thornton, Nestlé accused of double standards over added sugar in baby products sold in poorer countries, *BMJ* 385 (2024) q898.
- [30] A.M. Doherty, A.M. Lacko, B.M. Popkin, Sugar-sweetened beverage (SSB) consumption is associated with lower quality of the non-SSB diet in US adolescents and young adults, *Am. J. Clin. Nutr.* 113 (3) (2021) 657–664.
- [31] S.H. Kwon, H.R. Park, Y.M. Lee, S.Y. Kwon, O.S. Kim, H.Y. Kim, et al., Difference in food and nutrient intakes in Korean elderly people according to chewing difficulty: using data from the Korea national health and nutrition examination survey 2013 (6th), *Nutr. Res. Pract.* 11 (2) (2017) 139–146.
- [32] A.E. Özen, M. Bibiloni Mdel, A. Pons, J.A. Tur, Fluid intake from beverages across age groups: A systematic review, *J. Hum. Nutr. Diet.* 28 (5) (2015) 417–442.
- [33] A. Carriedo, A.D. Koon, L.M. Encarnación, K. Lee, R. Smith, H. Walls, The political economy of sugar-sweetened beverage taxation in Latin America: lessons from Mexico, Chile and Colombia, *Global Health* 17 (1) (2021) 5.
- [34] L. Fisher, M. Dahal, S. Hawkes, M. Puri, K. Buse, Barriers and opportunities to restricting marketing of unhealthy foods and beverages to children in Nepal: a policy analysis, *BMC Public Health* 21 (1) (2021) 1351.
- [35] A. Mendez Lopez, R. Loopstra, M. McKee, D. Stuckler, Is trade liberalisation a vector for the spread of sugar-sweetened beverages? A cross-national longitudinal analysis of 44 low- and middle-income countries, *Soc. Sci. Med.* 172 (2017) 21–27.
- [36] K.J. Hofman, N. Stacey, E.C. Swart, B.M. Popkin, S.W. Ng, South Africa's Health Promotion Levy: excise tax findings and equity potential, *Obes. Rev.* 22 (9) (2021) e13301.
- [37] N. Stacey, I. Edoka, K. Hofman, E.C. Swart, B. Popkin, S.W. Ng, Changes in beverage purchases following the announcement and implementation of South Africa's Health Promotion Levy: an observational study, *Lancet Planet Health* 5 (4) (2021) e200–e208.
- [38] M. Henderson, L. Page, Appraising the evidence: what is selection bias? *Evid. Based Ment. Health* 10 (3) (2007) 67–68.
- [39] P. Qin, Q. Li, Y. Zhao, Q. Chen, X. Sun, Y. Liu, et al., Sugar and artificially sweetened beverages and risk of obesity, type 2 diabetes mellitus, hypertension, and all-cause mortality: a dose-response meta-analysis of prospective cohort studies, *Eur. J. Epidemiol.* 35 (7) (2020) 655–671.
- [40] G. Bridge, S. Groisman, R. Bedi, Sugar-sweetened beverage taxes in Brazil: past, present, and future, *J. Public Health Policy* 43 (2) (2022) 281–291.
- [41] UNO. Department of economic and social affairs, Sustainable development. SDG Actions Platform, United Nations Organization, 2024 [cited July 28, 2024]. Available from: <https://sdgs.un.org/partnerships>.
- [42] WHO, Guideline: sugars intake for adults and children, Geneva, 2015. Available from: <https://apps.who.int/iris/handle/10665/149782>.
- [43] J.L. Pomeranz, Advanced policy options to regulate sugar-sweetened beverages to support public health, *J. Public Health Policy* 33 (1) (2012) 75–88.

5.6.1 Material Suplementar do Capítulo 6

Supplementary Figure 1. Framework for data acquisition and estimation of burden of high SSB consumption and attributed outcomes.



Supplementary Table 1. Summary exposure value of a high sugar-sweetened beverage consumption from 1990 to 2021 with projections to 2050 in 21 GBD regions and 204 countries.

Location	1990	1990-2021 APC (%)	1990-2021 TPC (%)	2021	2021-2050 APC (%)	2021-2050 TPC (%)	2050
Global	29.97 (22.97; 42.54)	0.14 (-0.07; 0.36)	1.96 (1.51; 2.40)	30.56 (22.83; 41.22)	0.75 (0.73; 0.78)	9.54 (9.08; 10.00)	33.56 (25.31; 46.35)
Central Europe, Eastern Europe, and Central Asia	28.09 (19.70; 40.97)	1.40 (0.97; 1.84)	20.64 (20.12; 21.17)	33.88 (24.95; 45.31)	1.04 (0.99; 1.09)	13.40 (12.96; 13.84)	38.65 (28.53; 50.54)
Central Asia	25.53 (16.90; 38.79)	0.93 (0.40; 1.47)	13.28 (12.68; 13.88)	28.92 (19.61; 41.34)	1.28 (1.22; 1.33)	16.69 (16.15; 17.23)	33.90 (23.51; 46.29)
Armenia	26.36 (17.00; 44.73)	-1.14 (-2.33; 0.07)	-14.25 (-14.93; -13.57)	22.61 (14.37; 36.86)	1.36 (1.32; 1.40)	14.88 (14.10; 15.65)	26.12 (15.96; 43.04)
Azerbaijan	23.18 (14.62; 38.44)	1.92 (1.63; 2.22)	29.20 (28.44; 29.96)	29.95 (17.95; 44.01)	1.72 (1.70; 1.74)	22.98 (22.32; 23.65)	37.10 (22.85; 53.01)
Georgia	22.71 (13.64; 37.00)	1.03 (0.58; 1.48)	14.76 (14.01; 15.51)	26.06 (14.60; 39.45)	1.55 (1.44; 1.66)	20.56 (19.85; 21.26)	31.74 (19.00; 46.42)
Kazakhstan	32.14 (18.25; 47.70)	1.39 (0.82; 1.97)	20.50 (19.85; 21.14)	38.72 (24.03; 53.19)	1.53 (1.44; 1.61)	20.19 (19.65; 20.74)	46.81 (31.04; 61.82)
Kyrgyzstan	22.90 (12.57; 36.73)	0.48 (0.14; 0.81)	6.60 (5.80; 7.39)	24.42 (12.49; 39.58)	0.67 (0.65; 0.69)	8.46 (7.66; 9.26)	26.56 (13.65; 42.09)
Mongolia	21.03 (12.24; 35.26)	-0.05 (-0.67; 0.57)	19.61 (18.82; 20.40)	25.15 (15.67; 39.52)	1.39 (1.29; 1.48)	18.22 (17.51; 18.92)	29.85 (18.82; 45.22)
Tajikistan	29.33 (19.54; 48.13)	-1.01 (-1.08; -0.94)	-12.77 (-13.45; -12.09)	25.59 (16.40; 44.25)	-0.80 (-0.82; -0.78)	-9.32 (-10.08; -8.56)	23.11 (14.26; 41.49)
Turkmenistan	24.74 (13.94; 38.87)	3.92 (3.27; 4.58)	67.86 (67.02; 68.70)	41.52 (24.75; 57.89)	2.37 (2.31; 2.43)	32.93 (32.34; 33.52)	55.81 (36.83; 73.37)
Uzbekistan	21.05 (11.87; 34.18)	-2.34 (-3.12; -1.57)	15.48 (14.72; 16.24)	24.31 (14.49; 37.50)	1.52 (1.49; 1.55)	20.11 (19.41; 20.81)	29.38 (17.91; 43.45)
Central Europe	35.60 (23.73; 49.65)	2.77 (2.48; 3.06)	44.46 (43.96; 44.97)	51.43 (39.07; 64.29)	1.40 (1.30; 1.50)	18.43 (18.10; 18.77)	61.41 (48.72; 72.66)
Albania	31.52 (16.50; 48.01)	3.84 (3.26; 4.41)	66.04 (65.32; 66.77)	52.34 (35.37; 68.56)	1.83 (1.73; 1.93)	24.70 (24.25; 25.14)	65.91 (46.94; 80.27)
Bosnia and Herzegovina	24.32 (12.42; 39.34)	4.02 (3.44; 4.60)	69.99 (69.13; 70.85)	41.35 (25.02; 57.05)	1.90 (1.79; 2.01)	25.72 (25.15; 26.28)	52.51 (34.35; 68.90)
Bulgaria	48.42 (33.01; 64.43)	0.53 (-1.25; 2.35)	7.41 (6.95; 7.88)	52.01 (34.37; 66.83)	1.09 (1.01; 1.17)	14.09 (13.63; 14.54)	59.79 (40.05; 75.00)
Croatia	40.29 (24.95; 57.67)	2.70 (1.42; 4.00)	43.19 (42.63; 43.76)	57.69 (41.42; 73.13)	0.39 (0.35; 0.43)	4.86 (4.45; 5.27)	60.67 (42.24; 77.38)
Czechia	41.30 (25.98; 57.53)	1.34 (1.22; 1.45)	19.59 (19.05; 20.13)	49.40 (33.40; 64.75)	0.74 (0.73; 0.76)	9.40 (8.96; 9.85)	54.24 (38.79; 69.96)
Hungary	39.77 (24.11; 56.27)	1.47 (0.80; 2.14)	21.70 (21.13; 22.26)	48.40 (32.55; 63.43)	1.18 (1.12; 1.24)	15.28 (14.80; 15.76)	56.18 (37.92; 73.04)
Montenegro	28.09 (15.79; 44.14)	-0.09 (-1.78; 1.62)	-1.22 (-1.92; 0.53)	27.74 (15.17; 42.09)	1.39 (1.33; 1.44)	18.25 (17.49; 19.01)	33.05 (17.95; 50.69)
North Macedonia	30.07 (16.50; 45.87)	2.41 (2.22; 2.60)	37.79 (37.08; 38.51)	41.43 (25.90; 57.63)	1.40 (1.35; 1.45)	18.42 (17.87; 18.97)	49.39 (32.28; 65.52)
Poland	35.87 (24.62; 50.08)	3.15 (2.60; 3.70)	51.76 (51.28; 52.24)	54.44 (42.91; 66.06)	1.71 (1.60; 1.82)	22.88 (22.55; 23.22)	67.56 (52.31; 80.99)
Romania	30.40 (16.94; 45.37)	5.55 (5.16; 5.94)	107 (106.35; 107.66)	62.92 (48.23; 76.27)	1.93 (1.76; 2.10)	26.18 (25.88; 26.49)	80.37 (63.70; 91.09)
Serbia	37.33 (22.40; 53.87)	-0.14 (-1.03; 0.77)	-1.81 (-2.41; -1.22)	36.66 (21.35; 52.53)	0.83 (0.75; 0.90)	10.53 (9.93; 11.12)	40.73 (25.31; 56.19)
Slovakia	22.89 (12.98; 37.54)	2.49 (0.23; 4.81)	39.36 (38.51; 40.20)	31.89 (17.94; 47.84)	0.00 (-0.01; 0.01)	-0.04 (-0.74; 0.65)	31.88 (17.07; 49.67)
Slovenia	35.77 (21.54; 51.66)	2.67 (2.07; 3.28)	42.66 (42.06; 43.26)	51.03 (35.52; 66.13)	0.95 (0.91; 0.99)	12.17 (11.74; 12.60)	57.54 (41.25; 72.79)
Eastern Europe	24.83 (17.18; 38.51)	0.54 (-0.03; 1.11)	7.46 (6.88; 8.04)	26.68 (18.33; 37.94)	1.06 (1.05; 1.07)	13.69 (13.12; 14.26)	30.45 (20.44; 43.76)
Belarus	23.60 (14.41; 38.17)	0.74 (0.67; 0.82)	10.54 (9.83; 11.25)	26.08 (17.54; 41.17)	0.72 (0.71; 0.73)	8.65 (8; 9.30)	28.42 (19.31; 44.02)
Estonia	25.74 (14.39; 40.49)	2.31 (2.09; 2.53)	36.26 (35.50; 37.03)	35.08 (22.15; 51.50)	1.37 (1.34; 1.40)	17.98 (17.33; 18.63)	41.66 (24.82; 59.82)
Latvia	24.49 (13.97; 38.66)	0.17 (-1.30; 1.67)	2.35 (1.64; 3.05)	25.07 (14.26; 38.35)	1.26 (1.23; 1.29)	16.44 (15.66; 17.22)	29.37 (15.88; 46.99)
Lithuania	27.51 (15.34; 43.08)	1.73 (0.77; 2.71)	26.01 (25.27; 26.75)	34.67 (20.55; 50.32)	1.26 (1.20; 1.31)	16.40 (15.75; 17.05)	40.64 (23.76; 58.17)
Republic of Moldova	23.45 (15.12; 38.92)	-0.52 (-0.70; -0.34)	-6.78 (-7.49; -6.07)	21.86 (13.88; 36.89)	0.22 (0.17; 0.26)	2.65 (1.90; 3.40)	22.46 (14.05; 37.46)
Russian Federation	27.13 (18.79; 41.01)	0.67 (0.11; 1.23)	9.40 (8.83; 9.97)	29.68 (20.24; 41.96)	0.92 (0.91; 0.93)	11.20 (10.64; 11.76)	33.13 (22.04; 47.59)
Ukraine	18.43 (11.84; 31.73)	-0.66 (-1.41; 0.10)	-8.51 (-9.24; -7.78)	16.86 (10.27; 28.34)	0.50 (0.45; 0.55)	6.22 (5.41; 7.03)	17.91 (10.76; 31.09)
High-income	40.75 (30.21; 53.43)	2.01 (1.70; 2.31)	30.68 (30.29; 31.07)	53.26 (42.47; 64.36)	0.97 (0.94; 1.01)	12.49 (12.20; 12.78)	60.19 (49.15; 71.23)
Australasia	45.31 (30.20; 60.94)	0.85 (0.39; 1.31)	12.04 (11.56; 12.51)	50.76 (34.89; 64.88)	0.78 (0.77; 0.79)	9.88 (9.45; 10.32)	55.97 (39.23; 71.32)
Australia	48.07 (31.95; 63.74)	0.72 (0.31; 1.14)	10.21 (9.74; 10.67)	52.98 (36.27; 67.46)	0.73 (0.71; 0.75)	9.26 (8.84; 9.68)	58.09 (40.81; 73.47)

New Zealand	31.29 (18.67; 47.73)	1.44 (0.71; 2.18)	21.24 (20.58; 21.91)	37.93 (22.81; 52.74)	1.28 (1.24; 1.31)	16.66 (16.07; 17.25)	44.52 (27.79; 61.67)
High-income Asia Pacific	28.21 (18.94; 41.24)	1.61 (1.05; 2.17)	24.03 (23.46; 24.61)	34.99 (24.20; 48.04)	1.31 (1.27; 1.34)	17.14 (16.64; 17.65)	41.26 (28.04; 54.68)
Brunei Darussalam	31.04 (21.64; 47.41)	0.08 (0.03; 0.14)	1.13 (0.55; 1.70)	31.39 (21.45; 45.89)	0.10 (0.10; 0.11)	1.27 (0.72; 1.82)	31.80 (21.86; 46.58)
Japan	32.04 (21.94; 45.42)	0.79 (0.42; 1.16)	11.16 (10.65; 11.67)	35.61 (25.16; 47.83)	0.87 (0.84; 0.90)	11.16 (10.69; 11.63)	39.75 (27.95; 52.49)
Republic of Korea	17.60 (10.13; 29.80)	4.90 (3.97; 5.84)	90.39 (89.47; 91.31)	33.51 (21.04; 46.66)	2.27 (2.16; 2.37)	31.36 (30.72; 32.01)	44.58 (27.17; 62.54)
Singapore	19.75 (11.19; 33.40)	3.62 (3.37; 3.87)	61.40 (60.48; 62.32)	31.88 (18.63; 47.44)	2.34 (2.29; 2.40)	32.53 (31.80; 33.27)	42.72 (25.14; 62.49)
High-income North America	47.32 (36.12; 60.26)	2.34 (1.48; 3.20)	36.47 (36.14; 36.81)	64.58 (53.84; 74.62)	0.46 (0.45; 0.48)	5.79 (5.54; 6.03)	68.46 (56.95; 80.91)
Canada	34.58 (22.19; 49.79)	2.82 (1.94; 3.70)	45.39 (44.76; 46.02)	50.28 (32.70; 66.64)	0.71 (0.71; 0.72)	9.01 (8.53; 9.50)	54.98 (36.93; 72.14)
Greenland	48.81 (33.60; 63.51)	2.17 (1.99; 2.36)	33.57 (33.14; 34.01)	65.20 (49.19; 79.26)	0.97 (0.94; 1.00)	12.47 (12.17; 12.78)	73.70 (59.37; 85.79)
United States of America	48.73 (37.18; 61.53)	2.30 (1.45; 3.16)	35.90 (35.57; 36.23)	66.23 (55.33; 76.17)	0.48 (0.46; 0.50)	5.99 (5.75; 6.23)	70.35 (58.64; 83.17)
Southern Latin America	50.60 (37.04; 64.39)	2.56 (2.21; 2.91)	40.52 (40.17; 40.87)	71.11 (58.68; 81.10)	1.21 (1.14; 1.28)	10.97 (10.76; 11.19)	79.23 (67.30; 88.26)
Argentina	57.25 (42.22; 72.33)	1.91 (1.52; 2.31)	29.06 (28.72; 29.40)	73.89 (59.84; 84.33)	0.58 (0.55; 0.60)	5.62 (5.37; 5.87)	78.18 (62.13; 89.81)
Chile	35.58 (21.70; 51.40)	4.60 (4.14; 5.07)	83.25 (82.68; 83.81)	65.20 (50.26; 77.21)	1.75 (1.65; 1.85)	23.47 (23.21; 23.74)	81.25 (68.81; 90.56)
Uruguay	45.72 (29.76; 61.87)	2.97 (2.79; 3.16)	48.32 (47.85; 48.78)	67.81 (52.79; 80.74)	1.29 (1.23; 1.34)	16.81 (16.55; 17.07)	79.70 (67.21; 89.05)
Western Europe	40.34 (28.77; 54.27)	1.49 (1.35; 1.63)	22.06 (21.62; 22.51)	49.24 (36.95; 62.30)	1.07 (1.05; 1.09)	13.76 (13.40; 14.13)	56.30 (43.08; 69.20)
Andorra	57.75 (41.06; 73.24)	0.04 (-0.13; 0.21)	0.53 (0.15; 0.91)	58.05 (42.80; 73.13)	-0.09 (-0.10; -0.09)	-1.12 (-1.49; -0.74)	57.38 (42.06; 73.05)
Austria	32.46 (18.66; 48.40)	2.89 (2.08; 3.71)	46.80 (46.13; 47.47)	47.65 (31.45; 63.08)	0.92 (0.90; 0.95)	11.82 (11.34; 12.29)	53.51 (37.06; 70.07)
Belgium	43.69 (28.98; 60.07)	2.39 (1.60; 3.18)	37.38 (36.89; 37.86)	60.03 (45.17; 73.99)	0.64 (0.62; 0.66)	8.10 (7.75; 8.46)	65.10 (48.47; 80.11)
Cyprus	44.38 (28.50; 59.81)	-0.77 (-1.09; -0.44)	-9.83 (-10.32; -9.35)	40.02 (25.85; 55.69)	-0.64 (-0.65; -0.63)	-7.49 (-8.02; -6.97)	36.91 (23.54; 52.74)
Denmark	38.24 (23.99; 54.32)	1.70 (1.49; 1.91)	25.50 (24.95; 26.06)	47.99 (32.84; 62.87)	0.89 (0.87; 0.92)	11.44 (10.98; 11.90)	53.72 (36.76; 69.06)
Finland	32.62 (18.94; 48.03)	2.29 (2.10; 2.48)	35.65 (35; 36.30)	44.24 (28.52; 59.39)	1.41 (1.37; 1.44)	18.51 (17.99; 19.04)	52.79 (34.49; 69.24)
France	36.01 (22.04; 52.68)	1.43 (0.99; 1.87)	21.12 (20.50; 21.74)	43.62 (28.00; 60.37)	1.27 (1.23; 1.30)	16.53 (15.98; 17.08)	51.13 (32.74; 68.58)
Germany	46.71 (31.27; 62.79)	1.36 (1.16; 1.56)	19.93 (19.46; 20.39)	56.01 (40.88; 70.58)	0.70 (0.70; 0.71)	8.91 (8.53; 9.29)	61.20 (45.41; 75.82)
Greece	35.91 (21.15; 51.21)	0.42 (0.08; 0.77)	5.88 (5.28; 6.47)	38.02 (22.71; 53.11)	0.05 (0.04; 0.06)	0.62 (0.04; 1.19)	38.27 (22.38; 53.51)
Iceland	46.35 (30.63; 62.95)	-0.51 (-1.10; 0.09)	-6.64 (-7.13; -6.16)	43.27 (27.60; 58.63)	0.20 (0.20; 0.20)	2.47 (1.96; 2.99)	44.38 (27.57; 59.74)
Ireland	46.33 (29.82; 62.74)	2.99 (2.63; 3.35)	48.79 (48.33; 49.26)	68.94 (54.07; 81.55)	1.27 (1.20; 1.34)	16.61 (16.33; 16.89)	80.93 (64.73; 91.95)
Israel	46.61 (30.02; 61.88)	2.36 (2.02; 2.69)	36.85 (36.39; 37.30)	63.79 (48.71; 76.88)	1.04 (0.99; 1.08)	13.35 (13.05; 13.65)	72.70 (58.70; 84.68)
Italy	33.83 (23.67; 47.19)	0.83 (0.78; 0.88)	11.77 (11.28; 12.26)	37.82 (27.37; 50.87)	0.67 (0.66; 0.68)	8.47 (8.03; 8.92)	41.15 (30.43; 54.37)
Luxembourg	55.04 (39.26; 68.74)	0.80 (-0.02; 1.63)	11.34 (10.98; 11.71)	61.29 (47.73; 74.87)	-0.11 (-0.12; -0.11)	-1.36 (-1.69; -1.02)	60.43 (44.91; 75.92)
Malta	60.73 (44.44; 75.40)	0.83 (0.12; 1.54)	11.71 (11.36; 12.05)	67.83 (53.42; 81.12)	0.03 (0.03; 0.04)	0.38 (0.06; 0.69)	68.10 (50.60; 83.43)
Monaco	81.65 (69.04; 91.65)	0.54 (0.42; 0.67)	7.59 (7.42; 7.76)	87.85 (78.77; 95.63)	0.28 (0.27; 0.28)	3.41 (3.28; 3.53)	90.97 (83.15; 96.86)
Netherlands	43.70 (27.62; 59.27)	2.32 (2.08; 2.56)	36.24 (35.73; 36.74)	59.54 (43.24; 73.92)	1.22 (1.18; 1.26)	15.94 (15.59; 16.30)	69.46 (53.65; 82.90)
Norway	35.40 (25.23; 49.06)	1.96 (1.42; 2.51)	29.93 (29.46; 30.40)	46.00 (35.43; 58.53)	0.68 (0.66; 0.69)	8.53 (8.15; 8.90)	50.08 (38.32; 64.40)
Portugal	28.49 (10.83; 50.94)	2.12 (1.97; 2.26)	32.64 (31.59; 33.70)	37.80 (14.58; 59.35)	1.69 (1.63; 1.76)	22.66 (21.77; 23.54)	46.75 (20.09; 69.92)
San Marino	54.25 (38.00; 69.81)	0.07 (-0.79; 0.93)	0.95 (0.54; 1.35)	54.76 (38.47; 68.98)	-0.40 (-0.42; -0.38)	-4.78 (-5.20; -4.37)	52.05 (34.46; 68.31)
Spain	38.94 (15.02; 61.64)	2.52 (2.18; 2.86)	39.84 (38.97; 40.70)	54.45 (27.31; 75.67)	1.44 (1.38; 1.51)	19.03 (18.42; 19.65)	65.28 (36.81; 83.64)
Sweden	31.71 (16.80; 50.66)	2.12 (1.66; 2.59)	32.68 (31.89; 33.47)	42.08 (23.38; 60.03)	0.99 (0.97; 1.01)	12.74 (12.13; 13.36)	47.66 (28.46; 65.21)
Switzerland	34.85 (20.63; 50.42)	1.33 (0.95; 1.71)	19.47 (18.84; 20.10)	41.64 (24.65; 56.99)	0.86 (0.85; 0.88)	11.03 (10.47; 11.59)	46.41 (28.61; 63.02)
United Kingdom	44.10 (34.74; 58.02)	1.11 (0.99; 1.23)	16.04 (15.68; 16.39)	51.17 (41.85; 63.04)	0.70 (0.69; 0.70)	8.79 (8.50; 9.08)	55.84 (46.39; 67.19)
Latin America and Caribbean	35.30 (26.48; 48.55)	1.61 (1.46; 1.76)	24 (23.55; 24.45)	43.78 (33.34; 56.20)	1.22 (1.20; 1.24)	15.86 (15.49; 16.24)	50.96 (39.99; 63.54)
Andean Latin America	27.45 (18.08; 40.24)	1.91 (1.20; 2.62)	28.96 (28.31; 29.61)	35.40 (21.80; 49.97)	2.01 (1.98; 2.03)	27.28 (26.67; 27.88)	45.44 (29.99; 62.58)
Bolivia (Plurinational State of)	25.78 (14.89; 39.74)	2.10 (2.02; 2.19)	32.31 (31.55; 33.08)	34.11 (19.53; 50.07)	1.48 (1.46; 1.51)	19.57 (18.92; 20.23)	41.03 (24.86; 57.51)

Ecuador	41.51 (26.51; 57.01)	0.55 (-0.31; 1.42)	7.67 (7.15; 8.19)	44.69 (29.57; 60.09)	1.29 (1.25; 1.33)	16.88 (16.38; 17.38)	52.48 (36.69; 69.42)
Peru	21.45 (12.93; 34.66)	2.84 (2.01; 3.67)	45.73 (44.89; 46.57)	31.25 (17.70; 46.36)	3.54 (2.55; 4.54)	36.53 (35.79; 37.28)	43.14 (25.44; 62.45)
Caribbean	28.77 (19.38; 41.27)	1.12 (0.70; 1.54)	16.15 (15.62; 16.68)	33.41 (23.75; 44.98)	0.26 (0.22; 0.31)	3.24 (2.77; 3.70)	34.52 (24.46; 46.81)
Antigua and Barbuda	27.02 (18.29; 43.95)	0.52 (0.35; 0.69)	7.28 (6.60; 7.95)	28.99 (19.26; 45.18)	0.53 (0.51; 0.55)	6.62 (5.97; 7.28)	30.96 (20.37; 48.08)
Bahamas	28.04 (18.25; 43.60)	0.30 (0.23; 0.37)	4.08 (3.46; 4.71)	29.19 (19.77; 43.91)	0.15 (0.15; 0.15)	1.84 (1.25; 2.43)	29.74 (20.20; 44.68)
Barbados	36.01 (21.02; 51.96)	-0.57 (-0.70; -0.44)	-7.36 (-7.95; -6.78)	33.36 (20.43; 48.92)	-0.15 (-0.15; -0.15)	-1.83 (-2.44; -1.22)	32.72 (19.49; 48.36)
Belize	22.50 (12.96; 36.16)	1.74 (0.99; 2.48)	26.08 (25.27; 26.89)	28.37 (16.09; 44.25)	0.54 (0.50; 0.58)	6.74 (6.04; 7.45)	30.34 (17.63; 45.86)
Bermuda	31.00 (19.92; 46.62)	0.51 (0.35; 0.68)	7.15 (6.55; 7.75)	33.22 (22.30; 48.31)	0.19 (0.18; 0.20)	2.36 (1.80; 2.91)	34.02 (22.94; 49.25)
Cuba	34.60 (20.12; 51.37)	2.67 (2.15; 3.19)	42.52 (41.87; 43.16)	49.30 (32.67; 64.53)	1.01 (0.97; 1.04)	13.63 (13.17; 14.08)	56.26 (39.65; 71.01)
Dominica	28.21 (15.33; 43.45)	1.50 (0.81; 2.19)	22.16 (21.46; 22.87)	34.46 (21.11; 49.24)	0.67 (0.63; 0.70)	7.38 (6.77; 7.98)	37.06 (22.18; 53.05)
Dominican Republic	22.30 (13.00; 36.52)	2.24 (2.12; 2.35)	34.67 (33.85; 35.48)	30.03 (17.67; 45.45)	1.80 (1.76; 1.84)	24.24 (23.56; 24.92)	37.57 (23.40; 53.83)
Grenada	22.28 (13.48; 36.27)	1.13 (0.89; 1.37)	16.33 (15.57; 17.09)	25.92 (16.64; 41.70)	1.18 (1.09; 1.26)	15.29 (14.57; 16.01)	29.98 (18.21; 46.04)
Guyana	22.70 (11.62; 36.23)	2.51 (2.32; 2.71)	39.66 (38.79; 40.53)	31.70 (17.03; 48.13)	2.22 (1.88; 2.56)	30.61 (29.84; 31.38)	42.04 (23.30; 61.84)
Haiti	20.43 (12.78; 35.78)	-0.28 (-0.42; -0.13)	-3.67 (-4.42; -2.92)	19.68 (12.42; 32.60)	0.33 (0.28; 0.39)	4.11 (3.36; 4.85)	20.49 (12.71; 33.94)
Jamaica	29.31 (16.48; 45.34)	0.46 (-0.03; 0.96)	6.43 (5.74; 7.11)	31.20 (18.27; 46.23)	0.27 (0.24; 0.30)	3.32 (2.67; 3.96)	32.24 (18.49; 47.73)
Puerto Rico	32.96 (21.69; 48.28)	1.01 (0.66; 1.36)	14.52 (13.95; 15.10)	37.74 (24.96; 52.34)	0.32 (0.32; 0.33)	4.01 (3.49; 4.54)	39.31 (25.97; 54.25)
Saint Kitts and Nevis	25.28 (15.24; 40.03)	0.65 (0.51; 0.79)	9.10 (8.41; 9.78)	27.58 (17.63; 41.90)	0.74 (0.73; 0.75)	9.40 (8.74; 10.06)	30.27 (19.17; 46.40)
Saint Lucia	23.77 (13.71; 38.17)	0.72 (0.60; 0.84)	10.14 (9.40; 10.88)	26.18 (15.51; 40.78)	0.87 (0.82; 0.93)	11.16 (10.45; 11.87)	29.17 (17.22; 44.91)
Saint Vincent and the Grenadines	22.13 (13.01; 35.44)	2.63 (1.85; 3.42)	41.90 (41.08; 42.72)	31.41 (18.08; 46.69)	1.27 (1.24; 1.30)	16.61 (15.92; 17.30)	36.80 (20.94; 53.59)
Suriname	28.00 (14.72; 42.78)	1.20 (1.16; 1.23)	17.04 (16.33; 17.76)	32.77 (19.83; 48.39)	0.97 (0.91; 1.02)	12.42 (11.80; 13.04)	36.94 (23.16; 52.52)
Trinidad and Tobago	32.59 (18.96; 48.05)	1.68 (1.42; 1.95)	25.22 (24.58; 25.86)	40.81 (26.35; 56.17)	1.02 (0.98; 1.06)	12.20 (11.68; 12.73)	45.95 (30.91; 61.93)
United States Virgin Islands	32.68 (20.85; 47.94)	1.93 (0.58; 3.30)	29.40 (28.79; 30.01)	42.28 (26.87; 56.39)	0.06 (0.03; 0.09)	0.73 (0.21; 1.25)	42.60 (26.14; 58.56)
Central Latin America	39.64 (30.21; 51.98)	1.12 (1.05; 1.19)	16.27 (15.86; 16.68)	46.08 (34.58; 58.66)	1.06 (1.05; 1.08)	13.74 (13.37; 14.11)	52.63 (40.81; 65.12)
Colombia	23.63 (14.01; 37.86)	4.10 (3.60; 4.59)	71.72 (70.88; 72.56)	40.58 (24.44; 56.10)	2.69 (2.62; 2.77)	38.12 (37.54; 38.70)	56.79 (38.32; 74.14)
Costa Rica	36.33 (22.42; 53.47)	1.75 (1.73; 1.77)	26.36 (25.75; 26.96)	45.91 (29.94; 60.89)	1.21 (1.18; 1.24)	15.78 (15.30; 16.26)	53.45 (37.17; 68.27)
El Salvador	24.45 (13.92; 38.31)	2.38 (2.05; 2.72)	37.27 (36.54; 38.01)	33.57 (21.39; 47.85)	1.27 (1.24; 1.30)	16.57 (15.98; 17.15)	39.36 (25.62; 54.58)
Guatemala	25.46 (14.77; 40.83)	1.36 (1.15; 1.57)	19.93 (19.20; 20.66)	30.54 (18.22; 45.00)	0.94 (0.92; 0.95)	11.99 (11.33; 12.64)	34.33 (21.45; 50.84)
Honduras	23.79 (13.69; 37.75)	1.82 (1.49; 2.15)	27.52 (26.76; 28.28)	30.34 (17.36; 44.49)	1.22 (1.19; 1.25)	14.76 (14.11; 15.41)	34.98 (20.51; 49.16)
Mexico	52.57 (41.56; 65.33)	0.64 (0.53; 0.74)	8.92 (8.60; 9.25)	57.26 (45.43; 69.85)	0.59 (0.56; 0.62)	7.37 (7.06; 7.67)	61.60 (48.90; 74.03)
Nicaragua	23.16 (14.29; 37.70)	1.52 (1.42; 1.61)	22.49 (21.72; 23.25)	28.37 (15.83; 42.41)	1.11 (1.08; 1.13)	14.31 (13.62; 15)	32.58 (18.73; 47.65)
Panama	26.28 (16.88; 41.79)	0.40 (0.17; 0.64)	25.98 (25.27; 26.69)	33.11 (20.82; 48.34)	2.07 (1.92; 2.22)	25.67 (25.03; 26.30)	41.94 (27.34; 59.06)
Venezuela (Bolivarian Republic of)	30.56 (17.77; 45.70)	-0.46 (-0.52; -0.40)	-6.05 (-6.68; -5.42)	28.71 (16.66; 43.27)	-0.39 (-0.39; -0.38)	-4.59 (-5.24; -3.95)	27.35 (15.73; 41.51)
Tropical Latin America	34.55 (24.88; 49.34)	2.06 (1.70; 2.43)	31.66 (31.18; 32.13)	45.49 (35.44; 57.29)	1.35 (1.32; 1.37)	17.64 (17.29; 17.99)	53.78 (42.54; 66.26)
Brazil	34.79 (25.05; 49.65)	2.10 (1.73; 2.47)	32.25 (31.78; 32.73)	46.01 (36.03; 57.89)	1.36 (1.33; 1.38)	17.82 (17.47; 18.17)	54.49 (43.21; 67.00)
Paraguay	24.45 (15.07; 38.38)	0.03 (-0.23; 0.30)	11.48 (10.79; 12.17)	27.26 (16.69; 41.24)	1.22 (1.14; 1.30)	15.89 (15.23; 16.55)	31.69 (20.27; 46.46)
North Africa and Middle East	24.41 (16.89; 37.00)	1.86 (1.74; 1.99)	28.17 (27.57; 28.76)	31.29 (22.43; 43.34)	0.97 (0.91; 1.02)	12.43 (11.92; 12.94)	35.39 (25.43; 49.45)
North Africa and Middle East	24.41 (16.89; 37.00)	1.86 (1.74; 1.99)	28.17 (27.57; 28.76)	31.29 (22.43; 43.34)	0.97 (0.91; 1.02)	12.43 (11.92; 12.94)	35.39 (25.43; 49.45)
Afghanistan	21.22 (13.14; 38.04)	1.20 (0.49; 1.91)	17.36 (16.46; 18.26)	24.90 (15.77; 44.60)	-0.03 (-0.05; -0.01)	3.56 (2.71; 4.41)	25.79 (15.66; 46.76)
Algeria	24.16 (15.77; 38.88)	0.74 (0.70; 0.77)	10.45 (9.75; 11.16)	26.68 (15.99; 41.15)	0.81 (0.77; 0.86)	10.35 (9.63; 11.07)	29.52 (17.43; 46.43)
Bahrain	31.37 (19.32; 46.88)	1.28 (1.06; 1.50)	18.67 (18.03; 19.30)	37.23 (22.98; 51.70)	1.03 (0.98; 1.07)	13.21 (12.63; 13.79)	42.38 (26.12; 58.26)
Egypt	17.17 (10.01; 29.31)	2.23 (1.82; 2.64)	34.56 (33.66; 35.47)	23.10 (12.47; 36.84)	2.66 (2.63; 2.69)	37.56 (36.69; 38.43)	32.13 (17.38; 49.71)
Iran (Islamic Republic of)	27.64 (19.28; 41.66)	0.95 (0.75; 1.16)	13.60 (13.01; 14.18)	31.40 (21.58; 44.91)	1.39 (1.33; 1.45)	16.34 (15.73; 16.95)	36.70 (24.20; 54.96)

Iraq	23.34 (14.48; 37.50)	0.94 (0.27; 1.62)	13.47 (12.75; 14.19)	26.48 (17.69; 42.08)	0.96 (0.86; 1.07)	12.35 (11.61; 13.10)	29.82 (17.77; 49.12)
Jordan	22.12 (13.69; 35.97)	1.17 (0.84; 1.49)	16.92 (16.19; 17.65)	25.86 (15.18; 38.81)	0.85 (0.82; 0.88)	9.53 (8.86; 10.21)	28.41 (16.80; 42.36)
Kuwait	29.64 (19.44; 45.35)	2.44 (0.70; 4.22)	38.46 (37.79; 39.12)	41.03 (27.11; 56.79)	0.00 (-0.01; 0.01)	-0.01 (-0.55; 0.53)	41.04 (25.00; 57.83)
Lebanon	24.07 (14.22; 38.12)	0.51 (0.41; 0.61)	7.07 (6.37; 7.76)	25.77 (15.95; 39.27)	0.55 (0.51; 0.58)	6.86 (6.19; 7.54)	27.57 (16.89; 42.72)
Libya	29.28 (17.17; 44.53)	-0.48 (-0.51; -0.45)	-13.88 (-14.52; -13.25)	25.22 (15.29; 40.31)	-0.36 (-0.42; -0.30)	-4.29 (-5.04; -3.55)	24.06 (12.10; 40.18)
Morocco	16.68 (10.13; 29.77)	0.02 (-0.96; 1.01)	0.27 (-0.55; 1.08)	16.72 (8.87; 27.77)	1.70 (1.68; 1.72)	24.52 (23.60; 25.43)	20.97 (10.98; 35.27)
Oman	33.20 (22.82; 53.17)	-0.75 (-1.10; -0.41)	-9.66 (-10.27; -9.05)	30.00 (19.43; 46.58)	0.29 (0.22; 0.36)	2.23 (1.57; 2.89)	30.68 (19.16; 48.07)
Palestine	29.26 (19.13; 48.47)	0.57 (0.14; 1.01)	8 (7.26; 8.74)	31.60 (20.55; 52.51)	0.36 (0.29; 0.43)	4.52 (3.77; 5.27)	33.04 (20.78; 55.49)
Qatar	44.53 (28.24; 60.96)	1.84 (1.42; 2.26)	27.83 (27.30; 28.36)	56.93 (39.44; 73.68)	0.73 (0.71; 0.74)	9.21 (8.80; 9.62)	62.38 (45.54; 77.46)
Saudi Arabia	43.29 (29.47; 58.91)	3.00 (2.56; 3.44)	48.86 (48.38; 49.34)	64.44 (48.59; 77.77)	1.18 (1.13; 1.24)	15.34 (15.04; 15.65)	74.80 (59.96; 86.75)
Sudan	20.69 (12.76; 35.71)	0.27 (0.22; 0.31)	3.66 (2.88; 4.44)	21.45 (13.34; 36.05)	0.48 (0.46; 0.51)	6.01 (5.20; 6.81)	22.77 (13.77; 39.59)
Syrian Arab Republic	20.80 (11.12; 34.00)	0.39 (-0.40; 1.17)	5.34 (4.57; 6.10)	21.91 (12.88; 34.75)	-0.10 (-0.15; -0.05)	-1.18 (-1.93; -0.43)	21.62 (11.14; 35.49)
Tunisia	25.14 (13.57; 38.96)	2.26 (1.77; 2.75)	35.09 (34.31; 35.86)	33.97 (18.42; 47.83)	1.56 (1.50; 1.62)	20.71 (20.06; 21.36)	41.20 (23.79; 56.97)
Turkey	26.11 (14.32; 40.98)	3.36 (2.35; 4.38)	56.04 (55.24; 56.84)	40.74 (25.00; 57.25)	2.52 (2.30; 2.74)	35.34 (34.78; 35.90)	56.18 (39.20; 72.47)
United Arab Emirates	54.37 (38.77; 69.85)	-2.17 (-2.66; -1.68)	-25.60 (-26; -25.21)	40.45 (25.83; 55.16)	-0.79 (-0.83; -0.76)	-9.20 (-9.73; -8.67)	36.65 (21.72; 52.49)
Yemen	29.15 (18.79; 49.09)	0.64 (0.35; 0.93)	8.97 (8.22; 9.72)	31.76 (20.94; 52.36)	1.14 (1.07; 1.22)	14.81 (14.09; 15.53)	36.52 (23.87; 57.03)
South Asia	18.05 (12.28; 29.07)	1.02 (0.52; 1.53)	14.69 (14.03; 15.36)	20.70 (13.63; 30.94)	2.10 (2.08; 2.12)	28.77 (28.09; 29.45)	26.90 (17.74; 40.12)
South Asia	18.05 (12.28; 29.07)	1.02 (0.52; 1.53)	14.69 (14.03; 15.36)	20.70 (13.63; 30.94)	2.10 (2.08; 2.12)	28.77 (28.09; 29.45)	26.90 (17.74; 40.12)
Bangladesh	37.84 (24.33; 59.85)	-2.00 (-2.26; -1.74)	-23.83 (-24.45; -23.20)	28.83 (18.10; 49.36)	-0.71 (-0.72; -0.69)	-8.29 (-9.07; -7.52)	26.33 (14.76; 46.49)
Bhutan	31.90 (20.26; 53.94)	-2.02 (-2.12; -1.91)	-23.87 (-24.55; -23.19)	24.28 (15.05; 42.41)	-1.16 (-1.20; -1.12)	-13.22 (-14.03; -12.42)	20.95 (11.40; 38.85)
India	13.68 (8.21; 23.22)	2.26 (1.66; 2.86)	35.06 (34.21; 35.92)	18.48 (10.93; 28.90)	2.86 (2.83; 2.90)	40.98 (40.16; 41.80)	26.41 (15.86; 40.56)
Nepal	31.52 (19.70; 52.89)	-3.22 (-3.85; -2.58)	-35.66 (-36.31; -35)	20.28 (12.22; 36.49)	-0.99 (-1.11; -0.87)	-11.39 (-12.25; -10.54)	17.84 (9.42; 33.97)
Pakistan	33.96 (22.90; 53.76)	-0.33 (-0.45; -0.21)	-4.37 (-5.02; -3.73)	32.48 (21.53; 52.73)	0.03 (0.03; 0.04)	1 (0.30; 1.71)	32.79 (20.46; 54.00)
Southeast Asia, East Asia, and Oceania	31.16 (21.43; 50.74)	-1.60 (-2.14; -1.06)	-19.55 (-20.13; -18.98)	25.07 (17.49; 38.27)	0.78 (0.70; 0.86)	9.92 (9.30; 10.54)	27.58 (18.96; 42.08)
East Asia	32.55 (22.07; 53.37)	-2.05 (-2.69; -1.41)	-24.35 (-24.93; -23.76)	24.63 (16.87; 38.29)	0.46 (0.38; 0.54)	5.75 (5.04; 6.46)	26.03 (15.04; 42.65)
China	32.80 (22.19; 53.78)	-2.11 (-2.75; -1.47)	-24.99 (-25.58; -24.41)	24.60 (16.87; 38.29)	0.44 (0.36; 0.53)	5.53 (4.81; 6.25)	25.95 (14.68; 42.91)
Democratic People's Republic of Korea	33.12 (21.43; 55.09)	-1.32 (-1.88; -0.75)	-16.33 (-17.01; -15.66)	27.71 (17.17; 47.02)	-0.33 (-0.34; -0.33)	-3.96 (-4.71; -3.21)	26.58 (15.82; 44.69)
Taiwan (Province of China)	18.51 (11.17; 31.77)	2.00 (1.13; 2.87)	30.55 (29.69; 31.40)	24.17 (13.49; 37.48)	2.09 (2.03; 2.14)	28.54 (27.68; 29.40)	31.40 (16.93; 51.04)
Oceania	19.40 (12.55; 31.08)	0.56 (0.34; 0.77)	7.80 (7.10; 8.51)	20.91 (13.44; 33.53)	0.70 (0.60; 0.79)	8.80 (8.06; 9.54)	22.77 (14.34; 37.99)
American Samoa	30.63 (17.41; 47.26)	0.00 (-0.13; 0.14)	0.04 (-0.62; 0.70)	30.64 (17.61; 45.24)	0.21 (0.17; 0.25)	2.62 (1.95; 3.29)	31.46 (17.14; 47.45)
Cook Islands	24.29 (12.62; 39.57)	3.65 (3.45; 3.86)	62.07 (61.23; 62.91)	39.36 (24.53; 55.39)	1.95 (1.89; 2.01)	26.44 (25.88; 27)	50.25 (34.21; 66.36)
Fiji	20.89 (11.85; 34.03)	1.68 (1.43; 1.93)	25.13 (24.31; 25.94)	26.14 (14.40; 40.24)	1.41 (1.37; 1.45)	18.56 (17.81; 19.31)	31.15 (17.37; 47.36)
Guam	42.18 (26.12; 58.38)	1.58 (1.34; 1.82)	23.46 (22.90; 24.01)	52.08 (34.71; 68.76)	0.59 (0.57; 0.61)	7.44 (6.97; 7.90)	56.09 (38.04; 72.55)
Kiribati	16.97 (9.73; 29.25)	0.37 (0.16; 0.58)	5.06 (4.26; 5.86)	17.83 (9.67; 28.67)	0.38 (0.36; 0.40)	4.22 (3.46; 4.99)	18.60 (9.96; 29.51)
Marshall Islands	18.18 (10.78; 31.20)	0.52 (0.46; 0.57)	7.30 (6.51; 8.09)	19.50 (11.41; 31.80)	0.52 (0.52; 0.53)	6.59 (5.83; 7.35)	20.84 (12.35; 34.08)
Micronesia (Federated States of)	18.27 (10.77; 31.14)	0.28 (0.20; 0.35)	3.78 (3; 4.55)	18.96 (10.80; 30.55)	0.22 (0.22; 0.23)	3 (2.24; 3.76)	19.55 (11.07; 31.95)
Nauru	25.64 (12.99; 40.24)	-0.36 (-1.38; 0.67)	-4.80 (-5.53; -4.06)	24.41 (12.75; 38.63)	1.08 (1.05; 1.11)	14.01 (13.21; 14.81)	27.95 (13.80; 43.36)
Niue	20.98 (11.08; 35.04)	1.59 (1.42; 1.77)	23.72 (22.87; 24.57)	25.95 (14.11; 40.32)	1.47 (1.42; 1.52)	19.42 (18.68; 20.17)	31.21 (18.27; 47.03)
Northern Mariana Islands	40.71 (25.30; 57.79)	-0.57 (-0.69; -0.44)	-7.34 (-7.89; -6.79)	37.72 (22.39; 53.64)	-0.18 (-0.20; -0.16)	-2.21 (-2.79; -1.63)	36.86 (21.80; 52.23)
Palau	22.78 (11.78; 36.37)	1.49 (1.35; 1.63)	22.03 (21.23; 22.83)	27.79 (14.69; 41.76)	1.15 (1.10; 1.19)	14.86 (14.14; 15.59)	32.01 (17.32; 46.98)
Papua New Guinea	17.53 (10.24; 29.63)	0.96 (0.78; 1.14)	13.73 (12.91; 14.55)	19.94 (12.08; 33.36)	0.92 (0.83; 1.00)	11.73 (10.91; 12.55)	22.32 (13.61; 38.65)
Samoa	20.77 (11.11; 33.24)	1.88 (1.15; 2.61)	28.53 (27.69; 29.36)	26.69 (13.89; 40.74)	0.58 (0.56; 0.59)	7.27 (6.52; 8.02)	28.68 (14.74; 44.54)

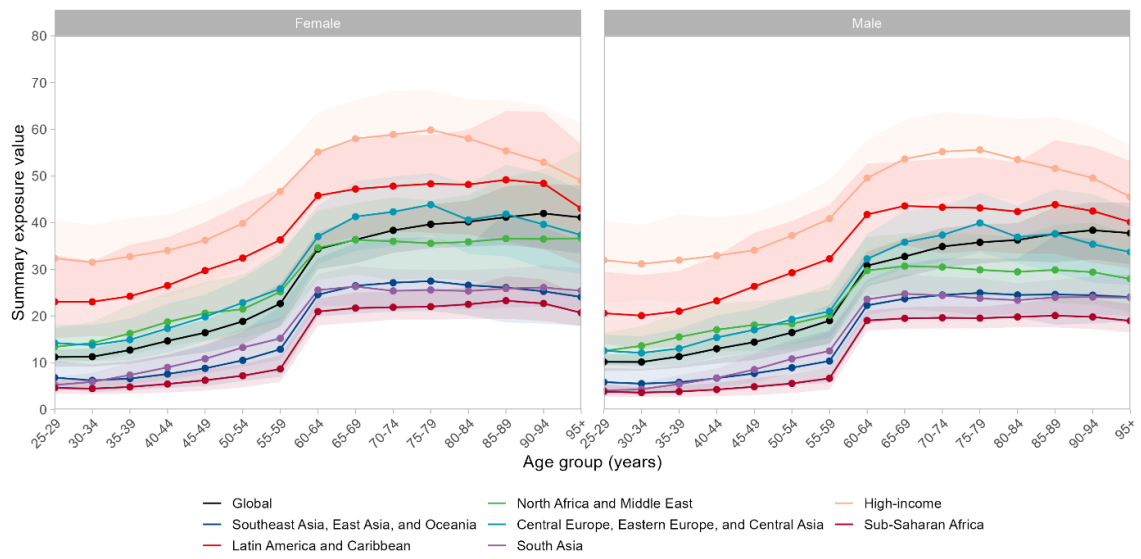
Solomon Islands	21.61 (13.24; 38.03)	-1.02 (-1.42; -0.63)	-12.95 (-13.68; -12.21)	18.82 (11.76; 31.38)	-0.07 (-0.14; 0.01)	-0.84 (-1.58; -0.10)	18.64 (11.38; 31.29)
Tokelau	20.26 (12.29; 33.90)	0.48 (0.32; 0.64)	13.56 (12.78; 14.34)	23.01 (13.23; 36.25)	1.48 (1.43; 1.54)	19.58 (18.79; 20.36)	27.64 (15.65; 43.87)
Tonga	18.75 (11.10; 31.44)	0.89 (0.76; 1.03)	12.69 (11.89; 13.49)	21.13 (11.62; 33.75)	0.71 (0.66; 0.75)	8.94 (8.19; 9.69)	23.07 (13.01; 35.75)
Tuvalu	22.11 (14.14; 37.51)	-0.30 (-0.37; -0.23)	-3.97 (-4.69; -3.25)	21.24 (12.99; 34.75)	-0.07 (-0.08; -0.07)	0.25 (-0.51; 1.01)	21.29 (12.69; 36.38)
Vanuatu	18.41 (10.91; 31.48)	0.15 (0.03; 0.27)	1.98 (1.21; 2.76)	18.77 (10.71; 30.34)	0.32 (0.29; 0.35)	3.91 (3.16; 4.66)	19.52 (11.02; 31.12)
Southeast Asia	26.77 (18.71; 42.84)	-0.17 (-0.36; 0.02)	-2.29 (-2.86; -1.71)	26.16 (19.18; 38.47)	1.16 (1.08; 1.23)	14.99 (14.43; 15.55)	30.18 (21.59; 43.51)
Cambodia	21.28 (12.60; 37.15)	-0.66 (-1.07; -0.25)	-8.51 (-9.25; -7.76)	19.47 (11.96; 32.11)	0.51 (0.49; 0.53)	6.40 (5.63; 7.18)	20.74 (12.48; 34.84)
Indonesia	31.13 (20.86; 51.34)	-0.99 (-1.37; -0.62)	-12.56 (-13.21; -11.92)	27.22 (18.75; 44.76)	0.24 (0.08; 0.40)	2.97 (2.20; 3.75)	27.95 (14.90; 47.83)
Lao People's Democratic Republic	22.41 (13.85; 39.43)	-0.35 (-0.63; -0.07)	-4.58 (-5.33; -3.83)	21.38 (13.00; 34.52)	0.60 (0.59; 0.62)	7.56 (6.82; 8.29)	23.03 (14.00; 36.93)
Malaysia	17.36 (10.48; 29.99)	2.31 (1.32; 3.31)	35.97 (35.06; 36.89)	23.60 (12.66; 37.80)	3.24 (3.07; 3.40)	47.31 (46.45; 48.18)	35.25 (19.81; 52.51)
Maldives	26.91 (17.43; 44.91)	0.40 (0.18; 0.62)	5.50 (4.77; 6.23)	28.39 (19.09; 47.19)	0.51 (0.43; 0.59)	6.36 (5.61; 7.12)	30.22 (18.89; 51.39)
Mauritius	21.95 (12.26; 35.25)	2.76 (2.36; 3.17)	44.36 (43.54; 45.18)	31.69 (18.78; 46.51)	1.86 (1.83; 1.89)	25.14 (24.48; 25.79)	39.96 (24.63; 56.00)
Myanmar	25.95 (15.85; 44.16)	-1.66 (-2.36; -0.96)	-20.18 (-20.85; -19.52)	20.71 (13.03; 32.88)	-0.02 (-0.03; 0.00)	-0.23 (-0.93; 0.47)	20.65 (12.25; 33.51)
Philippines	28.28 (19.91; 42.01)	1.04 (0.47; 1.61)	14.92 (14.37; 15.48)	32.50 (22.65; 44.78)	1.72 (1.67; 1.78)	23.09 (22.57; 23.62)	40.28 (28.97; 54.82)
Seychelles	31.93 (21.66; 50.14)	0.18 (0.02; 0.35)	2.50 (1.86; 3.14)	32.73 (22.65; 51.66)	0.65 (0.64; 0.67)	8.22 (7.54; 8.90)	35.50 (22.73; 56.59)
Sri Lanka	19.04 (11.27; 32.75)	2.02 (1.82; 2.22)	30.85 (30.01; 31.70)	24.91 (14.48; 38.45)	1.92 (1.85; 2.00)	26.06 (25.34; 26.78)	31.62 (19.33; 46.28)
Thailand	19.09 (11.24; 32.83)	5.09 (4.95; 5.22)	95.07 (94.08; 96.07)	37.24 (22.54; 53.68)	3.18 (3.05; 3.31)	46.35 (45.73; 46.96)	55.33 (37.11; 71.55)
Timor-Leste	22.04 (13.36; 39.07)	2.36 (1.81; 2.90)	36.84 (35.94; 37.74)	30.15 (19.99; 50.04)	1.65 (1.62; 1.67)	21.88 (21.13; 22.62)	37.04 (24.76; 58.34)
Vietnam	27.13 (17.25; 47.44)	-3.75 (-4.54; -2.96)	-40.25 (-40.90; -39.60)	16.21 (9.98; 28.24)	-1.00 (-1.18; -0.83)	-11.55 (-12.36; -10.74)	14.22 (7.44; 26.11)
Sub-Saharan Africa	30.53 (22.42; 46.07)	-1.34 (-1.80; -0.87)	-16.58 (-17.10; -16.07)	25.46 (18.28; 39.18)	-0.15 (-0.18; -0.11)	-1.77 (-2.35; -1.19)	24.98 (17.60; 38.65)
Central Sub-Saharan Africa	21.43 (14.11; 34.92)	-0.40 (-0.71; -0.09)	-5.29 (-5.97; -4.62)	20.30 (13.47; 33.57)	0.38 (0.35; 0.42)	4.77 (4.06; 5.48)	21.28 (14.21; 34.74)
Angola	32.11 (21.37; 53.15)	-1.77 (-2.57; -0.96)	-21.36 (-21.98; -20.75)	25.25 (16.54; 40.23)	0.39 (0.32; 0.46)	4.87 (4.14; 5.60)	26.46 (15.68; 43.84)
Central African Republic	20.47 (12.64; 35.12)	-1.08 (-1.43; -0.73)	-13.59 (-14.33; -12.85)	17.69 (10.38; 30.81)	-2.39 (-2.55; -2.22)	-8.39 (-9.20; -7.59)	16.16 (9.14; 29.06)
Congo	24.77 (15.98; 40.91)	-0.20 (-0.46; 0.06)	-2.69 (-3.36; -2.02)	24.11 (16.05; 37.94)	0.45 (0.42; 0.49)	5.67 (5; 6.34)	25.50 (16.95; 40.59)
Democratic Republic of the Congo	18.29 (10.43; 30.61)	-0.06 (-0.20; 0.08)	-0.82 (-1.60; 0.04)	18.14 (11.14; 31.30)	0.28 (0.26; 0.30)	3.43 (2.64; 4.22)	18.78 (11.70; 31.99)
Equatorial Guinea	20.33 (12.57; 36.39)	4.01 (2.52; 5.51)	69.76 (68.86; 70.65)	34.51 (21.95; 49.68)	1.60 (1.48; 1.73)	21.32 (20.66; 21.99)	42.06 (25.21; 61.83)
Gabon	27.74 (18.26; 43.98)	0.11 (-0.01; 0.23)	1.45 (0.82; 2.08)	28.15 (17.89; 41.91)	0.50 (0.46; 0.54)	6.23 (5.56; 6.91)	29.93 (18.43; 48.01)
Eastern Sub-Saharan Africa	23.80 (16.61; 38.69)	-0.17 (-0.31; -0.03)	-5.24 (-5.86; -4.61)	22.55 (15.64; 35.45)	0.23 (0.19; 0.26)	2.82 (2.19; 3.45)	23.18 (15.79; 36.05)
Burundi	18.69 (11.35; 32.63)	-0.66 (-0.99; -0.34)	-8.59 (-9.34; -7.84)	17.08 (10.39; 28.90)	-0.26 (-0.26; -0.26)	-2.59 (-3.34; -1.84)	16.63 (10.28; 28.13)
Comoros	19.12 (10.75; 32.62)	-0.16 (-0.18; -0.14)	-2.26 (-3.06; -1.47)	18.69 (10.35; 31.50)	0.26 (0.25; 0.27)	3.20 (2.38; 4.02)	19.30 (10.46; 32.36)
Djibouti	44.04 (25.92; 83.97)	-3.64 (-4.58; -2.69)	-39.29 (-40.09; -38.49)	26.74 (14.04; 53.77)	-0.92 (-1.00; -0.83)	-10.62 (-11.69; -9.55)	23.77 (10.62; 51.10)
Eritrea	18.04 (10.68; 32.41)	-0.28 (-0.36; -0.21)	-3.78 (-4.57; -2.98)	17.36 (10.29; 29.09)	0.15 (0.09; 0.20)	1.78 (1.03; 2.54)	17.67 (10.49; 28.97)
Ethiopia	32.84 (21.75; 53.86)	-1.39 (-1.61; -1.17)	-17.18 (-17.83; -16.53)	27.19 (18.34; 46.31)	-0.53 (-0.62; -0.43)	-6.21 (-6.93; -5.48)	25.40 (16.28; 43.79)
Kenya	29.68 (20.86; 45.92)	-0.25 (-0.38; -0.12)	-3.28 (-3.85; -2.72)	28.70 (20.26; 42.18)	0.16 (0.15; 0.16)	1.92 (1.37; 2.47)	29.28 (20.17; 43.12)
Madagascar	18.58 (10.87; 32.11)	-0.05 (-0.14; 0.04)	-0.65 (-1.43; 0.13)	18.46 (10.81; 30.54)	0.39 (0.32; 0.45)	4.79 (4.02; 5.57)	19.35 (11.04; 31.70)
Malawi	17.77 (10.83; 32.15)	0.11 (0.08; 0.14)	1.46 (0.63; 2.29)	18.03 (9.16; 29.51)	0.25 (0.22; 0.28)	3.06 (2.22; 3.90)	18.59 (9.28; 31.55)
Mozambique	18.25 (11.06; 32.04)	-0.29 (-0.65; 0.07)	-3.86 (-4.65; -3.08)	17.55 (9.39; 28.70)	0.23 (0.21; 0.24)	5.29 (4.49; 6.10)	18.50 (9.97; 30.67)
Rwanda	19.98 (12.20; 34.80)	-0.46 (-0.71; -0.22)	-6.07 (-6.84; -5.30)	18.76 (10.85; 31.79)	0.45 (0.40; 0.50)	5.57 (4.77; 6.36)	19.81 (11.47; 32.73)
Somalia	18.84 (11.40; 33.96)	-0.20 (-0.37; -0.03)	-2.70 (-3.52; -1.87)	18.33 (10.73; 32.16)	0.09 (0.09; 0.10)	1.15 (0.32; 1.97)	18.54 (10.89; 32.30)
South Sudan	21.48 (11.90; 34.61)	0.79 (0.56; 1.02)	11.19 (10.38; 12.01)	23.89 (11.60; 38.41)	0.22 (0.17; 0.27)	6.37 (5.56; 7.19)	25.43 (12.47; 40.77)
Uganda	18.27 (11.30; 31.38)	0.40 (0.39; 0.41)	5.48 (4.68; 6.27)	19.27 (11.34; 32.31)	0.93 (0.84; 1.01)	11.88 (11.08; 12.69)	21.59 (12.36; 35.35)
United Republic of Tanzania	18.34 (10.64; 30.66)	0.60 (0.56; 0.64)	8.45 (7.65; 9.25)	19.89 (11.63; 33.26)	1.30 (1.26; 1.35)	17.03 (16.20; 17.85)	23.35 (13.39; 38.23)

Zambia	21.96 (13.84; 38.06)	0.48 (0.27; 0.69)	6.66 (5.87; 7.45)	23.43 (14.54; 39.28)	0.69 (0.65; 0.74)	7.69 (6.90; 8.47)	25.28 (15.74; 42.84)
Southern Sub-Saharan Africa	27.97 (19.60; 41.42)	1.02 (0.86; 1.19)	14.71 (14.16; 15.26)	32.09 (22.00; 43.82)	1.02 (0.96; 1.07)	13.07 (12.56; 13.57)	36.41 (25.35; 49.38)
Botswana	26.87 (17.62; 43.59)	0.55 (0.32; 0.78)	7.63 (6.96; 8.31)	28.92 (19.42; 44.57)	1.23 (1.09; 1.37)	16.03 (15.36; 16.70)	33.61 (21.08; 50.77)
Eswatini	22.96 (14.36; 37.85)	0.57 (0.43; 0.72)	7.99 (7.27; 8.70)	24.79 (15.68; 38.73)	0.60 (0.55; 0.65)	7.54 (6.86; 8.22)	26.70 (16.75; 41.54)
Lesotho	19.68 (10.14; 33.04)	2.36 (2.02; 2.70)	36.93 (35.99; 37.87)	26.94 (13.64; 42.48)	1.51 (1.48; 1.53)	19.92 (19.14; 20.71)	32.50 (17.26; 48.35)
Namibia	26.50 (17.58; 44.08)	0.72 (0.52; 0.92)	10.10 (9.41; 10.79)	29.18 (19.88; 45.13)	0.74 (0.64; 0.83)	9.35 (8.73; 9.97)	31.93 (21.68; 47.72)
South Africa	29.61 (20.40; 42.62)	1.28 (1.09; 1.47)	18.62 (18.06; 19.17)	35.12 (23.79; 48.00)	1.45 (1.42; 1.49)	19.17 (18.66; 19.68)	42.09 (28.88; 55.65)
Zimbabwe	22.93 (14.38; 37.42)	-0.87 (-1.16; -0.59)	-11.12 (-11.81; -10.44)	20.38 (12.44; 33.68)	-0.16 (-0.17; -0.14)	-1.88 (-2.63; -1.14)	19.97 (11.74; 33.40)
Western Sub-Saharan Africa	39.75 (28.70; 60.10)	-2.53 (-3.31; -1.75)	-29.19 (-29.68; -28.70)	28.15 (20.06; 43.74)	-0.53 (-0.57; -0.50)	-6.30 (-6.91; -5.69)	26.29 (17.38; 42.30)
Benin	37.67 (25.16; 60.38)	-3.45 (-4.51; -2.37)	-37.64 (-38.22; -37.06)	23.49 (15.11; 41.39)	-1.34 (-1.50; -1.17)	-15.11 (-15.91; -14.30)	19.79 (10.55; 37.50)
Burkina Faso	40.19 (27.05; 62.30)	-3.74 (-4.80; -2.67)	-40.15 (-40.68; -39.61)	24.06 (15.15; 40.41)	-2.25 (-2.27; -2.23)	-24.07 (-24.82; -23.33)	18.11 (8.69; 34.04)
Cabo Verde	40.83 (27.83; 62.40)	-1.29 (-1.38; -1.19)	-15.99 (-16.56; -15.41)	34.30 (23.06; 54.95)	-0.93 (-0.93; -0.92)	-10.24 (-10.93; -9.56)	30.66 (19.19; 53.54)
Cameroon	36.63 (24.54; 58.23)	-2.67 (-3.24; -2.10)	-30.58 (-31.17; -29.98)	25.43 (16.08; 43.45)	-0.91 (-0.95; -0.86)	-10.48 (-11.25; -9.72)	22.65 (13.52; 41.07)
Chad	45.90 (32.45; 68.19)	-2.38 (-3.04; -1.72)	-27.69 (-28.21; -27.17)	33.19 (22.13; 54.18)	-1.51 (-1.56; -1.46)	-16.92 (-17.62; -16.23)	27.44 (15.55; 48.63)
Côte d'Ivoire	29.06 (18.82; 48.13)	-1.96 (-2.39; -1.53)	-23.41 (-24.05; -22.78)	22.26 (14.36; 36.80)	-0.74 (-0.84; -0.64)	-8.65 (-9.37; -7.93)	20.22 (12.60; 35.33)
Gambia	31.49 (20.77; 50.82)	-2.21 (-2.91; -1.50)	-25.96 (-26.59; -25.34)	23.32 (14.27; 39.85)	-0.52 (-0.65; -0.39)	-6.11 (-6.88; -5.34)	21.79 (13.08; 38.09)
Ghana	38.32 (26.05; 60.67)	-4.04 (-5.39; -2.67)	-42.60 (-43.13; -42.06)	22.00 (13.32; 35.28)	-0.83 (-0.93; -0.73)	-9.59 (-10.32; -8.87)	19.79 (10.34; 33.34)
Guinea	32.86 (21.48; 55.55)	-3.00 (-3.53; -2.47)	-33.64 (-34.28; -33)	21.80 (14.08; 38.85)	-2.04 (-2.21; -1.87)	-22.16 (-22.90; -21.41)	16.81 (9.50; 30.16)
Guinea-Bissau	37.35 (24.50; 59.19)	-1.81 (-2.14; -1.49)	-21.85 (-22.48; -21.23)	29.19 (19.10; 50.38)	-1.16 (-1.28; -1.04)	-13.21 (-13.96; -12.46)	25.19 (15.22; 45.51)
Liberia	28.12 (17.80; 47.75)	-1.11 (-1.34; -0.88)	-13.96 (-14.68; -13.25)	24.19 (15.29; 41.81)	-0.48 (-0.54; -0.43)	-5.74 (-6.51; -4.97)	22.75 (14.01; 40.22)
Mali	32.20 (21.11; 53.07)	-3.13 (-4.29; -1.95)	-34.83 (-35.44; -34.22)	20.98 (13.15; 35.92)	-1.47 (-1.51; -1.43)	-16.39 (-17.15; -15.64)	17.46 (8.76; 30.88)
Mauritania	30.18 (19.55; 50.02)	-2.12 (-2.90; -1.34)	-25.08 (-25.72; -24.44)	22.61 (14.15; 37.96)	-0.16 (-0.20; -0.12)	-1.94 (-2.70; -1.18)	22.13 (12.97; 37.69)
Niger	31.84 (20.52; 52.90)	-3.56 (-4.72; -2.40)	-38.66 (-39.26; -38.05)	19.53 (12.44; 33.30)	-2.12 (-2.21; -2.03)	-22.95 (-23.74; -22.16)	14.94 (6.28; 28.67)
Nigeria	43.22 (31.23; 63.86)	-2.19 (-2.98; -1.39)	-25.77 (-26.26; -25.29)	32.08 (22.85; 49.50)	-0.02 (-0.05; 0.02)	-0.18 (-0.82; 0.45)	31.98 (19.93; 50.64)
Sao Tome and Principe	32.15 (20.90; 51.55)	-2.06 (-2.68; -1.44)	-24.46 (-25.09; -23.83)	24.29 (15.13; 41.60)	-0.28 (-0.29; -0.27)	-3.40 (-4.18; -2.62)	23.42 (13.70; 40.84)
Senegal	41.90 (29.36; 65.47)	-1.06 (-1.17; -0.94)	-13.34 (-13.94; -12.73)	36.31 (24.09; 59.52)	-0.61 (-0.68; -0.53)	-7.12 (-7.82; -6.43)	33.59 (21.30; 57.06)
Sierra Leone	42.83 (29.25; 66.15)	-1.94 (-2.37; -1.50)	-23.17 (-23.75; -22.60)	32.90 (21.28; 54.08)	-0.98 (-1.05; -0.90)	-11.24 (-11.94; -10.55)	29.07 (17.78; 49.49)
Togo	40.93 (27.65; 63.22)	-3.54 (-4.52; -2.55)	-38.41 (-38.95; -37.88)	25.21 (16.10; 41.66)	-1.25 (-1.35; -1.15)	-14.22 (-14.93; -13.50)	21.46 (12.00; 37.23)

Footnote:

Different colors reflect different geographic levels. Red: Global; Blue: Super-regions; Green: Regions; Yellow: Country.

Supplementary Figure 2. Burden of high sugar-sweetened beverages by sex in 2021.



Supplementary Table 2. Burden of non-communicable diseases attributed to a diet high in sugar-sweetened beverages in 21 GBD regions and 204 countries in 2021.

	Deaths (per 100,000)			YLDs (per 100,000)			YLLs (per 100,000)			DALYs (per 100,000)		
Location	NCD	Cardiovascular diseases	Diabetes and Kidney diseases	NCD	Cardiovascular diseases	Diabetes and Kidney diseases	NCD	Cardiovascular diseases	Diabetes and Kidney diseases	NCD	Cardiovascular diseases	Diabetes and Kidney diseases
Global	0.89 (0.40 ; 1.38)	0.17 (0.02; 0.31)	0.72 (0.37; 1.06)	21.49 (10.48; 35.37)	0.44 (0.17; 0.76)	21.05 (10.31; 34.63)	19.89 (8.63; 30.75)	3.71 (0.18; 7.08)	16.19 (8.49; 23.74)	41.39 (19.52; 63.92)	4.15 (0.36; 7.81)	37.24 (18.74; 56.15)
Central Europe, Eastern Europe, and Central Asia	0.98 (0.39 ; 1.55)	0.38 (0.07; 0.68)	0.60 (0.31; 0.88)	21.49 (10.10; 34.93)	0.65 (0.25; 1.11)	20.84 (9.85; 33.91)	20.51 (7.69; 32.77)	7.53 (0.90; 14.03)	12.97 (6.73; 18.87)	42.00 (18.29; 66.07)	8.19 (1.14; 15.09)	33.81 (17.03; 51.28)
Central Asia	0.82 (0.30 ; 1.35)	0.27 (0.01; 0.52)	0.55 (0.28; 0.82)	19.16 (8.84; 31.52)	0.42 (0.15; 0.72)	18.75 (8.69; 30.73)	20.26 (7.14; 34.33)	6.01 (-0.10; 11.82)	14.25 (7.33; 21.77)	39.43 (16.79; 62.94)	6.43 (0.07; 12.59)	32.99 (16.38; 51.11)
Armenia	0.31 (0.10 ; 0.53)	0.10 (0.00; 0.21)	0.20 (0.10; 0.32)	7.07 (3.21; 12.38)	0.16 (0.05; 0.30)	6.91 (3.15; 12.11)	7.07 (2.32; 12.05)	2.26 (-0.11; 4.62)	4.81 (2.47; 7.54)	14.14 (5.53; 23.34)	2.42 (-0.06; 4.89)	11.71 (5.76; 18.77)
Azerbaijan	0.86 (0.24 ; 1.54)	0.26 (-0.02; 0.56)	0.60 (0.25; 1.03)	17.63 (8.11; 30.25)	0.38 (0.12; 0.68)	17.25 (7.98; 29.60)	20.86 (5.72; 37.43)	5.82 (-0.54; 12.18)	15.04 (6.27; 25.84)	38.49 (13.97; 64.80)	6.20 (-0.42; 12.80)	32.29 (14.07; 52.62)
Georgia	0.64 (0.24 ; 1.05)	0.16 (0.02; 0.30)	0.48 (0.22; 0.78)	17.13 (7.67; 29.71)	0.25 (0.08; 0.45)	16.88 (7.58; 29.30)	15.20 (5.50; 25.05)	3.64 (0.19; 7.13)	11.56 (5.37; 18.53)	32.33 (13.63; 53.45)	3.89 (0.28; 7.51)	28.44 (13.23; 46.13)
Kazakhstan	0.88 (0.30 ; 1.53)	0.39 (0.04; 0.77)	0.49 (0.23; 0.80)	35.57 (15.74; 60.91)	0.66 (0.23; 1.20)	34.91 (15.49; 59.70)	19.19 (6.60; 33.81)	7.63 (0.32; 15.07)	11.56 (5.64; 18.60)	54.76 (22.87; 89.35)	8.29 (0.57; 16.24)	46.46 (21.65; 75.48)
Kyrgyzstan	0.50 (0.12 ; 0.93)	0.24 (0.00; 0.51)	0.26 (0.11; 0.43)	13.42 (5.74; 23.83)	0.32 (0.11; 0.59)	13.10 (5.60; 23.33)	12.36 (3.07; 22.13)	5.47 (-0.04; 11.12)	6.89 (3.13; 11.22)	25.78 (9.25; 44.34)	5.79 (0.08; 11.68)	19.99 (9.05; 33.35)
Mongolia	0.38 (0.11 ; 0.69)	0.15 (-0.01; 0.31)	0.23 (0.11; 0.39)	10.49 (4.77; 18.15)	0.36 (0.14; 0.64)	10.14 (4.57; 17.57)	9.65 (2.88; 17.63)	3.40 (-0.25; 7.29)	6.25 (2.88; 10.74)	20.14 (8.05; 34.77)	3.76 (-0.08; 7.92)	16.38 (7.72; 27.70)
Tajikistan	0.18 (0.05 ; 0.32)	0.08 (0.01; 0.16)	0.10 (0.04; 0.17)	3.06 (1.33; 5.60)	0.11 (0.04; 0.20)	2.96 (1.29; 5.40)	4.29 (1.25; 7.53)	1.69 (0.04; 3.36)	2.60 (1.18; 4.44)	7.36 (2.71; 12.72)	1.80 (0.08; 3.56)	5.55 (2.56; 9.30)
Turkmenistan	2.08 (0.75 ; 3.68)	0.70 (0.08; 1.45)	1.38 (0.66; 2.30)	25.20 (11.44; 42.51)	1.20 (0.48; 2.12)	24.00 (10.88; 40.78)	56.11 (20.25; 98.02)	17.10 (0.71; 35.50)	39.00 (18.80; 65.54)	81.30 (32.64; 138.67)	18.30 (1.22; 37.57)	63.00 (29.90; 101.86)
Uzbekistan	0.94 (0.33 ; 1.63)	0.25 (-0.01; 0.52)	0.69 (0.32; 1.16)	16.08 (7.30; 28.09)	0.32 (0.12; 0.59)	15.76 (7.17; 27.64)	24.28 (8.79; 42.61)	5.83 (-0.50; 12.63)	18.45 (8.45; 30.80)	40.36 (16.50; 67.86)	6.15 (-0.34; 13.24)	34.21 (16.22; 56.36)
Central Europe	1.50 (0.64 ; 2.34)	0.54 (0.13; 0.96)	0.96 (0.49; 1.40)	39.26 (18.14; 64.01)	1.14 (0.41; 1.98)	38.12 (17.71; 62.31)	30.51 (12.28; 47.67)	10.26 (1.84; 18.45)	20.24 (10.34; 29.46)	69.77 (31.87; 109.40)	11.40 (2.26; 20.45)	58.37 (29.46; 90.35)
Albania	0.89 (0.31 ; 1.55)	0.50 (0.09; 0.96)	0.39 (0.20; 0.63)	29.13 (13.47; 49.25)	0.93 (0.32; 1.68)	28.19 (13.06; 47.89)	16.25 (5.01; 28.50)	8.70 (0.80; 17.26)	7.54 (3.91; 12.12)	45.37 (19.51; 75.72)	9.64 (1.12; 18.66)	35.74 (17.43; 58.35)
Bosnia and Herzegovina	2.07 (0.87 ; 3.61)	0.40 (0.08; 0.76)	1.67 (0.79; 2.85)	41.58 (18.17; 72.04)	0.95 (0.35; 1.72)	40.64 (17.76; 70.21)	41.32 (17.54; 73.42)	7.60 (1.12; 15.29)	33.72 (16.08; 58.99)	82.90 (38.26; 137.85)	8.54 (1.58; 16.95)	74.36 (36.08; 122.50)
Bulgaria	2.15 (0.80 ; 3.53)	0.90 (0.20; 1.64)	1.25 (0.62; 1.93)	44.42 (20.29; 76.13)	1.33 (0.49; 2.31)	43.09 (19.59; 73.65)	48.37 (17.85; 79.34)	19.38 (3.07; 36.01)	28.99 (14.76; 44.64)	92.79 (37.71; 153.08)	20.71 (3.64; 37.88)	72.08 (34.53; 117.65)
Croatia	1.64 (0.73 ; 2.52)	0.44 (0.09; 0.78)	1.20 (0.61; 1.81)	43.10 (19.75; 71.39)	1.11 (0.40; 1.96)	41.99 (19.30; 69.67)	30.48 (13.06; 47.02)	7.77 (1.20; 14.26)	22.71 (11.49; 33.78)	73.58 (33.03; 117.49)	8.88 (1.68; 16.16)	64.70 (32.19; 101.91)
Czechia	1.50 (0.63 ; 2.44)	0.29 (0.04; 0.55)	1.21 (0.60; 1.92)	39.56 (18.30; 69.24)	0.95 (0.35; 1.70)	38.61 (17.88; 67.81)	27.68 (11.25; 46.08)	5.46 (0.36; 10.70)	22.22 (11.00; 35.49)	67.24 (31.07; 113.06)	6.42 (0.72; 12.28)	60.83 (30.06; 101.21)

Hungary	1.24 (0.50 ; 2.01)	0.32 (0.02; 0.63)	0.92 (0.48; 1.41)	38.31 (17.58; 64.26)	0.72 (0.24; 1.33)	37.59 (17.28; 63.29)	27.08 (10.42; 44.20)	7.12 (0.20; 14.20)	19.96 (10.33; 30.00)	65.39 (28.62; 105.84)	7.84 (0.48; 15.49)	57.55 (28.13; 91.49)
Montenegro	0.99 (0.37 ; 1.74)	0.32 (0.04; 0.63)	0.67 (0.31; 1.11)	21.94 (9.56; 38.32)	0.45 (0.14; 0.83)	21.49 (9.42; 37.59)	18.30 (6.88; 31.96)	5.37 (0.22; 11.04)	12.93 (6.23; 21.24)	40.24 (17.19; 68.08)	5.82 (0.35; 11.83)	34.42 (16.13; 57.42)
North Macedonia	2.57 (1.10 ; 4.34)	0.81 (0.27; 1.48)	1.77 (0.82; 2.87)	41.98 (18.94; 73.50)	0.84 (0.31; 1.55)	41.14 (18.57; 72.07)	46.51 (18.44; 76.71)	12.71 (3.19; 23.89)	33.80 (15.75; 53.81)	88.49 (40.12; 144.87)	13.55 (3.50; 25.36)	74.94 (35.38; 120.51)
Poland	1.39 (0.62 ; 2.18)	0.43 (0.10; 0.78)	0.97 (0.50; 1.45)	43.84 (20.55; 72.05)	1.06 (0.36; 1.83)	42.78 (20.12; 70.16)	28.78 (12.60; 45.37)	8.10 (1.36; 15.11)	20.69 (11.02; 30.61)	72.63 (34.28; 113.20)	9.16 (1.80; 17.03)	63.47 (31.92; 99.05)
Romania	1.74 (0.70 ; 2.76)	1.05 (0.34; 1.79)	0.69 (0.35; 1.05)	36.97 (17.15; 62.23)	1.96 (0.80; 3.40)	35.01 (16.22; 59.33)	35.57 (13.02; 58.44)	19.58 (4.62; 34.44)	15.99 (8.06; 24.22)	72.54 (30.58; 116.44)	21.54 (5.43; 37.42)	51.00 (24.67; 80.34)
Serbia	1.50 (0.63 ; 2.49)	0.44 (0.10; 0.83)	1.06 (0.51; 1.72)	33.77 (15.42; 57.91)	0.59 (0.20; 1.06)	33.19 (15.19; 56.92)	29.74 (12.18; 49.98)	7.82 (1.29; 15.46)	21.92 (10.40; 34.44)	63.51 (28.08; 105.33)	8.41 (1.50; 16.54)	55.11 (25.92; 90.69)
Slovakia	0.87 (0.32 ; 1.46)	0.41 (0.07; 0.75)	0.46 (0.22; 0.72)	21.92 (10.05; 36.61)	1.06 (0.42; 1.82)	20.86 (9.57; 34.97)	16.75 (5.87; 28.26)	7.14 (0.88; 13.43)	9.61 (4.76; 15.01)	38.67 (16.63; 62.75)	8.21 (1.32; 15.10)	30.47 (15.04; 48.92)
Slovenia	0.83 (0.37 ; 1.31)	0.23 (0.06; 0.39)	0.60 (0.29; 0.92)	31.72 (15.28; 53.23)	0.85 (0.27; 1.48)	30.87 (15.02; 51.83)	15.79 (6.86; 24.80)	3.66 (0.79; 6.49)	12.13 (6.07; 18.33)	47.51 (22.80; 76.56)	4.51 (1.09; 7.94)	43.00 (21.52; 69.13)
Eastern Europe	0.64 (0.22 ; 1.07)	0.29 (0.04; 0.52)	0.36 (0.18; 0.55)	11.12 (5.21; 17.95)	0.41 (0.15; 0.71)	10.71 (5.02; 17.26)	13.73 (4.42; 23.19)	6.05 (0.40; 11.52)	7.68 (3.94; 11.67)	24.86 (9.58; 39.24)	6.46 (0.58; 12.16)	18.39 (8.88; 27.62)
Belarus	0.27 (0.03 ; 0.53)	0.20 (0.00; 0.41)	0.07 (0.03; 0.12)	5.08 (2.25; 9.13)	0.20 (0.06; 0.38)	4.88 (2.18; 8.77)	6.21 (0.55; 12.32)	4.45 (- 0.27; 9.59)	1.76 (0.78; 2.89)	11.29 (3.34; 21.27)	4.66 (- 0.20; 9.89)	6.63 (3.16; 11.57)
Estonia	0.65 (0.26 ; 1.05)	0.14 (0.01; 0.27)	0.51 (0.24; 0.79)	21.39 (9.48; 36.98)	0.47 (0.17; 0.84)	20.92 (9.32; 36.08)	14.15 (5.39; 22.99)	2.75 (0.16; 5.52)	11.40 (5.36; 17.90)	35.54 (15.17; 59.21)	3.22 (0.32; 6.35)	32.32 (14.93; 53.35)
Latvia	0.62 (0.23 ; 1.07)	0.23 (0.04; 0.45)	0.38 (0.19; 0.62)	12.97 (5.67; 22.34)	0.38 (0.15; 0.72)	12.59 (5.51; 21.65)	13.93 (5.26; 24.08)	4.44 (0.53; 8.71)	9.49 (4.68; 15.09)	26.90 (11.38; 46.55)	4.82 (0.68; 9.31)	22.08 (10.41; 36.82)
Lithuania	0.75 (0.26 ; 1.35)	0.32 (0.04; 0.62)	0.44 (0.21; 0.73)	17.89 (8.40; 30.20)	0.55 (0.21; 1.00)	17.34 (8.22; 29.07)	16.83 (5.95; 29.67)	6.13 (0.42; 12.27)	10.70 (5.31; 17.50)	34.72 (15.07; 57.91)	6.68 (0.64; 13.06)	28.04 (14.10; 44.71)
Republic of Moldova	0.20 (0.05 ; 0.34)	0.10 (0.01; 0.20)	0.10 (0.05; 0.16)	5.68 (2.48; 9.62)	0.15 (0.05; 0.28)	5.53 (2.43; 9.39)	4.79 (1.27; 8.42)	2.31 (0.05; 4.62)	2.48 (1.22; 3.93)	10.48 (3.85; 17.19)	2.47 (0.11; 4.87)	8.01 (3.75; 12.73)
Russian Federation	0.82 (0.31 ; 1.35)	0.34 (0.05; 0.62)	0.49 (0.25; 0.75)	13.50 (6.38; 22.01)	0.50 (0.18; 0.86)	13.00 (6.17; 21.27)	17.41 (6.13; 29.09)	7.14 (0.61; 13.57)	10.27 (5.28; 15.62)	30.90 (12.14; 48.98)	7.64 (0.81; 14.29)	23.26 (11.22; 35.17)
Ukraine	0.20 (0.03 ; 0.38)	0.17 (0.01; 0.32)	0.04 (0.02; 0.06)	4.55 (2.11; 7.51)	0.18 (0.07; 0.33)	4.37 (2.05; 7.25)	4.58 (0.48; 8.76)	3.50 (- 0.04; 7.02)	1.08 (0.50; 1.73)	9.13 (2.69; 15.82)	3.69 (0.04; 7.32)	5.45 (2.54; 8.73)
High-income	0.94 (0.42 ; 1.44)	0.17 (0.02; 0.32)	0.77 (0.40; 1.12)	43.36 (21.12; 70.78)	0.89 (0.36; 1.52)	42.47 (20.73; 69.34)	20.85 (8.88; 32.01)	3.95 (- 0.01; 7.87)	16.90 (9.03; 24.49)	64.21 (30.68; 99.16)	4.84 (0.35; 9.27)	59.37 (30.13; 91.44)
Australasia	0.82 (0.38 ; 1.26)	0.17 (0.04; 0.30)	0.64 (0.34; 0.97)	24.95 (11.57; 41.10)	0.87 (0.36; 1.45)	24.08 (11.18; 39.85)	15.17 (6.73; 23.80)	2.94 (0.31; 5.55)	12.24 (6.46; 18.08)	40.13 (18.52; 62.96)	3.81 (0.70; 6.80)	36.31 (17.72; 56.54)
Australia	0.85 (0.40 ; 1.33)	0.17 (0.04; 0.31)	0.68 (0.35; 1.04)	25.34 (11.66; 42.21)	0.92 (0.38; 1.53)	24.42 (11.23; 40.95)	15.66 (6.95; 24.60)	2.96 (0.31; 5.57)	12.71 (6.63; 18.72)	41.01 (18.85; 65.03)	3.88 (0.72; 6.91)	37.12 (18.06; 58.58)
New Zealand	0.61 (0.27 ; 0.98)	0.17 (0.04; 0.30)	0.44 (0.22; 0.68)	22.86 (10.57; 36.44)	0.62 (0.25; 1.05)	22.24 (10.28; 35.36)	12.46 (5.42; 19.83)	2.83 (0.30; 5.38)	9.63 (4.99; 14.68)	35.32 (15.95; 55.33)	3.44 (0.54; 6.44)	31.88 (15.39; 49.03)
High-income Asia Pacific	0.28 (0.13 ; 0.45)	0.09 (0.02; 0.15)	0.20 (0.10; 0.30)	29.75 (14.33; 48.89)	0.67 (0.29; 1.16)	29.08 (13.98; 48.00)	5.61 (2.42; 8.82)	1.54 (0.28; 2.86)	4.07 (2.13; 6.06)	35.36 (17.03; 56.96)	2.21 (0.57; 3.89)	33.15 (16.39; 53.35)

Brunei Darussalam	1.21 (0.55 ; 2.01)	0.10 (0.01; 0.19)	1.11 (0.53; 1.85)	30.69 (13.59; 54.33)	0.29 (0.12; 0.51)	30.40 (13.45; 53.93)	28.36 (12.04; 48.34)	2.35 (-0.04; 4.99)	26.01 (11.97; 43.51)	59.06 (26.69; 101.11)	2.64 (0.10; 5.40)	56.42 (26.28; 96.96)
Japan	0.24 (0.10 ; 0.40)	0.09 (0.02; 0.16)	0.15 (0.08; 0.25)	25.81 (12.40; 43.03)	0.68 (0.29; 1.18)	25.13 (12.05; 41.99)	4.45 (1.76; 7.13)	1.56 (0.26; 2.92)	2.88 (1.52; 4.41)	30.25 (14.35; 49.11)	2.24 (0.56; 3.99)	28.01 (13.83; 45.72)
Republic of Korea	0.45 (0.21 ; 0.71)	0.08 (0.02; 0.15)	0.36 (0.18; 0.56)	36.94 (17.14; 61.69)	0.59 (0.25; 1.02)	36.35 (16.89; 60.88)	8.98 (4.24; 14.08)	1.46 (0.30; 2.63)	7.52 (3.85; 11.49)	45.92 (21.90; 74.42)	2.05 (0.58; 3.62)	43.87 (21.23; 70.93)
Singapore	0.21 (0.07 ; 0.36)	0.07 (0.00; 0.15)	0.13 (0.07; 0.21)	34.35 (16.58; 56.99)	0.58 (0.25; 1.02)	33.77 (16.32; 56.04)	4.11 (1.23; 7.12)	1.61 (-0.09; 3.38)	2.50 (1.32; 3.78)	38.46 (18.18; 63.81)	2.19 (0.20; 4.21)	36.27 (17.70; 59.74)
High-income North America	1.61 (0.72 ; 2.44)	0.28 (0.01; 0.54)	1.33 (0.71; 1.92)	69.05 (33.61; 112.16)	1.51 (0.63; 2.57)	67.54 (32.94; 109.48)	39.00 (16.71; 60.01)	7.20 (-0.26; 14.64)	31.80 (17.02; 45.62)	108.05 (51.86; 166.17)	8.71 (0.36; 17.00)	99.34 (50.76; 151.96)
Canada	0.66 (0.28 ; 1.02)	0.10 (0.00; 0.20)	0.55 (0.27; 0.83)	34.29 (15.99; 60.43)	0.57 (0.22; 1.01)	33.72 (15.81; 59.46)	13.84 (5.84; 22.36)	2.33 (-0.14; 4.92)	11.51 (5.95; 17.43)	48.13 (21.94; 81.16)	2.90 (0.08; 5.91)	45.23 (21.37; 75.58)
Greenland	1.24 (0.53 ; 2.07)	0.26 (0.01; 0.58)	0.98 (0.52; 1.52)	29.92 (14.14; 50.52)	0.57 (0.21; 1.05)	29.35 (13.91; 49.59)	29.64 (11.65; 50.96)	6.67 (-0.57; 15.12)	22.97 (12.28; 35.81)	59.56 (26.21; 97.51)	7.24 (-0.37; 16.10)	52.32 (26.73; 82.25)
United States of America	1.72 (0.77 ; 2.63)	0.31 (0.01; 0.59)	1.42 (0.76; 2.07)	73.20 (35.48; 119.25)	1.62 (0.67; 2.76)	71.58 (34.76; 116.37)	42.01 (18.03; 64.39)	7.78 (-0.27; 15.78)	34.23 (18.32; 49.21)	115.21 (55.02; 176.36)	9.41 (0.39; 18.29)	105.80 (53.99; 160.94)
Southern Latin America	2.02 (0.96 ; 3.01)	0.26 (0.04; 0.49)	1.75 (0.91; 2.55)	53.28 (24.57; 88.57)	1.00 (0.40; 1.69)	52.28 (24.15; 86.93)	43.26 (20.19; 65.33)	5.75 (0.18; 11.16)	37.52 (19.71; 54.20)	96.55 (44.43; 150.92)	6.75 (0.57; 12.78)	89.80 (43.52; 137.20)
Argentina	2.35 (1.12 ; 3.53)	0.30 (0.05; 0.55)	2.05 (1.08; 3.02)	53.13 (24.56; 87.63)	1.13 (0.47; 1.89)	52.00 (24.12; 85.94)	51.44 (24.06; 78.12)	6.44 (0.20; 12.64)	45.00 (23.69; 66.18)	104.57 (48.33; 164.25)	7.57 (0.64; 14.32)	97.00 (47.65; 149.21)
Chile	1.30 (0.59 ; 1.97)	0.19 (0.03; 0.34)	1.11 (0.55; 1.64)	54.28 (24.35; 90.56)	0.76 (0.28; 1.28)	53.52 (24.07; 89.44)	25.62 (10.89; 39.77)	4.00 (0.14; 7.92)	21.62 (10.63; 31.62)	79.90 (35.51; 128.01)	4.76 (0.43; 8.91)	75.13 (34.98; 119.87)
Uruguay	2.07 (0.96 ; 3.18)	0.30 (0.05; 0.57)	1.77 (0.89; 2.66)	49.10 (22.95; 83.27)	0.86 (0.34; 1.52)	48.24 (22.55; 81.64)	43.73 (19.28; 67.16)	6.76 (0.26; 13.88)	36.97 (18.58; 55.25)	92.83 (43.18; 146.56)	7.62 (0.59; 15.24)	85.21 (42.56; 133.68)
Western Europe	0.67 (0.30 ; 1.04)	0.13 (0.02; 0.23)	0.55 (0.28; 0.81)	30.32 (14.17; 49.88)	0.49 (0.17; 0.86)	29.83 (14.02; 48.98)	11.93 (5.03; 18.46)	2.37 (0.07; 4.63)	9.55 (4.88; 13.97)	42.25 (19.73; 67.01)	2.87 (0.26; 5.39)	39.38 (19.35; 62.65)
Andorra	0.87 (0.37 ; 1.43)	0.15 (0.03; 0.29)	0.72 (0.34; 1.17)	32.93 (15.71; 55.73)	0.63 (0.22; 1.15)	32.31 (15.43; 54.66)	15.55 (6.16; 26.40)	2.77 (0.19; 5.44)	12.78 (5.92; 21.29)	48.49 (22.33; 77.80)	3.40 (0.42; 6.52)	45.09 (21.71; 72.01)
Austria	0.87 (0.38 ; 1.40)	0.16 (0.02; 0.30)	0.71 (0.35; 1.11)	19.62 (9.04; 32.91)	0.80 (0.31; 1.35)	18.83 (8.68; 31.58)	14.28 (5.94; 22.77)	2.67 (0.09; 5.17)	11.61 (5.86; 17.74)	33.90 (15.08; 54.02)	3.46 (0.44; 6.41)	30.44 (14.56; 48.72)
Belgium	0.64 (0.28 ; 0.99)	0.16 (0.03; 0.28)	0.48 (0.24; 0.72)	41.47 (19.50; 68.70)	0.70 (0.28; 1.23)	40.76 (19.20; 67.81)	11.44 (4.70; 18.06)	2.84 (0.34; 5.40)	8.60 (4.36; 12.80)	52.90 (24.05; 83.81)	3.54 (0.62; 6.67)	49.37 (23.44; 78.53)
Cyprus	1.25 (0.53 ; 2.07)	0.13 (0.01; 0.25)	1.13 (0.52; 1.82)	24.01 (10.57; 40.99)	0.19 (0.05; 0.36)	23.82 (10.50; 40.59)	20.60 (8.65; 32.68)	2.28 (-0.06; 4.72)	18.32 (8.87; 28.65)	44.62 (20.17; 70.63)	2.47 (0.01; 5.08)	42.15 (19.84; 65.35)
Denmark	0.83 (0.39 ; 1.32)	0.14 (0.03; 0.25)	0.69 (0.35; 1.07)	20.49 (10.15; 33.70)	0.50 (0.19; 0.86)	19.99 (9.97; 32.83)	14.45 (6.47; 22.47)	2.33 (0.34; 4.41)	12.12 (6.13; 18.21)	34.94 (16.48; 55.77)	2.82 (0.52; 5.28)	32.12 (16.29; 50.60)
Finland	0.40 (0.15 ; 0.66)	0.15 (0.02; 0.29)	0.25 (0.13; 0.37)	33.65 (16.31; 55.80)	0.61 (0.23; 1.09)	33.04 (16.06; 54.81)	7.59 (2.56; 12.34)	2.80 (0.07; 5.46)	4.78 (2.54; 7.06)	41.24 (18.92; 67.96)	3.42 (0.32; 6.38)	37.82 (18.61; 61.98)
France	0.52 (0.23 ; 0.82)	0.09 (0.02; 0.17)	0.43 (0.21; 0.66)	17.10 (8.02; 28.63)	0.52 (0.18; 0.91)	16.58 (7.79; 27.81)	9.18 (4.00; 14.18)	1.58 (0.14; 3.04)	7.60 (3.87; 11.25)	26.28 (12.19; 41.80)	2.10 (0.36; 3.87)	24.18 (11.83; 38.32)
Germany	0.92 (0.39 ; 1.47)	0.15 (0.01; 0.28)	0.77 (0.37; 1.18)	29.90 (14.47; 48.17)	0.56 (0.19; 0.96)	29.34 (14.27; 47.26)	16.63 (6.86; 25.95)	2.93 (-0.10; 5.77)	13.70 (6.87; 20.31)	46.53 (20.76; 72.75)	3.49 (0.12; 6.70)	43.04 (21.08; 66.07)

Greece	0.68 (0.29 ; 1.15)	0.21 (0.04; 0.42)	0.47 (0.24; 0.74)	29.19 (13.46; 49.36)	0.47 (0.18; 0.83)	28.72 (13.27; 48.65)	12.71 (4.85; 21.13)	3.99 (0.15; 7.90)	8.71 (4.53; 13.36)	41.89 (18.12; 69.74)	4.46 (0.37; 8.69)	37.43 (17.33; 61.60)
Iceland	0.36 (0.13 ; 0.62)	0.12 (0.01; 0.23)	0.24 (0.12; 0.39)	24.10 (11.30; 41.25)	0.55 (0.21; 1.00)	23.55 (11.08; 40.33)	6.47 (2.00; 11.25)	2.31 (0.01; 4.78)	4.15 (2.04; 6.56)	30.56 (14.05; 51.50)	2.86 (0.22; 5.71)	27.70 (13.62; 46.74)
Ireland	0.70 (0.28 ; 1.13)	0.20 (0.03; 0.39)	0.50 (0.25; 0.76)	32.80 (15.73; 53.41)	0.67 (0.22; 1.18)	32.12 (15.49; 52.37)	11.93 (4.13; 19.73)	3.76 (0.07; 7.44)	8.17 (4.11; 12.11)	44.73 (20.12; 71.21)	4.44 (0.28; 8.55)	40.29 (19.94; 63.60)
Israel	1.78 (0.86 ; 2.76)	0.11 (0.01; 0.22)	1.67 (0.84; 2.55)	42.53 (20.49; 71.24)	0.64 (0.21; 1.16)	41.89 (20.27; 70.17)	31.57 (14.99; 47.61)	2.05 (0.03; 3.96)	29.51 (14.99; 43.84)	74.10 (36.95; 116.14)	2.69 (0.25; 5.13)	71.40 (36.52; 111.16)
Italy	0.62 (0.27 ; 0.98)	0.13 (0.03; 0.23)	0.49 (0.24; 0.75)	17.92 (8.41; 30.14)	0.35 (0.12; 0.63)	17.57 (8.28; 29.47)	10.25 (4.56; 16.13)	1.93 (0.29; 3.63)	8.32 (4.23; 12.59)	28.16 (13.67; 45.61)	2.28 (0.41; 4.21)	25.88 (13.06; 41.55)
Luxembourg	0.51 (0.22 ; 0.83)	0.10 (0.01; 0.19)	0.42 (0.21; 0.66)	30.73 (14.83; 51.46)	0.39 (0.11; 0.73)	30.34 (14.67; 50.89)	9.53 (3.92; 15.44)	1.95 (- 0.03; 3.98)	7.58 (3.88; 11.45)	40.26 (18.31; 65.10)	2.34 (0.09; 4.64)	37.92 (18.28; 60.81)
Malta	1.44 (0.65 ; 2.33)	0.20 (0.01; 0.40)	1.24 (0.63; 1.98)	53.82 (25.76; 91.05)	0.53 (0.15; 0.99)	53.29 (25.54; 90.07)	28.15 (12.03; 45.21)	4.61 (- 0.34; 9.79)	23.54 (12.14; 35.86)	81.98 (38.78; 135.04)	5.14 (- 0.17; 10.72)	76.84 (38.76; 124.64)
Monaco	1.45 (0.56 ; 2.42)	0.74 (0.19; 1.39)	0.71 (0.36; 1.08)	47.86 (22.64; 77.09)	2.18 (0.81; 3.65)	45.68 (21.84; 73.76)	25.82 (8.17; 44.27)	13.49 (1.95; 25.82)	12.33 (6.17; 18.71)	73.68 (32.39; 115.99)	15.67 (2.87; 29.19)	58.01 (29.35; 89.74)
Netherlands	0.83 (0.39 ; 1.36)	0.16 (0.04; 0.30)	0.67 (0.34; 1.07)	30.23 (13.97; 51.64)	0.66 (0.25; 1.14)	29.57 (13.68; 50.50)	13.85 (6.28; 22.25)	2.65 (0.42; 4.86)	11.21 (5.74; 17.11)	44.08 (20.83; 70.31)	3.31 (0.66; 5.91)	40.78 (19.86; 64.94)
Norway	0.47 (0.19 ; 0.75)	0.13 (0.03; 0.24)	0.34 (0.16; 0.51)	22.99 (11.18; 38.47)	0.79 (0.33; 1.37)	22.20 (10.78; 37.22)	7.98 (3.21; 12.60)	2.09 (0.29; 3.95)	5.88 (2.95; 8.83)	30.97 (14.81; 49.92)	2.88 (0.60; 5.25)	28.09 (14.21; 45.69)
Portugal	0.91 (0.43 ; 1.42)	0.16 (0.05; 0.30)	0.75 (0.38; 1.11)	38.58 (18.42; 64.16)	0.36 (0.13; 0.62)	38.22 (18.28; 63.53)	15.65 (7.15; 24.39)	2.72 (0.47; 5.17)	12.93 (6.61; 19.35)	54.23 (25.75; 86.92)	3.08 (0.62; 5.76)	51.15 (25.02; 82.04)
San Marino	0.42 (0.16 ; 0.75)	0.12 (0.03; 0.23)	0.30 (0.13; 0.52)	30.21 (13.81; 50.89)	0.71 (0.26; 1.28)	29.50 (13.58; 49.80)	7.39 (2.66; 13.39)	2.03 (0.34; 4.10)	5.36 (2.33; 9.53)	37.60 (17.18; 61.29)	2.75 (0.63; 5.04)	34.85 (16.32; 56.79)
Spain	0.70 (0.32 ; 1.11)	0.12 (0.01; 0.21)	0.59 (0.30; 0.90)	53.39 (25.46; 89.17)	0.57 (0.20; 0.97)	52.82 (25.26; 88.27)	12.23 (5.09; 19.57)	2.49 (- 0.05; 4.96)	9.74 (5.12; 14.51)	65.62 (30.63; 106.49)	3.05 (0.20; 5.87)	62.56 (30.27; 100.87)
Sweden	0.58 (0.25 ; 0.92)	0.11 (0.02; 0.21)	0.47 (0.23; 0.72)	23.81 (11.05; 39.23)	0.59 (0.19; 1.06)	23.22 (10.85; 38.13)	9.70 (4.22; 15.42)	1.79 (0.11; 3.58)	7.91 (4.03; 12.02)	33.52 (15.62; 53.50)	2.38 (0.34; 4.46)	31.14 (15.11; 49.30)
Switzerland	0.38 (0.16 ; 0.64)	0.07 (0.00; 0.14)	0.32 (0.15; 0.49)	35.20 (16.95; 58.49)	0.27 (0.09; 0.48)	34.92 (16.84; 57.99)	6.51 (2.56; 10.33)	1.17 (- 0.02; 2.40)	5.35 (2.56; 7.97)	41.71 (19.64; 68.15)	1.44 (0.07; 2.85)	40.27 (19.54; 65.97)
United Kingdom	0.38 (0.14 ; 0.65)	0.10 (0.00; 0.22)	0.28 (0.13; 0.43)	37.29 (17.53; 63.05)	0.32 (0.09; 0.59)	36.97 (17.45; 62.53)	7.53 (2.53; 12.98)	2.38 (- 0.17; 5.14)	5.15 (2.66; 7.93)	44.82 (20.01; 73.92)	2.69 (- 0.06; 5.63)	42.12 (20.03; 69.67)
Latin America and Caribbean	2.43 (1.19 ; 3.66)	0.20 (0.02; 0.37)	2.24 (1.17; 3.30)	42.24 (20.44; 67.89)	0.35 (0.10; 0.64)	41.89 (20.35; 67.37)	59.16 (29.00; 88.09)	4.88 (- 0.12; 9.59)	54.28 (29.10; 78.89)	101.40 (48.36; 151.21)	5.23 (0.00; 10.29)	96.17 (48.24; 142.52)
Andean Latin America	1.52 (0.70 ; 2.38)	0.10 (0.00; 0.21)	1.41 (0.69; 2.18)	28.01 (12.79; 45.51)	0.26 (0.07; 0.47)	27.75 (12.70; 45.03)	36.90 (16.42; 59.00)	2.63 (- 0.07; 5.33)	34.27 (16.40; 53.17)	64.91 (30.58; 100.72)	2.89 (0.01; 5.76)	62.02 (30.49; 95.00)
Bolivia (Plurinational State of)	2.20 (0.90 ; 3.68)	0.12 (0.01; 0.28)	2.07 (0.91; 3.45)	27.49 (11.72; 49.77)	0.18 (0.04; 0.35)	27.31 (11.64; 49.45)	50.60 (20.72; 86.48)	2.86 (- 0.02; 6.92)	47.74 (21.08; 79.57)	78.09 (34.63; 131.26)	3.05 (0.03; 7.26)	75.05 (34.60; 124.88)
Ecuador	2.38 (1.07 ; 3.82)	0.18 (0.01; 0.35)	2.20 (1.06; 3.51)	53.60 (25.24; 88.90)	0.46 (0.15; 0.80)	53.14 (25.08; 88.19)	58.84 (26.25; 94.13)	4.65 (- 0.15; 9.41)	54.20 (26.32; 85.32)	112.44 (50.42; 174.56)	5.10 (- 0.01; 10.15)	107.34 (50.46; 164.73)
Peru	0.95 (0.43 ; 1.61)	0.07 (0.00; 0.14)	0.88 (0.43; 1.46)	15.74 (6.93; 26.66)	0.19 (0.04; 0.36)	15.55 (6.90; 26.31)	22.72 (9.70; 40.03)	1.64 (- 0.03; 3.58)	21.09 (9.86; 35.75)	38.46 (18.19; 61.60)	1.82 (0.02; 3.87)	36.64 (18.26; 58.46)

Caribbean	1.41 (0.65 ; 2.17)	0.19 (0.02; 0.36)	1.23 (0.63; 1.83)	37.82 (18.35; 61.86)	0.27 (0.08; 0.48)	37.55 (18.25; 61.41)	34.10 (15.32; 53.40)	4.42 (0.12; 8.75)	29.68 (15.15; 45.08)	71.92 (36.18; 112.20)	4.69 (0.21; 9.19)	67.23 (35.57; 102.77)
Antigua and Barbuda	0.82 (0.39 ; 1.33)	0.04 (0.01; 0.09)	0.78 (0.38; 1.26)	16.57 (7.39; 29.26)	0.07 (0.01; 0.14)	16.49 (7.38; 29.14)	17.53 (8.32; 28.27)	0.85 (0.06; 1.69)	16.68 (8.17; 26.74)	34.10 (16.35; 56.45)	0.92 (0.08; 1.82)	33.17 (16.35; 54.95)
Bahamas	0.81 (0.35 ; 1.35)	0.07 (0.00; 0.14)	0.74 (0.35; 1.22)	21.68 (9.20; 39.48)	0.12 (0.02; 0.23)	21.56 (9.16; 39.28)	20.52 (8.44; 35.11)	1.64 (- 0.03; 3.61)	18.88 (8.49; 31.71)	42.19 (18.23; 72.39)	1.76 (0.01; 3.81)	40.44 (18.26; 69.23)
Barbados	2.46 (1.17 ; 3.93)	0.18 (0.05; 0.32)	2.28 (1.11; 3.61)	43.78 (18.97; 74.56)	0.29 (0.09; 0.53)	43.49 (18.88; 73.99)	51.62 (24.25; 84.46)	3.18 (0.75; 6.05)	48.45 (23.47; 79.08)	95.40 (43.76; 156.41)	3.46 (0.84; 6.56)	91.94 (42.81; 150.11)
Belize	1.84 (0.84 ; 2.92)	0.08 (0.00; 0.15)	1.76 (0.84; 2.76)	31.03 (13.74; 54.92)	0.13 (0.02; 0.25)	30.90 (13.72; 54.70)	46.44 (21.54; 75.59)	1.80 (- 0.08; 3.80)	44.64 (21.66; 72.13)	77.47 (36.14; 127.98)	1.93 (- 0.04; 4.06)	75.54 (35.95; 124.52)
Bermuda	0.42 (0.17 ; 0.73)	0.07 (0.01; 0.14)	0.35 (0.17; 0.60)	14.25 (6.13; 26.44)	0.16 (0.04; 0.31)	14.09 (6.08; 26.15)	8.89 (3.58; 15.23)	1.37 (0.09; 2.87)	7.53 (3.51; 12.61)	23.15 (9.88; 40.68)	1.53 (0.14; 3.11)	21.62 (9.68; 37.58)
Cuba	1.06 (0.45 ; 1.71)	0.28 (0.04; 0.52)	0.78 (0.40; 1.19)	48.39 (22.77; 81.94)	0.46 (0.14; 0.83)	47.93 (22.66; 81.24)	24.38 (10.18; 39.52)	6.38 (0.31; 12.42)	18.00 (9.10; 27.84)	72.77 (33.92; 117.85)	6.84 (0.42; 13.14)	65.93 (32.81; 105.44)
Dominica	3.29 (1.57 ; 5.39)	0.20 (0.04; 0.39)	3.09 (1.51; 5.06)	53.98 (24.95; 98.02)	0.24 (0.07; 0.45)	53.74 (24.87; 97.57)	72.96 (35.25; 119.19)	3.94 (0.45; 7.88)	69.03 (34.33; 111.64)	126.94 (62.80; 207.47)	4.18 (0.53; 8.27)	122.76 (61.52; 200.34)
Dominican Republic	1.18 (0.50 ; 2.03)	0.19 (0.01; 0.39)	0.99 (0.48; 1.66)	34.27 (16.04; 57.46)	0.24 (0.07; 0.44)	34.03 (15.91; 56.99)	31.13 (12.17; 53.80)	5.02 (- 0.12; 10.41)	26.11 (12.00; 43.17)	65.39 (28.62; 108.50)	5.26 (- 0.03; 10.80)	60.14 (28.46; 98.04)
Grenada	1.60 (0.70 ; 2.69)	0.09 (0.01; 0.17)	1.51 (0.69; 2.54)	25.02 (10.99; 45.56)	0.11 (0.03; 0.22)	24.90 (10.95; 45.37)	36.84 (15.90; 61.11)	1.86 (0.08; 3.75)	34.98 (15.72; 57.12)	61.85 (26.87; 102.29)	1.97 (0.12; 3.99)	59.88 (26.82; 98.52)
Guyana	3.81 (1.74 ; 6.33)	0.35 (0.06; 0.67)	3.46 (1.68; 5.72)	73.10 (33.39; 121.58)	0.33 (0.11; 0.58)	72.77 (33.24; 121.10)	98.12 (44.62; 166.84)	7.87 (0.73; 15.35)	90.26 (44.09; 151.84)	171.23 (77.89; 279.76)	8.19 (0.83; 16.00)	163.03 (78.41; 265.29)
Haiti	0.81 (0.35 ; 1.46)	0.09 (0.00; 0.19)	0.72 (0.33; 1.30)	12.67 (5.49; 22.08)	0.05 (0.01; 0.09)	12.63 (5.48; 22.00)	20.04 (8.40; 36.05)	2.21 (- 0.16; 4.90)	17.84 (8.17; 31.57)	32.72 (14.62; 56.27)	2.26 (- 0.15; 4.99)	30.46 (14.81; 51.40)
Jamaica	2.41 (1.08 ; 4.03)	0.09 (0.01; 0.17)	2.33 (1.07; 3.87)	33.08 (14.59; 55.65)	0.12 (0.02; 0.26)	32.96 (14.57; 55.38)	53.12 (23.66; 89.35)	1.84 (0.07; 3.88)	51.28 (23.36; 85.78)	86.20 (40.86; 140.32)	1.97 (0.09; 4.11)	84.24 (40.38; 136.95)
Puerto Rico	1.51 (0.67 ; 2.49)	0.07 (0.00; 0.15)	1.43 (0.66; 2.35)	40.16 (18.26; 68.11)	0.23 (0.06; 0.43)	39.93 (18.20; 67.73)	38.28 (15.58; 63.01)	1.95 (- 0.11; 4.10)	36.33 (15.67; 59.48)	78.44 (35.04; 128.46)	2.18 (- 0.05; 4.48)	76.27 (34.86; 124.65)
Saint Kitts and Nevis	1.28 (0.56 ; 2.12)	0.12 (0.02; 0.22)	1.16 (0.54; 1.89)	25.44 (11.81; 45.26)	0.14 (0.04; 0.26)	25.30 (11.76; 45.03)	27.67 (11.83; 45.18)	2.25 (0.30; 4.37)	25.42 (11.41; 40.98)	53.11 (24.61; 87.68)	2.39 (0.34; 4.58)	50.72 (23.89; 83.86)
Saint Lucia	1.40 (0.60 ; 2.34)	0.08 (0.02; 0.15)	1.32 (0.58; 2.22)	32.37 (14.41; 55.65)	0.13 (0.03; 0.25)	32.24 (14.35; 55.47)	31.83 (14.16; 52.22)	1.48 (0.24; 2.80)	30.35 (14.02; 49.49)	64.20 (30.07; 105.54)	1.61 (0.27; 3.00)	62.59 (29.78; 102.80)
Saint Vincent and the Grenadines	2.75 (1.29 ; 4.48)	0.15 (0.02; 0.29)	2.60 (1.29; 4.18)	51.85 (25.50; 89.22)	0.18 (0.05; 0.35)	51.67 (25.42; 88.90)	65.83 (31.01; 107.26)	3.23 (0.10; 6.60)	62.60 (30.87; 100.54)	117.68 (59.76; 190.97)	3.42 (0.17; 6.90)	114.26 (59.62; 184.67)
Suriname	1.87 (0.85 ; 3.25)	0.16 (0.01; 0.32)	1.71 (0.80; 2.91)	52.70 (23.89; 93.87)	0.25 (0.07; 0.47)	52.45 (23.81; 93.41)	49.56 (22.19; 83.99)	4.05 (0.03; 8.71)	45.51 (21.68; 75.85)	102.26 (45.68; 168.10)	4.30 (0.11; 9.09)	97.96 (45.55; 159.26)
Trinidad and Tobago	5.15 (2.33 ; 8.63)	0.23 (0.01; 0.47)	4.92 (2.31; 8.20)	78.36 (35.34; 133.47)	0.32 (0.07; 0.63)	78.04 (35.23; 132.87)	126.01 (56.42; 209.91)	5.88 (- 0.22; 12.74)	120.13 (55.48; 197.53)	204.37 (97.64; 336.58)	6.20 (- 0.13; 13.19)	198.18 (97.60; 325.44)
United States Virgin Islands	1.81 (0.76 ; 3.00)	0.19 (0.01; 0.38)	1.62 (0.77; 2.63)	81.68 (38.21; 137.41)	0.36 (0.10; 0.64)	81.32 (38.10; 136.83)	43.94 (18.10; 73.40)	4.74 (- 0.29; 10.16)	39.21 (18.61; 63.87)	125.62 (61.51; 211.09)	5.09 (- 0.15; 10.74)	120.53 (61.56; 200.82)
Central Latin America	3.57 (1.70 ; 5.50)	0.20 (- 0.01; 0.41)	3.37 (1.71; 5.09)	56.15 (27.77; 90.43)	0.38 (0.10; 0.69)	55.77 (27.67; 89.89)	89.07 (43.19; 135.08)	5.34 (- 0.60; 11.04)	83.73 (43.55; 123.98)	145.21 (68.85; 221.12)	5.71 (- 0.50; 11.59)	139.50 (69.52; 210.22)

Colombia	0.90 (0.36 ; 1.47)	0.12 (0.00; 0.25)	0.78 (0.37; 1.22)	40.11 (19.42; 66.62)	0.24 (0.06; 0.47)	39.87 (19.37; 66.20)	21.36 (8.48; 34.83)	2.85 (- 0.26; 6.18)	18.52 (8.88; 28.65)	61.48 (28.56; 99.31)	3.09 (- 0.19; 6.63)	58.39 (29.01; 92.63)
Costa Rica	1.41 (0.67 ; 2.27)	0.12 (0.00; 0.24)	1.29 (0.66; 2.04)	53.85 (24.33; 90.48)	0.34 (0.09; 0.64)	53.50 (24.19; 89.81)	32.52 (14.97; 52.10)	3.20 (- 0.24; 6.90)	29.32 (14.83; 45.23)	86.36 (40.43; 137.99)	3.54 (- 0.13; 7.52)	82.82 (40.44; 130.74)
El Salvador	2.20 (0.98 ; 3.53)	0.12 (0.00; 0.25)	2.08 (1.01; 3.32)	32.06 (14.17; 55.37)	0.18 (0.05; 0.34)	31.87 (14.10; 55.02)	57.98 (26.28; 94.59)	3.15 (- 0.28; 6.67)	54.83 (26.27; 87.89)	90.03 (41.30; 147.89)	3.33 (- 0.22; 7.00)	86.70 (41.11; 140.92)
Guatemala	2.56 (1.27 ; 4.10)	0.10 (0.00; 0.20)	2.47 (1.27; 3.94)	37.49 (17.50; 67.16)	0.13 (0.03; 0.23)	37.36 (17.47; 66.92)	69.10 (33.71; 109.97)	2.31 (- 0.23; 5.06)	66.80 (34.03; 105.64)	106.59 (52.37; 172.08)	2.43 (- 0.20; 5.28)	104.16 (52.13; 166.97)
Honduras	1.39 (0.56 ; 2.31)	0.19 (0.01; 0.39)	1.19 (0.56; 1.97)	36.47 (16.30; 66.04)	0.14 (0.03; 0.26)	36.33 (16.25; 65.79)	33.22 (12.99; 55.50)	4.22 (- 0.09; 8.61)	29.00 (12.94; 48.04)	69.68 (30.93; 117.65)	4.36 (- 0.05; 8.86)	65.33 (31.36; 109.29)
Mexico	5.72 (2.74 ; 8.89)	0.28 (- 0.01; 0.56)	5.44 (2.76; 8.37)	74.61 (37.54; 121.07)	0.54 (0.16; 0.97)	74.08 (37.39; 120.10)	140.96 (68.96; 214.51)	7.43 (- 0.84; 15.32)	133.53 (69.27; 199.85)	215.57 (103.15 ; 335.27)	7.97 (- 0.67; 16.21)	207.60 (104.09; 318.73)
Nicaragua	1.20 (0.54 ; 2.04)	0.08 (0.00; 0.16)	1.12 (0.52; 1.88)	31.32 (14.01; 53.78)	0.12 (0.03; 0.23)	31.20 (13.97; 53.54)	30.38 (13.16; 51.21)	1.81 (- 0.22; 3.83)	28.57 (13.43; 47.86)	61.70 (27.66; 100.60)	1.93 (- 0.19; 4.01)	59.77 (27.82; 96.73)
Panama	1.01 (0.44 ; 1.69)	0.07 (0.01; 0.14)	0.94 (0.44; 1.56)	26.26 (12.26; 45.90)	0.16 (0.04; 0.30)	26.11 (12.21; 45.59)	24.13 (10.26; 39.30)	1.60 (0.02; 3.24)	22.52 (10.38; 36.29)	50.39 (22.67; 83.92)	1.76 (0.08; 3.49)	48.63 (23.09; 80.54)
Venezuela (Bolivarian Republic of)	1.93 (0.83 ; 3.15)	0.18 (- 0.01; 0.36)	1.76 (0.83; 2.81)	30.28 (13.70; 52.64)	0.19 (0.05; 0.35)	30.10 (13.63; 52.34)	45.88 (19.15; 75.77)	4.38 (- 0.43; 9.61)	41.49 (19.72; 66.52)	76.16 (35.49; 123.09)	4.57 (- 0.38; 9.95)	71.59 (35.64; 113.19)
Tropical Latin America	1.75 (0.84 ; 2.64)	0.21 (0.04; 0.39)	1.54 (0.80; 2.25)	32.62 (14.71; 52.12)	0.37 (0.11; 0.66)	32.25 (14.57; 51.45)	40.04 (18.33; 60.37)	5.03 (0.40; 9.80)	35.01 (17.81; 51.38)	72.67 (33.31; 110.72)	5.40 (0.52; 10.37)	67.27 (32.86; 100.74)
Brazil	1.76 (0.83 ; 2.66)	0.21 (0.04; 0.39)	1.55 (0.80; 2.25)	32.96 (14.81; 52.54)	0.38 (0.11; 0.67)	32.58 (14.66; 51.94)	40.14 (18.34; 60.46)	5.10 (0.40; 9.95)	35.04 (17.81; 51.26)	73.10 (33.49; 111.52)	5.48 (0.52; 10.54)	67.62 (33.04; 101.32)
Paraguay	1.57 (0.72 ; 2.62)	0.10 (0.01; 0.20)	1.47 (0.69; 2.44)	18.88 (8.37; 33.08)	0.16 (0.04; 0.30)	18.72 (8.33; 32.80)	36.32 (15.91; 60.40)	2.26 (0.12; 4.55)	34.06 (15.56; 56.55)	55.20 (25.75; 91.73)	2.42 (0.17; 4.80)	52.78 (25.20; 86.48)
North Africa and Middle East	1.37 (0.58 ; 2.16)	0.28 (0.03; 0.54)	1.09 (0.55; 1.64)	29.80 (13.93; 49.74)	0.47 (0.16; 0.82)	29.33 (13.77; 49.09)	30.94 (11.87; 49.23)	6.80 (0.20; 13.62)	24.14 (12.05; 36.13)	60.74 (27.50; 96.58)	7.26 (0.39; 14.32)	53.47 (26.95; 83.86)
North Africa and Middle East	1.37 (0.58 ; 2.16)	0.28 (0.03; 0.54)	1.09 (0.55; 1.64)	29.80 (13.93; 49.74)	0.47 (0.16; 0.82)	29.33 (13.77; 49.09)	30.94 (11.87; 49.23)	6.80 (0.20; 13.62)	24.14 (12.05; 36.13)	60.74 (27.50; 96.58)	7.26 (0.39; 14.32)	53.47 (26.95; 83.86)
Afghanistan	0.35 (0.12 ; 0.66)	0.10 (0.01; 0.20)	0.26 (0.11; 0.45)	7.71 (3.47; 13.38)	0.08 (0.03; 0.15)	7.63 (3.45; 13.25)	9.02 (2.87; 16.61)	2.56 (0.06; 5.34)	6.46 (2.90; 11.48)	16.73 (6.71; 28.46)	2.63 (0.09; 5.45)	14.09 (6.62; 23.36)
Algeria	0.87 (0.33 ; 1.52)	0.27 (0.05; 0.54)	0.60 (0.27; 1.01)	28.10 (12.71; 50.30)	0.44 (0.16; 0.80)	27.66 (12.56; 49.52)	17.55 (6.20; 30.34)	5.20 (0.48; 10.39)	12.35 (5.54; 20.89)	45.65 (19.20; 81.34)	5.64 (0.66; 11.17)	40.02 (18.71; 69.83)
Bahrain	6.04 (2.55 ; 10.04)	0.39 (0.07; 0.74)	5.65 (2.50; 9.36)	67.87 (29.08; 117.79)	0.56 (0.18; 1.03)	67.31 (28.90; 116.75)	111.99 (48.94; 179.30)	7.46 (0.93; 14.02)	104.52 (47.93; 166.16)	179.86 (78.27; 295.51)	8.02 (1.12; 14.97)	171.84 (76.92; 281.95)
Egypt	2.15 (0.84 ; 3.54)	0.44 (0.03; 0.86)	1.70 (0.81; 2.70)	24.70 (11.73; 43.26)	0.33 (0.11; 0.63)	24.37 (11.59; 42.55)	47.73 (18.11; 79.22)	10.39 (0.05; 20.85)	37.33 (17.81; 59.10)	72.43 (31.13; 118.18)	10.73 (0.15; 21.40)	61.70 (31.43; 97.95)
Iran (Islamic Republic of)	0.78 (0.32 ; 1.35)	0.16 (0.02; 0.33)	0.63 (0.30; 1.06)	19.66 (8.65; 34.88)	0.31 (0.10; 0.59)	19.35 (8.52; 34.37)	16.67 (6.41; 28.61)	3.61 (0.19; 7.58)	13.05 (6.12; 21.55)	36.32 (16.07; 61.44)	3.92 (0.32; 8.07)	32.40 (15.44; 54.20)
Iraq	0.78 (0.30 ; 1.34)	0.18 (0.03; 0.34)	0.60 (0.27; 1.01)	17.90 (7.79; 31.89)	0.21 (0.07; 0.38)	17.69 (7.69; 31.53)	17.24 (6.08; 29.70)	3.77 (0.36; 7.61)	13.47 (5.79; 23.13)	35.14 (15.29; 58.62)	3.97 (0.43; 7.95)	31.17 (14.47; 51.47)
Jordan	1.27 (0.56 ; 2.14)	0.18 (0.04; 0.35)	1.09 (0.52; 1.84)	34.00 (14.85; 62.14)	0.53 (0.20; 0.94)	33.47 (14.61; 61.22)	26.46 (11.58; 44.55)	3.65 (0.52; 7.13)	22.81 (11.04; 37.75)	60.46 (27.04; 101.71)	4.18 (0.70; 8.14)	56.29 (26.09; 94.12)

Kuwait	1.53 (0.63 ; 2.50)	0.24 (0.02; 0.48)	1.29 (0.60; 2.04)	74.97 (34.09; 129.20)	0.78 (0.25; 1.42)	74.19 (33.72; 127.98)	30.74 (11.78; 50.89)	5.82 (-0.08; 12.85)	24.92 (11.75; 39.23)	105.71 (45.70; 172.19)	6.60 (0.22; 14.11)	99.11 (45.93; 161.59)
Lebanon	0.83 (0.35 ; 1.42)	0.10 (0.01; 0.19)	0.73 (0.34; 1.23)	29.34 (12.76; 50.85)	0.36 (0.12; 0.66)	28.99 (12.64; 50.29)	17.20 (7.22; 29.20)	2.10 (0.03; 4.17)	15.11 (7.05; 25.72)	46.55 (20.80; 78.09)	2.45 (0.14; 4.72)	44.09 (20.30; 73.52)
Libya	0.74 (0.25 ; 1.34)	0.15 (0.00; 0.31)	0.59 (0.25; 1.02)	21.93 (9.39; 38.26)	0.23 (0.07; 0.41)	21.70 (9.34; 37.86)	18.12 (5.88; 31.57)	4.10 (-0.23; 8.57)	14.03 (5.81; 23.85)	40.06 (15.33; 68.42)	4.33 (-0.15; 8.92)	35.72 (15.12; 60.08)
Morocco	0.69 (0.26 ; 1.21)	0.23 (0.02; 0.45)	0.46 (0.21; 0.75)	23.33 (10.66; 40.00)	0.29 (0.10; 0.50)	23.04 (10.56; 39.54)	15.80 (5.79; 27.30)	5.25 (0.25; 10.48)	10.55 (4.78; 16.91)	39.13 (16.82; 65.23)	5.54 (0.34; 10.98)	33.59 (16.08; 55.11)
Oman	1.14 (0.49 ; 2.07)	0.16 (0.01; 0.35)	0.98 (0.46; 1.75)	17.04 (7.74; 31.78)	0.33 (0.13; 0.60)	16.71 (7.63; 31.19)	23.87 (10.34; 43.67)	3.48 (0.12; 7.45)	20.40 (9.83; 36.31)	40.92 (18.08; 75.43)	3.81 (0.26; 8.03)	37.11 (17.15; 67.16)
Palestine	0.37 (0.16 ; 0.60)	0.05 (0.01; 0.11)	0.31 (0.15; 0.49)	5.16 (2.29; 8.94)	0.06 (0.02; 0.11)	5.10 (2.27; 8.83)	7.30 (3.06; 11.85)	1.14 (0.03; 2.26)	6.16 (3.04; 9.75)	12.47 (5.52; 20.12)	1.21 (0.05; 2.38)	11.26 (5.49; 17.88)
Qatar	7.10 (3.10 ; 11.38)	0.53 (0.12; 0.96)	6.57 (2.98; 10.48)	117.80 (53.39; 204.82)	1.43 (0.49; 2.50)	116.37 (52.81; 202.03)	128.21 (54.05; 212.15)	9.66 (1.59; 18.16)	118.55 (52.87; 192.23)	246.02 (112.86 ; 403.30)	11.09 (2.12; 20.39)	234.93 (111.09; 384.15)
Saudi Arabia	4.42 (1.89 ; 7.06)	0.86 (0.06; 1.65)	3.56 (1.78; 5.49)	86.72 (41.21; 143.41)	1.29 (0.43; 2.32)	85.43 (40.86; 141.46)	112.80 (45.45; 188.46)	24.84 (-0.05; 51.54)	87.96 (43.48; 137.00)	199.52 (86.31; 311.49)	26.13 (0.35; 53.77)	173.39 (85.07; 261.73)
Sudan	0.35 (0.10 ; 0.64)	0.12 (0.00; 0.27)	0.22 (0.11; 0.38)	7.61 (3.48; 13.66)	0.12 (0.04; 0.23)	7.49 (3.43; 13.43)	8.53 (2.42; 15.80)	3.22 (-0.13; 7.33)	5.30 (2.51; 9.11)	16.14 (6.33; 28.66)	3.35 (-0.08; 7.58)	12.79 (6.41; 21.73)
Syrian Arab Republic	0.71 (0.22 ; 1.30)	0.25 (0.00; 0.54)	0.46 (0.21; 0.77)	17.19 (7.21; 30.18)	0.26 (0.08; 0.48)	16.94 (7.11; 29.77)	16.27 (4.66; 29.73)	6.18 (-0.34; 13.67)	10.09 (4.70; 17.20)	33.46 (12.44; 57.03)	6.44 (-0.25; 14.10)	27.02 (12.57; 44.25)
Tunisia	1.06 (0.35 ; 1.91)	0.25 (0.01; 0.53)	0.81 (0.34; 1.39)	41.78 (18.10; 73.08)	0.41 (0.13; 0.75)	41.37 (17.95; 72.39)	23.59 (7.47; 42.57)	5.85 (0.02; 12.72)	17.74 (7.54; 30.43)	65.37 (26.97; 114.59)	6.26 (0.20; 13.39)	59.10 (26.53; 101.42)
Turkey	1.90 (0.79 ; 3.09)	0.32 (0.05; 0.63)	1.58 (0.75; 2.50)	41.05 (18.97; 67.92)	0.74 (0.25; 1.31)	40.31 (18.67; 66.55)	38.16 (15.74; 61.88)	6.37 (0.46; 12.80)	31.80 (15.35; 49.39)	79.21 (35.08; 127.67)	7.11 (0.72; 14.07)	72.11 (34.85; 113.42)
United Arab Emirates	3.25 (1.34 ; 5.14)	0.52 (0.12; 0.96)	2.73 (1.26; 4.24)	50.23 (23.17; 84.58)	1.29 (0.51; 2.21)	48.94 (22.58; 82.52)	61.88 (25.54; 98.31)	9.55 (1.72; 17.22)	52.33 (24.37; 81.35)	112.11 (49.37; 174.04)	10.84 (2.32; 19.11)	101.27 (46.96; 157.75)
Yemen	0.15 (0.04 ; 0.28)	0.07 (0.00; 0.15)	0.08 (0.04; 0.14)	2.77 (1.22; 4.78)	0.05 (0.01; 0.09)	2.72 (1.21; 4.70)	3.61 (0.85; 6.80)	1.77 (-0.01; 3.74)	1.85 (0.90; 3.24)	6.38 (2.30; 11.22)	1.82 (0.00; 3.81)	4.56 (2.23; 7.70)
South Asia	0.76 (0.32 ; 1.17)	0.13 (0.00; 0.25)	0.63 (0.32; 0.94)	11.60 (5.54; 19.03)	0.16 (0.05; 0.29)	11.44 (5.46; 18.75)	17.57 (6.94; 27.41)	3.37 (-0.22; 6.87)	14.20 (7.20; 21.09)	29.17 (12.57; 45.15)	3.54 (-0.16; 7.15)	25.64 (12.70; 38.25)
South Asia	0.76 (0.32 ; 1.17)	0.13 (0.00; 0.25)	0.63 (0.32; 0.94)	11.60 (5.54; 19.03)	0.16 (0.05; 0.29)	11.44 (5.46; 18.75)	17.57 (6.94; 27.41)	3.37 (-0.22; 6.87)	14.20 (7.20; 21.09)	29.17 (12.57; 45.15)	3.54 (-0.16; 7.15)	25.64 (12.70; 38.25)
Bangladesh	0.16 (0.07 ; 0.27)	0.03 (0.00; 0.06)	0.13 (0.06; 0.21)	2.51 (1.09; 4.23)	0.04 (0.02; 0.08)	2.46 (1.08; 4.16)	3.13 (1.21; 5.19)	0.74 (0.03; 1.48)	2.39 (1.11; 3.75)	5.63 (2.47; 9.24)	0.78 (0.05; 1.55)	4.85 (2.29; 7.66)
Bhutan	0.24 (0.10 ; 0.42)	0.03 (0.00; 0.07)	0.21 (0.09; 0.36)	3.19 (1.39; 5.29)	0.04 (0.01; 0.08)	3.15 (1.37; 5.22)	5.01 (1.90; 8.86)	0.80 (-0.04; 1.69)	4.21 (1.89; 7.13)	8.20 (3.50; 13.25)	0.85 (-0.03; 1.76)	7.36 (3.50; 11.70)
India	0.89 (0.37 ; 1.38)	0.15 (0.00; 0.29)	0.74 (0.37; 1.10)	13.77 (6.61; 22.72)	0.19 (0.06; 0.34)	13.58 (6.52; 22.39)	20.73 (8.18; 32.59)	3.97 (-0.28; 8.05)	16.76 (8.54; 24.97)	34.50 (14.88; 53.25)	4.16 (-0.21; 8.38)	30.34 (15.14; 45.39)
Nepal	0.23 (0.08 ; 0.41)	0.04 (0.00; 0.09)	0.18 (0.08; 0.32)	3.95 (1.81; 6.54)	0.04 (0.01; 0.08)	3.91 (1.80; 6.46)	4.88 (1.69; 8.71)	0.97 (-0.03; 2.11)	3.90 (1.71; 6.77)	8.83 (3.70; 14.84)	1.02 (-0.02; 2.18)	7.81 (3.68; 12.95)
Pakistan	0.26 (0.10 ; 0.45)	0.05 (0.00; 0.10)	0.22 (0.10; 0.35)	3.38 (1.51; 5.71)	0.06 (0.02; 0.12)	3.31 (1.48; 5.57)	5.90 (2.20; 10.24)	1.17 (-0.04; 2.57)	4.73 (2.11; 7.82)	9.28 (3.77; 15.81)	1.23 (-0.02; 2.69)	8.05 (3.72; 13.27)

Southeast Asia, East Asia, and Oceania	0.43 (0.18 ; 0.66)	0.11 (0.02; 0.21)	0.31 (0.15; 0.47)	10.61 (5.30; 17.75)	0.32 (0.13; 0.55)	10.29 (5.17; 17.28)	9.63 (3.96; 14.98)	2.37 (0.29; 4.50)	7.26 (3.64; 10.69)	20.24 (9.31; 32.27)	2.69 (0.42; 5.03)	17.55 (8.85; 27.41)
East Asia	0.30 (0.13 ; 0.50)	0.12 (0.03; 0.21)	0.19 (0.09; 0.28)	10.68 (5.19; 18.12)	0.35 (0.15; 0.62)	10.32 (5.00; 17.55)	6.27 (2.52; 10.24)	2.30 (0.40; 4.28)	3.97 (2.00; 6.00)	16.94 (7.78; 27.31)	2.65 (0.56; 4.89)	14.29 (7.06; 23.04)
China	0.30 (0.12 ; 0.48)	0.12 (0.03; 0.22)	0.18 (0.09; 0.27)	10.65 (5.17; 18.15)	0.36 (0.15; 0.62)	10.29 (4.98; 17.55)	6.13 (2.44; 10.09)	2.34 (0.41; 4.37)	3.79 (1.90; 5.71)	16.77 (7.74; 27.01)	2.70 (0.58; 4.98)	14.08 (6.92; 22.84)
Democratic People's Republic of Korea	0.11 (0.04 ; 0.20)	0.04 (0.01; 0.08)	0.07 (0.03; 0.12)	2.42 (1.08; 4.11)	0.09 (0.03; 0.15)	2.34 (1.03; 3.97)	2.77 (0.80; 4.96)	0.99 (0.07; 1.99)	1.78 (0.75; 2.90)	5.19 (1.92; 8.71)	1.08 (0.10; 2.13)	4.12 (1.81; 6.82)
Taiwan (Province of China)	0.76 (0.37 ; 1.20)	0.05 (0.01; 0.09)	0.72 (0.36; 1.11)	19.77 (8.87; 34.32)	0.46 (0.19; 0.81)	19.31 (8.70; 33.49)	15.40 (7.33; 23.58)	1.06 (0.03; 2.08)	14.34 (7.28; 21.74)	35.17 (16.40; 56.23)	1.52 (0.24; 2.82)	33.65 (16.04; 53.58)
Oceania	2.18 (0.94 ; 3.38)	0.13 (0.00; 0.26)	2.05 (0.94; 3.14)	20.06 (9.31; 34.64)	0.26 (0.10; 0.46)	19.80 (9.22; 34.25)	54.06 (23.35; 84.63)	3.40 (- 0.29; 7.16)	50.66 (23.55; 78.22)	74.12 (33.57; 116.63)	3.66 (- 0.19; 7.51)	70.45 (33.81; 109.38)
American Samoa	5.52 (2.64 ; 8.97)	0.32 (0.02; 0.64)	5.19 (2.61; 8.31)	87.26 (41.73; 155.20)	0.89 (0.40; 1.50)	86.37 (41.26; 154.01)	137.89 (63.35; 222.96)	8.49 (- 0.30; 18.13)	129.40 (62.24; 206.30)	225.15 (106.10 ; 363.08)	9.39 (0.03; 19.47)	215.77 (105.38; 345.32)
Cook Islands	6.91 (3.12 ; 10.98)	0.29 (0.03; 0.57)	6.62 (3.11; 10.44)	112.87 (49.63; 190.35)	1.38 (0.58; 2.32)	111.50 (49.17; 188.20)	166.33 (75.04; 270.98)	7.22 (- 0.07; 15.32)	159.11 (74.91; 257.03)	279.21 (131.48 ; 452.16)	8.60 (0.47; 17.27)	270.61 (130.70; 436.44)
Fiji	9.04 (3.82 ; 15.40)	0.36 (0.02; 0.73)	8.68 (3.84; 14.71)	52.78 (22.25; 94.66)	0.85 (0.34; 1.52)	51.92 (21.85; 93.35)	223.62 (92.90; 379.50)	9.21 (- 0.60; 19.63)	214.40 (95.89; 360.90)	276.39 (118.15 ; 466.81)	10.07 (- 0.21; 21.19)	266.33 (118.29; 446.02)
Guam	2.24 (0.93 ; 3.68)	0.41 (- 0.04; 0.94)	1.83 (0.94; 2.84)	67.29 (32.07; 113.88)	1.74 (0.76; 3.02)	65.54 (31.18; 110.69)	67.82 (25.16; 116.64)	14.63 (- 1.93; 36.19)	53.19 (26.52; 84.66)	135.11 (60.83; 227.54)	16.38 (- 1.13; 38.71)	118.73 (61.91; 191.83)
Kiribati	3.90 (1.84 ; 6.81)	0.22 (0.02; 0.45)	3.68 (1.80; 6.48)	28.50 (12.55; 51.86)	0.52 (0.23; 0.89)	27.98 (12.29; 50.85)	102.10 (46.96; 180.19)	5.92 (- 0.10; 12.98)	96.17 (45.84; 168.22)	130.60 (61.06; 227.18)	6.45 (0.17; 13.59)	124.15 (60.44; 214.73)
Marshall Islands	3.45 (1.39 ; 6.30)	0.22 (- 0.01; 0.44)	3.23 (1.39; 5.91)	40.47 (17.93; 72.91)	0.32 (0.13; 0.56)	40.15 (17.79; 72.45)	92.31 (36.79; 171.46)	6.18 (- 0.69; 13.20)	86.13 (36.50; 157.62)	132.79 (55.90; 233.85)	6.51 (- 0.52; 13.75)	126.28 (57.01; 220.30)
Micronesia (Federated States of)	2.32 (1.06 ; 4.18)	0.19 (- 0.02; 0.41)	2.14 (1.08; 3.78)	24.25 (10.95; 43.70)	0.29 (0.13; 0.54)	23.96 (10.82; 43.29)	61.11 (27.97; 110.38)	5.56 (- 0.75; 13.13)	55.55 (27.94; 98.94)	85.37 (40.45; 147.16)	5.85 (- 0.60; 13.51)	79.51 (40.40; 137.64)
Nauru	5.58 (2.49 ; 9.26)	0.57 (- 0.03; 1.20)	5.01 (2.44; 8.14)	51.55 (22.73; 90.90)	0.76 (0.32; 1.33)	50.80 (22.40; 89.50)	152.15 (65.11; 262.58)	17.36 (- 1.90; 37.95)	134.79 (64.43; 224.28)	203.70 (91.67; 344.79)	18.11 (- 1.53; 39.18)	185.59 (92.43; 303.65)
Niue	4.87 (2.20 ; 8.32)	0.37 (0.03; 0.73)	4.50 (2.17; 7.60)	64.72 (28.64; 109.06)	0.93 (0.40; 1.61)	63.79 (28.04; 107.65)	117.77 (50.46; 198.15)	9.11 (- 0.05; 19.23)	108.65 (50.70; 184.08)	182.49 (80.43; 300.81)	10.05 (0.44; 20.63)	172.44 (80.40; 281.54)
Northern Mariana Islands	4.26 (2.07 ; 6.81)	0.34 (0.02; 0.67)	3.92 (2.03; 6.15)	55.47 (24.73; 93.24)	0.94 (0.40; 1.72)	54.53 (24.23; 91.64)	103.23 (47.87; 168.83)	8.63 (- 0.27; 18.86)	94.60 (46.63; 148.21)	158.70 (72.37; 254.92)	9.57 (0.17; 20.54)	149.13 (72.36; 234.49)
Palau	4.75 (2.06 ; 7.89)	0.43 (0.05; 0.85)	4.32 (2.02; 7.09)	65.65 (30.62; 114.67)	1.03 (0.45; 1.84)	64.62 (30.21; 113.32)	116.91 (51.32; 193.79)	11.31 (0.02; 25.03)	105.60 (51.04; 170.19)	182.56 (85.05; 298.33)	12.34 (0.58; 26.57)	170.22 (83.95; 274.86)
Papua New Guinea	0.96 (0.43 ; 1.60)	0.07 (0.00; 0.15)	0.90 (0.43; 1.47)	11.83 (5.19; 21.49)	0.08 (0.03; 0.14)	11.75 (5.16; 21.33)	25.22 (11.03; 42.29)	1.86 (- 0.20; 4.32)	23.36 (10.85; 38.90)	37.04 (16.99; 64.24)	1.93 (- 0.17; 4.44)	35.11 (16.58; 60.21)
Samoa	3.91 (1.71 ; 6.56)	0.32 (0.00; 0.66)	3.59 (1.70; 5.97)	58.06 (26.35; 100.96)	0.82 (0.33; 1.48)	57.24 (26.03; 99.75)	99.34 (43.25; 168.81)	8.52 (- 0.60; 18.72)	90.82 (42.77; 149.97)	157.40 (67.79; 264.99)	9.34 (- 0.13; 19.97)	148.06 (67.71; 242.34)
Solomon Islands	1.28 (0.56 ; 2.15)	0.11 (- 0.01; 0.23)	1.18 (0.56; 1.94)	8.96 (4.05; 15.76)	0.11 (0.04; 0.20)	8.85 (4.01; 15.56)	35.88 (15.50; 61.99)	3.16 (- 0.56; 6.95)	32.73 (15.32; 55.21)	44.84 (20.39; 76.25)	3.27 (- 0.51; 7.11)	41.58 (20.14; 69.92)
Tokelau	2.61 (1.16 ; 4.06)	0.24 (0.01; 0.50)	2.37 (1.15; 3.98)	47.31 (21.85; 80.66)	0.51 (0.21; 0.89)	46.80 (21.51; 79.87)	66.04 (28.89; 103.79)	6.15 (- 0.34; 13.30)	59.88 (29.02; 100.73)	113.35 (52.08; 186.01)	6.67 (- 0.12; 14.07)	106.68 (52.36; 174.19)

	; 4.49)						113.43)					
Tonga	2.55 (1.08 ; 4.31)	0.12 (0.00; 0.25)	2.44 (1.08; 4.07)	31.15 (12.75; 56.63)	0.34 (0.12; 0.60)	30.82 (12.62; 56.01)	63.21 (26.46; 110.93)	3.08 (- 0.22; 6.88)	60.13 (27.29; 104.40)	94.36 (40.85; 162.02)	3.42 (- 0.08; 7.41)	90.95 (40.92; 154.32)
Tuvalu	2.09 (0.90 ; 3.72)	0.18 (- 0.02; 0.40)	1.92 (0.91; 3.34)	20.45 (8.72; 37.36)	0.17 (0.06; 0.32)	20.28 (8.64; 37.02)	54.17 (23.17; 96.18)	5.34 (- 0.92; 12.86)	48.83 (23.13; 85.59)	74.62 (32.07; 131.30)	5.51 (- 0.83; 13.16)	69.11 (31.86; 119.99)
Vanuatu	1.80 (0.75 ; 3.01)	0.21 (- 0.01; 0.45)	1.59 (0.73; 2.65)	19.29 (8.46; 34.33)	0.36 (0.14; 0.69)	18.92 (8.33; 33.71)	47.55 (19.15; 78.97)	6.11 (- 0.70; 13.20)	41.44 (19.45; 67.48)	66.84 (28.17; 110.50)	6.48 (- 0.54; 13.75)	60.36 (28.00; 98.60)
Southeast Asia	0.81 (0.35 ; 1.24)	0.09 (0.01; 0.19)	0.72 (0.35; 1.07)	11.85 (5.55; 19.86)	0.20 (0.07; 0.36)	11.65 (5.47; 19.56)	19.31 (8.19; 29.66)	2.38 (- 0.06; 4.91)	16.94 (8.28; 25.01)	31.17 (14.42; 48.23)	2.58 (0.03; 5.22)	28.59 (14.20; 43.33)
Cambodia	0.48 (0.21 ; 0.83)	0.06 (0.00; 0.13)	0.42 (0.19; 0.71)	6.47 (2.85; 11.57)	0.07 (0.02; 0.12)	6.41 (2.83; 11.45)	11.52 (4.77; 19.95)	1.44 (- 0.08; 3.04)	10.08 (4.71; 17.57)	17.99 (7.69; 30.90)	1.51 (- 0.05; 3.17)	16.48 (7.70; 27.84)
Indonesia	0.25 (0.11 ; 0.42)	0.06 (0.01; 0.11)	0.20 (0.10; 0.30)	3.01 (1.38; 4.90)	0.09 (0.03; 0.17)	2.92 (1.33; 4.78)	5.98 (2.43; 9.74)	1.34 (0.04; 2.66)	4.64 (2.34; 7.14)	9.00 (3.82; 14.37)	1.43 (0.07; 2.80)	7.56 (3.68; 11.70)
Lao People's Democratic Republic	0.64 (0.24 ; 1.08)	0.10 (0.00; 0.21)	0.54 (0.24; 0.90)	8.80 (3.82; 15.50)	0.11 (0.04; 0.19)	8.69 (3.79; 15.35)	15.88 (6.11; 26.70)	2.59 (- 0.18; 5.57)	13.30 (5.85; 21.45)	24.69 (10.18; 41.23)	2.69 (- 0.14; 5.76)	21.99 (9.75; 36.09)
Malaysia	0.83 (0.34 ; 1.34)	0.19 (0.01; 0.36)	0.64 (0.32; 0.99)	21.47 (9.63; 36.43)	0.59 (0.24; 1.03)	20.87 (9.38; 35.50)	20.49 (8.08; 34.07)	4.59 (- 0.09; 9.10)	15.90 (8.00; 24.15)	41.95 (17.61; 67.24)	5.18 (0.16; 10.05)	36.77 (17.10; 57.75)
Maldives	0.25 (0.10 ; 0.44)	0.04 (0.00; 0.08)	0.21 (0.09; 0.35)	6.03 (2.62; 10.63)	0.10 (0.03; 0.18)	5.94 (2.58; 10.46)	5.34 (2.05; 8.97)	0.85 (- 0.01; 1.76)	4.49 (1.98; 7.40)	11.37 (4.78; 19.32)	0.94 (0.03; 1.93)	10.43 (4.69; 17.37)
Mauritius	4.86 (2.43 ; 7.77)	0.19 (0.02; 0.37)	4.67 (2.37; 7.39)	47.56 (21.12; 85.19)	0.58 (0.23; 1.06)	46.98 (20.86; 84.12)	121.42 (58.53; 198.23)	4.96 (0.11; 10.36)	116.46 (59.00; 188.61)	168.98 (79.21; 282.60)	5.54 (0.38; 11.39)	163.44 (78.62; 271.08)
Myanmar	0.88 (0.37 ; 1.46)	0.09 (0.01; 0.18)	0.79 (0.36; 1.29)	11.28 (5.39; 20.30)	0.13 (0.05; 0.24)	11.14 (5.33; 20.07)	21.27 (8.78; 35.68)	2.12 (- 0.02; 4.45)	19.15 (8.63; 31.90)	32.54 (14.60; 53.50)	2.25 (0.04; 4.65)	30.29 (14.25; 49.28)
Philippines	1.73 (0.74 ; 2.79)	0.20 (- 0.01; 0.41)	1.54 (0.75; 2.37)	16.50 (7.81; 27.14)	0.29 (0.10; 0.50)	16.21 (7.71; 26.65)	45.08 (18.47; 72.18)	5.82 (- 0.67; 12.65)	39.25 (19.00; 59.81)	61.57 (26.76; 97.02)	6.11 (- 0.56; 13.07)	55.46 (27.18; 84.69)
Seychelles	0.34 (0.14 ; 0.55)	0.05 (0.01; 0.10)	0.28 (0.14; 0.45)	11.36 (4.95; 20.92)	0.16 (0.06; 0.30)	11.20 (4.87; 20.67)	7.80 (3.32; 12.94)	1.25 (0.03; 2.58)	6.55 (3.22; 10.56)	19.16 (8.88; 32.91)	1.42 (0.10; 2.86)	17.74 (8.44; 30.27)
Sri Lanka	1.33 (0.54 ; 2.39)	0.12 (0.01; 0.24)	1.21 (0.52; 2.15)	28.91 (12.09; 52.55)	0.22 (0.08; 0.40)	28.70 (12.01; 52.13)	29.36 (11.23; 52.38)	2.56 (0.04; 5.72)	26.80 (11.25; 46.76)	58.27 (24.88; 100.90)	2.78 (0.12; 6.09)	55.50 (24.37; 94.52)
Thailand	1.41 (0.62 ; 2.31)	0.11 (0.01; 0.21)	1.30 (0.61; 2.10)	29.69 (14.17; 50.17)	0.46 (0.17; 0.80)	29.23 (13.97; 49.51)	36.00 (15.75; 58.31)	2.92 (0.08; 6.00)	33.08 (15.77; 52.87)	65.69 (30.76; 103.78)	3.37 (0.26; 6.68)	62.32 (30.50; 97.83)
Timor-Leste	0.21 (0.07 ; 0.35)	0.04 (0.00; 0.09)	0.16 (0.07; 0.27)	3.99 (1.79; 6.96)	0.04 (0.01; 0.07)	3.95 (1.77; 6.87)	4.92 (1.75; 8.49)	1.10 (- 0.09; 2.39)	3.81 (1.63; 6.23)	8.91 (3.51; 14.61)	1.14 (- 0.07; 2.46)	7.76 (3.62; 12.85)
Vietnam	0.43 (0.19 ; 0.69)	0.05 (0.01; 0.09)	0.38 (0.18; 0.61)	4.87 (2.17; 7.99)	0.08 (0.03; 0.14)	4.79 (2.14; 7.87)	9.10 (3.83; 14.98)	1.03 (0.06; 2.00)	8.07 (3.69; 13.05)	13.97 (6.27; 22.19)	1.11 (0.09; 2.13)	12.86 (6.08; 20.10)
Sub-Saharan Africa	0.92 (0.45 ; 1.37)	0.07 (0.01; 0.13)	0.85 (0.44; 1.24)	7.41 (3.50; 12.24)	0.14 (0.05; 0.25)	7.27 (3.44; 11.97)	20.42 (9.93; 30.54)	1.55 (0.11; 2.96)	18.87 (9.78; 27.63)	27.83 (13.65; 42.52)	1.69 (0.16; 3.19)	26.14 (13.46; 38.77)
Central Sub- Saharan Africa	0.69 (0.30 ; 1.10)	0.08 (0.01; 0.16)	0.61 (0.29; 0.95)	6.74 (3.10; 11.21)	0.14 (0.06; 0.23)	6.60 (3.05; 11.00)	16.12 (7.05; 25.95)	1.66 (0.13; 3.39)	14.47 (6.86; 22.58)	22.86 (10.69; 36.04)	1.80 (0.19; 3.63)	21.07 (10.46; 32.49)
Angola	0.72 (0.29 ; 1.20)	0.07 (0.00; 0.15)	0.64 (0.29; 1.06)	9.22 (4.05; 16.15)	0.11 (0.04; 0.19)	9.11 (4.00; 15.99)	17.07 (7.08; 29.62)	1.65 (- 0.04; 3.50)	15.42 (6.99; 26.39)	26.29 (11.29; 43.21)	1.75 (0.01; 3.67)	24.54 (11.24; 40.11)
Central African Republic	0.66 (0.28	0.08 (0.01; 0.18)	0.58 (0.27; 1.00)	7.24 (3.13; 13.19)	0.12 (0.05; 0.22)	7.12 (3.08; 12.96)	16.61 (6.77; 29.47)	1.90 (0.11; 4.22)	14.71 (6.76; 25.52)	23.85 (10.15; 41.34)	2.02 (0.15; 4.43)	21.83 (10.11; 37.31)

	; 1.18)											
Congo	0.91 (0.41 ; 1.49)	0.09 (0.00; 0.18)	0.83 (0.40; 1.32)	8.00 (3.68; 14.43)	0.11 (0.04; 0.19)	7.89 (3.63; 14.24)	21.98 (9.79; 36.88)	2.00 (- 0.05; 4.17)	19.98 (9.57; 32.82)	29.98 (13.81; 49.77)	2.11 (0.02; 4.36)	27.87 (13.56; 45.86)
Democratic Republic of the Congo	0.58 (0.24 ; 0.98)	0.07 (0.01; 0.15)	0.50 (0.23; 0.83)	5.09 (2.31; 8.49)	0.13 (0.05; 0.24)	4.95 (2.24; 8.28)	13.45 (5.37; 22.36)	1.48 (0.16; 3.10)	11.97 (5.28; 19.46)	18.53 (7.63; 30.17)	1.61 (0.21; 3.31)	16.92 (7.55; 27.07)
Equatorial Guinea	2.95 (1.26 ; 5.32)	0.31 (0.06; 0.64)	2.64 (1.18; 4.66)	28.13 (12.45; 50.27)	0.71 (0.29; 1.24)	27.42 (12.13; 49.15)	69.07 (29.63; 128.42)	6.22 (0.70; 13.43)	62.85 (27.70; 114.84)	97.20 (43.72; 169.44)	6.93 (0.99; 14.52)	90.27 (42.35; 154.01)
Gabon	2.31 (1.00 ; 3.79)	0.19 (0.04; 0.36)	2.11 (0.96; 3.49)	20.77 (8.83; 36.86)	0.50 (0.21; 0.89)	20.27 (8.63; 36.09)	54.33 (23.32; 92.91)	3.89 (0.50; 7.49)	50.44 (22.83; 85.44)	75.10 (31.64; 126.61)	4.39 (0.67; 8.23)	70.71 (31.07; 119.33)
Eastern Sub-Saharan Africa	0.62 (0.30 ; 0.95)	0.05 (0.00; 0.09)	0.57 (0.30; 0.86)	4.15 (1.98; 6.80)	0.10 (0.03; 0.18)	4.05 (1.95; 6.63)	14.39 (6.94; 22.62)	1.14 (0.02; 2.28)	13.25 (6.91; 20.29)	18.54 (9.15; 28.54)	1.24 (0.05; 2.45)	17.30 (9.05; 25.95)
Burundi	0.44 (0.17 ; 0.78)	0.04 (0.00; 0.08)	0.40 (0.17; 0.71)	2.91 (1.34; 5.12)	0.06 (0.02; 0.11)	2.85 (1.32; 5.03)	10.20 (3.91; 18.09)	0.93 (0.00; 2.02)	9.27 (3.85; 16.05)	13.11 (5.22; 23.12)	0.99 (0.02; 2.15)	12.12 (5.25; 21.19)
Comoros	0.86 (0.34 ; 1.51)	0.06 (0.00; 0.12)	0.80 (0.34; 1.41)	9.36 (4.03; 16.75)	0.11 (0.03; 0.21)	9.25 (3.99; 16.55)	19.85 (7.67; 34.75)	1.32 (- 0.05; 2.94)	18.53 (7.67; 32.42)	29.21 (12.66; 49.58)	1.43 (- 0.02; 3.12)	27.78 (12.55; 46.72)
Djibouti	0.65 (0.29 ; 1.12)	0.05 (0.00; 0.11)	0.59 (0.28; 1.00)	4.31 (1.89; 7.69)	0.11 (0.03; 0.20)	4.20 (1.86; 7.49)	14.56 (6.24; 25.64)	1.26 (0.00; 2.68)	13.30 (6.09; 23.04)	18.88 (8.12; 32.37)	1.37 (0.04; 2.86)	17.50 (8.05; 29.42)
Eritrea	0.74 (0.33 ; 1.29)	0.05 (0.00; 0.11)	0.69 (0.32; 1.19)	5.65 (2.48; 10.53)	0.07 (0.02; 0.13)	5.58 (2.45; 10.41)	17.37 (7.84; 31.09)	1.26 (- 0.09; 2.78)	16.12 (7.67; 28.51)	23.02 (10.67; 40.23)	1.33 (- 0.07; 2.89)	21.69 (10.46; 37.76)
Ethiopia	0.36 (0.17 ; 0.60)	0.03 (0.00; 0.05)	0.34 (0.17; 0.55)	3.30 (1.55; 5.94)	0.06 (0.02; 0.11)	3.24 (1.52; 5.84)	8.12 (3.83; 12.76)	0.60 (0.02; 1.23)	7.52 (3.87; 11.60)	11.41 (5.54; 18.39)	0.66 (0.03; 1.31)	10.76 (5.48; 17.21)
Kenya	0.75 (0.34 ; 1.28)	0.06 (0.01; 0.11)	0.69 (0.32; 1.18)	4.18 (1.82; 7.24)	0.16 (0.06; 0.30)	4.02 (1.76; 6.95)	17.12 (7.56; 29.12)	1.20 (0.07; 2.40)	15.92 (7.50; 26.71)	21.31 (9.83; 35.02)	1.36 (0.12; 2.69)	19.95 (9.55; 32.50)
Madagascar	0.52 (0.21 ; 0.89)	0.07 (0.01; 0.14)	0.45 (0.20; 0.76)	3.93 (1.74; 7.04)	0.11 (0.04; 0.20)	3.81 (1.70; 6.85)	12.21 (4.92; 21.36)	1.63 (- 0.01; 3.46)	10.59 (4.84; 18.32)	16.14 (6.92; 27.87)	1.74 (0.03; 3.64)	14.40 (6.95; 24.46)
Malawi	0.95 (0.42 ; 1.57)	0.08 (0.01; 0.16)	0.87 (0.40; 1.42)	4.10 (1.84; 7.28)	0.14 (0.04; 0.26)	3.96 (1.79; 7.06)	22.71 (9.84; 38.00)	1.90 (0.05; 3.95)	20.81 (9.53; 34.36)	26.81 (11.81; 44.83)	2.04 (0.09; 4.19)	24.77 (11.39; 40.94)
Mozambique	0.79 (0.35 ; 1.31)	0.05 (0.01; 0.10)	0.74 (0.33; 1.21)	5.26 (2.30; 9.14)	0.09 (0.03; 0.18)	5.17 (2.26; 9.00)	19.62 (8.58; 32.31)	1.11 (0.14; 2.19)	18.51 (8.43; 30.36)	24.88 (10.88; 39.66)	1.20 (0.16; 2.36)	23.67 (10.72; 37.54)
Rwanda	0.57 (0.23 ; 1.02)	0.04 (0.00; 0.08)	0.53 (0.22; 0.95)	3.15 (1.39; 5.31)	0.06 (0.02; 0.12)	3.08 (1.37; 5.20)	12.77 (5.06; 22.70)	0.81 (- 0.04; 1.78)	11.96 (5.06; 21.20)	15.91 (6.58; 27.39)	0.87 (- 0.02; 1.89)	15.04 (6.47; 25.59)
Somalia	0.44 (0.20 ; 0.75)	0.03 (0.00; 0.06)	0.42 (0.20; 0.70)	2.57 (1.18; 4.62)	0.05 (0.01; 0.09)	2.53 (1.17; 4.54)	10.79 (4.94; 18.28)	0.65 (- 0.03; 1.44)	10.14 (4.89; 16.92)	13.36 (6.12; 22.26)	0.70 (- 0.01; 1.51)	12.66 (6.11; 20.96)
South Sudan	1.75 (0.76 ; 3.08)	0.10 (0.01; 0.22)	1.65 (0.74; 2.89)	8.98 (3.77; 16.20)	0.19 (0.06; 0.35)	8.79 (3.66; 15.85)	41.95 (18.04; 75.23)	2.40 (- 0.02; 5.52)	39.55 (17.77; 70.59)	50.93 (22.24; 89.16)	2.58 (0.03; 5.86)	48.34 (21.88; 85.51)
Uganda	0.63 (0.26 ; 1.07)	0.04 (0.00; 0.09)	0.59 (0.26; 1.01)	3.95 (1.68; 6.93)	0.09 (0.03; 0.16)	3.86 (1.65; 6.78)	14.44 (5.78; 25.15)	0.93 (- 0.03; 2.09)	13.51 (5.73; 23.46)	18.39 (7.50; 31.26)	1.02 (0.00; 2.22)	17.37 (7.55; 29.12)
United Republic of Tanzania	0.71 (0.30 ; 1.19)	0.07 (0.00; 0.15)	0.64 (0.29; 1.04)	4.80 (2.13; 8.51)	0.14 (0.05; 0.26)	4.66 (2.08; 8.26)	16.49 (7.05; 28.39)	1.70 (- 0.04; 3.61)	14.79 (6.73; 24.57)	21.29 (9.55; 35.91)	1.85 (0.02; 3.82)	19.44 (9.28; 32.21)
Zambia	0.57 (0.26 ; 0.93)	0.06 (0.01; 0.11)	0.51 (0.25; 0.83)	5.55 (2.48; 9.63)	0.11 (0.04; 0.19)	5.44 (2.42; 9.45)	13.50 (6.16; 22.51)	1.27 (0.10; 2.60)	12.23 (5.84; 20.04)	19.05 (8.97; 31.13)	1.38 (0.14; 2.77)	17.67 (8.56; 28.58)
Southern Sub-Saharan Africa	3.26 (1.63	0.15 (0.02; 0.27)	3.11 (1.60; 4.58)	25.09 (12.23; 41.26)	0.33 (0.13; 0.57)	24.76 (12.09; 40.68)	72.79 (35.26; 110.32)	3.33 (0.26; 6.36)	69.46 (35.22; 102.20)	97.87 (48.44; 147.38)	3.66 (0.38; 6.86)	94.21 (47.98; 140.43)

	; 4.84)						108.54)					
Botswana	0.92 (0.43 ; 1.56)	0.06 (0.01; 0.11)	0.86 (0.41; 1.47)	7.86 (3.52; 14.64)	0.13 (0.05; 0.25)	7.72 (3.46; 14.43)	19.97 (9.17; 35.54)	1.21 (0.05; 2.48)	18.75 (8.92; 33.41)	27.82 (13.05; 47.80)	1.35 (0.10; 2.68)	26.48 (12.63; 45.25)
Eswatini	2.23 (0.99 ; 3.75)	0.10 (0.01; 0.21)	2.13 (0.98; 3.59)	12.30 (5.62; 21.52)	0.14 (0.05; 0.25)	12.15 (5.57; 21.32)	53.31 (23.56; 90.72)	2.33 (0.10; 5.16)	50.97 (22.94; 86.76)	65.60 (29.28; 108.88)	2.48 (0.16; 5.35)	63.12 (29.41; 104.77)
Lesotho	3.57 (1.56 ; 6.15)	0.16 (0.02; 0.33)	3.41 (1.55; 5.88)	18.48 (8.16; 32.44)	0.21 (0.07; 0.37)	18.27 (8.09; 32.09)	84.68 (35.68; 142.49)	3.60 (0.25; 7.85)	81.08 (35.44; 135.88)	103.16 (45.10; 173.47)	3.81 (0.31; 8.19)	99.35 (44.79; 166.30)
Namibia	0.84 (0.35 ; 1.47)	0.07 (0.01; 0.13)	0.77 (0.33; 1.35)	4.99 (2.17; 8.98)	0.11 (0.04; 0.19)	4.88 (2.12; 8.80)	18.61 (7.76; 33.88)	1.46 (0.15; 2.96)	17.15 (7.46; 30.75)	23.60 (10.17; 41.83)	1.57 (0.19; 3.13)	22.03 (9.93; 39.02)
South Africa	3.69 (1.84 ; 5.51)	0.17 (0.03; 0.30)	3.53 (1.81; 5.26)	29.60 (14.29; 48.73)	0.38 (0.15; 0.67)	29.21 (14.14; 48.07)	83.46 (40.59; 124.85)	3.74 (0.29; 7.15)	79.72 (40.54; 118.25)	113.05 (55.88; 168.54)	4.12 (0.43; 7.84)	108.93 (55.39; 160.75)
Zimbabwe	0.88 (0.40 ; 1.53)	0.06 (0.00; 0.13)	0.81 (0.38; 1.40)	5.82 (2.59; 10.44)	0.08 (0.03; 0.16)	5.74 (2.55; 10.27)	20.79 (9.06; 36.43)	1.45 (- 0.02; 3.13)	19.34 (8.71; 33.06)	26.61 (11.79; 46.54)	1.53 (0.02; 3.26)	25.08 (11.55; 43.21)
Western Sub-Saharan Africa	0.51 (0.23 ; 0.78)	0.07 (0.01; 0.12)	0.44 (0.21; 0.65)	5.29 (2.39; 9.06)	0.12 (0.05; 0.22)	5.17 (2.35; 8.84)	11.00 (4.83; 17.21)	1.37 (0.15; 2.62)	9.62 (4.64; 14.57)	16.29 (7.42; 25.23)	1.49 (0.20; 2.78)	14.79 (7.19; 22.50)
Benin	0.37 (0.16 ; 0.65)	0.04 (0.01; 0.08)	0.32 (0.15; 0.56)	5.98 (2.76; 10.84)	0.07 (0.03; 0.12)	5.91 (2.72; 10.72)	8.00 (3.48; 14.23)	0.85 (0.09; 1.72)	7.15 (3.26; 12.43)	13.98 (6.39; 24.79)	0.92 (0.11; 1.84)	13.06 (6.22; 22.94)
Burkina Faso	0.31 (0.14 ; 0.49)	0.03 (0.00; 0.07)	0.27 (0.13; 0.43)	3.57 (1.73; 6.36)	0.05 (0.02; 0.08)	3.52 (1.71; 6.28)	6.95 (3.12; 11.02)	0.72 (0.01; 1.48)	6.23 (3.05; 9.62)	10.52 (4.93; 16.74)	0.77 (0.03; 1.56)	9.75 (4.90; 15.37)
Cabo Verde	0.30 (0.13 ; 0.52)	0.04 (0.01; 0.09)	0.25 (0.12; 0.43)	5.03 (2.29; 8.74)	0.09 (0.04; 0.17)	4.94 (2.25; 8.59)	6.16 (2.62; 10.34)	0.97 (0.08; 1.98)	5.20 (2.48; 8.49)	11.20 (4.95; 18.84)	1.06 (0.11; 2.15)	10.14 (4.76; 16.61)
Cameroon	0.55 (0.23 ; 0.92)	0.07 (0.01; 0.13)	0.48 (0.21; 0.79)	4.89 (2.05; 8.55)	0.12 (0.05; 0.21)	4.77 (2.00; 8.36)	12.44 (4.98; 20.88)	1.40 (0.20; 2.81)	11.04 (4.60; 18.39)	17.33 (7.15; 27.94)	1.52 (0.25; 2.99)	15.81 (6.86; 25.33)
Chad	0.22 (0.09 ; 0.37)	0.04 (0.01; 0.07)	0.18 (0.09; 0.30)	2.50 (1.13; 4.37)	0.05 (0.02; 0.09)	2.45 (1.11; 4.28)	4.90 (2.14; 8.39)	0.76 (0.06; 1.50)	4.14 (2.04; 6.91)	7.40 (3.37; 12.20)	0.82 (0.08; 1.59)	6.59 (3.27; 10.68)
Côte d'Ivoire	0.62 (0.29 ; 1.05)	0.08 (0.01; 0.16)	0.54 (0.27; 0.90)	7.37 (3.28; 13.83)	0.13 (0.04; 0.23)	7.24 (3.24; 13.61)	14.05 (6.35; 23.43)	1.78 (0.13; 3.71)	12.27 (5.93; 20.35)	21.43 (9.85; 37.60)	1.91 (0.18; 3.91)	19.52 (9.73; 33.55)
Gambia	0.45 (0.18 ; 0.78)	0.07 (0.01; 0.14)	0.38 (0.17; 0.65)	4.62 (2.04; 8.11)	0.09 (0.03; 0.17)	4.53 (2.00; 7.94)	10.07 (4.21; 17.12)	1.49 (0.09; 3.12)	8.59 (3.91; 14.30)	14.70 (6.42; 24.77)	1.58 (0.13; 3.28)	13.12 (6.16; 21.69)
Ghana	1.02 (0.47 ; 1.74)	0.19 (0.06; 0.36)	0.83 (0.39; 1.40)	9.68 (4.48; 16.93)	0.39 (0.16; 0.69)	9.29 (4.31; 16.31)	22.66 (9.81; 37.68)	3.54 (0.92; 6.85)	19.12 (8.76; 31.21)	32.34 (14.37; 52.86)	3.93 (1.09; 7.44)	28.41 (13.07; 46.24)
Guinea	0.41 (0.20 ; 0.71)	0.06 (0.01; 0.12)	0.35 (0.18; 0.59)	3.86 (1.73; 6.80)	0.09 (0.03; 0.16)	3.77 (1.69; 6.64)	9.15 (4.28; 15.85)	1.22 (0.12; 2.60)	7.93 (4.09; 13.60)	13.01 (6.37; 21.91)	1.31 (0.16; 2.76)	11.70 (6.06; 19.48)
Guinea-Bissau	0.35 (0.15 ; 0.58)	0.05 (0.00; 0.10)	0.30 (0.14; 0.50)	3.30 (1.56; 5.79)	0.05 (0.02; 0.09)	3.25 (1.53; 5.70)	8.19 (3.39; 14.43)	1.15 (0.03; 2.40)	7.04 (3.28; 12.08)	11.48 (5.00; 19.22)	1.20 (0.04; 2.49)	10.28 (5.00; 16.76)
Liberia	0.32 (0.13 ; 0.55)	0.04 (0.01; 0.08)	0.28 (0.13; 0.48)	3.65 (1.63; 6.36)	0.07 (0.02; 0.12)	3.58 (1.61; 6.24)	7.39 (3.07; 12.58)	0.93 (0.08; 1.89)	6.46 (2.96; 10.89)	11.04 (4.65; 18.01)	1.00 (0.10; 2.00)	10.04 (4.64; 16.04)
Mali	0.57 (0.23 ; 0.92)	0.07 (0.02; 0.13)	0.50 (0.22; 0.81)	10.70 (4.70; 18.56)	0.16 (0.07; 0.28)	10.53 (4.63; 18.30)	12.70 (5.28; 20.65)	1.48 (0.26; 2.79)	11.23 (5.05; 18.12)	23.40 (10.46; 37.82)	1.64 (0.32; 3.05)	21.76 (10.14; 34.86)
Mauritania	0.68 (0.28 ; 1.18)	0.10 (0.02; 0.20)	0.57 (0.27; 1.00)	5.52 (2.33; 9.85)	0.18 (0.06; 0.32)	5.34 (2.26; 9.52)	14.20 (5.82; 24.99)	2.00 (0.25; 4.02)	12.20 (5.62; 21.42)	19.72 (8.48; 34.57)	2.18 (0.31; 4.32)	17.54 (8.27; 30.53)
Niger	0.30 (0.13 ; 0.43)	0.04 (0.01; 0.09)	0.25 (0.12; 0.43)	4.65 (2.00; 8.11)	0.10 (0.03; 0.18)	4.56 (1.96; 7.95)	6.52 (2.72; 11.51)	0.88 (0.10; 1.76)	5.64 (2.65; 9.80)	11.18 (5.04; 18.69)	0.98 (0.13; 1.89)	10.20 (4.78; 16.89)

	; 0.51)											
Nigeria	0.50 (0.21 ; 0.81)	0.06 (0.00; 0.11)	0.44 (0.20; 0.70)	4.67 (2.02; 8.17)	0.10 (0.03; 0.18)	4.57 (1.96; 7.99)	10.59 (4.37; 17.45)	1.19 (0.04; 2.36)	9.40 (4.36; 15.21)	15.26 (6.58; 24.64)	1.29 (0.07; 2.54)	13.97 (6.49; 22.28)
Sao Tome and Principe	0.30 (0.12 ; 0.51)	0.07 (0.01; 0.13)	0.23 (0.11; 0.38)	6.35 (2.76; 11.32)	0.15 (0.06; 0.27)	6.20 (2.70; 11.07)	6.34 (2.47; 10.79)	1.41 (0.14; 2.80)	4.94 (2.26; 8.34)	12.69 (5.16; 21.08)	1.56 (0.21; 3.06)	11.13 (5.03; 18.47)
Senegal	0.26 (0.11 ; 0.42)	0.04 (0.01; 0.07)	0.22 (0.10; 0.36)	3.36 (1.54; 5.83)	0.06 (0.02; 0.11)	3.30 (1.52; 5.73)	5.60 (2.30; 9.42)	0.77 (0.10; 1.53)	4.83 (2.20; 7.90)	8.97 (3.98; 14.73)	0.83 (0.12; 1.63)	8.13 (3.84; 13.19)
Sierra Leone	0.19 (0.07 ; 0.33)	0.04 (0.00; 0.07)	0.16 (0.07; 0.26)	2.47 (1.04; 4.39)	0.05 (0.02; 0.09)	2.42 (1.02; 4.31)	4.32 (1.66; 7.43)	0.79 (0.04; 1.64)	3.53 (1.58; 5.74)	6.79 (2.72; 11.47)	0.84 (0.06; 1.71)	5.95 (2.66; 9.81)
Togo	0.31 (0.14 ; 0.53)	0.05 (0.01; 0.10)	0.25 (0.12; 0.42)	2.53 (1.08; 4.41)	0.07 (0.03; 0.12)	2.46 (1.05; 4.30)	6.68 (2.90; 11.42)	1.11 (0.12; 2.19)	5.58 (2.71; 9.36)	9.22 (4.12; 15.50)	1.17 (0.15; 2.28)	8.04 (3.83; 13.50)

Footnote:

Different colors reflect different geographic levels. Red: Global; Blue: Super-regions; Green: Regions; Yellow: Country.

5.7 Capítulo 7 – [Livro digital] Os primeiros mil dias de vida: a odontologia na perspectiva DOHaD

Versão em português

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Organizadoras
Cecilia Claudia Costa Ribeiro
Ana Estela Haddad
Ana Emilia Figueiredo de Oliveira

OS PRIMEIROS MIL DIAS DE VIDA

A Odontologia na
perspectiva DOHaD



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OS PRIMEIROS MIL DIAS DE VIDA

**A Odontologia na
perspectiva DOHaD**

São Luís



EDUFMA
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PREFÁCIO

Nas últimas quatro décadas, dediquei-me intensamente à prática clínica, pesquisa e ao ensino da Odontopediatria. Durante esse tempo, tive o privilégio de aprender e de conviver com grandes nomes da Odontologia nacional e internacional, que muito me fizeram crescer como profissional e ser humano. Nesse caminho, tive dificuldades e obstáculos, que seguramente foram superados com amor, foco e determinação com que sempre tratei as ações desta natureza no campo da nossa profissão. Falo de desafios! Estes fazem parte da nossa rotina e do nosso dia a dia, tanto como clínico, educador e pesquisador. Quando superados, independente das dificuldades, fazem-nos crescer! Esse sentimento me transporta para mais próximo das autoras dessa obra, certamente por haver uma identificação com os mesmos sentimentos profissionais e acadêmicos.

Antes de ir à obra propriamente dita, não poderia aqui deixar de registrar a minha gratidão por ter sido considerado entre tantos para prefaciá-la. Imaginem a minha honra, felicidade e responsabilidade quando recebi o convite da Profa. Cecilia em nome dos demais colegas para prefaciar um livro de autores merecedores da minha maior consideração e respeito pelo muito que têm feito pelo crescimento e visibilidade da Odontopediatria brasileira, a melhor do mundo!

Tenho acompanhado o trabalho desenvolvido por essas professoras há algum tempo à frente da Universidade Aberta do SUS/UFMA e do Grupo de Pesquisa SAITE – Saúde, Inovação, Tecnologia e Educação. Com um conteúdo científico robusto e escrito por gestoras, empreendedoras e, por que não, protagonistas, nada mais justo iniciar por elas esta difícil tarefa que me foi designada.

Conheci a Profa. Cecilia Claudia Costa Ribeiro há quase 25 anos, quando da sua defesa de Mestrado lá na UFSC, em 1998. De lá para cá, continuamos muito próximos tanto no Lato Sensu (edições das primeiras turmas do Curso de Especialização em Odontopediatria da ABO-MA) quanto no Stricto Sensu (fiz parte da sua banca de Doutorado e, mais recentemente, da banca examinadora do seu concurso para o cargo de Profa. Titular da UFMA, além de participar como parceiro e colaborador de vários projetos de pesquisa encabeçados por ela até os dias de hoje), seguramente por conta de sentimentos pessoais e profissionais do mesmo valor. Continuo até hoje seu seguidor fiel, não com a mesma intensidade vivida há alguns anos, mas o suficiente para testemunhar o seu talento e brilho como Odontopediatra, docente e pesquisadora de ponta. Referência nacional e internacional, é protagonista de várias ações dentro e fora da Universidade Federal do Maranhão, atuando nas áreas da Odontologia e Saúde Coletiva – Epidemiologia, especialmente nos temas

“Doenças Não Transmissíveis, Bucais e Sistêmicas, com foco nos seus fatores de risco comuns ao longo do seu ciclo vital”. Desenvolve pesquisas sobre fatores de risco comportamentais nos Primeiros Mil Dias de Vida, na perspectiva DOHaD, foco desse e-book, intitulado “Os primeiros mil dias de vida: a Odontologia na perspectiva DOHaD”. Por tudo acima referido à sua pessoa como cirurgiã-dentista, sem dúvidas, trata-se de um grande expoente e referência atual da Odontopediatria brasileira, marcando o estado do Maranhão como uma das lideranças incontestáveis da nossa especialidade.

Ana Estela Haddad tem dentro de si a busca pelo protagonismo quando o assunto é inovar, sempre pensando no macro, mantendo a ética e os interesses da população à frente da sua trajetória como docente. Um exemplo de cidadã e uma referência da literatura odontológica. Protagonista de um dos projetos mais bonitos que já tivemos no atendimento em larga escala, o Telessaúde Brasil tem o seu dedo. Na Educação, com o PROUNI, propiciou o acesso a um ensino de qualidade para uma população que necessitava disso em todas as regiões do país. Acrescento, ainda, a UNA-SUS, Universidade que trabalha de forma séria, organizada, com metodologia e muito labor, que proporciona a formação de toda uma comunidade de saúde que atua no Sistema Único de Saúde. Não falo de volume, mas, sim, de qualidade! São tantas ações de magnitude nacional que faltariam páginas para elencar, discutir e refletir. A expectativa ao ler essa obra é exatamente a possibilidade de fazermos uma reflexão. Ela é essencial! O essencialismo nos dias de hoje só é destacado por quem já viveu, vive e busca se manter na vanguarda do conhecimento técnico-científico.

Já a Profa. Ana Emilia Figueiredo de Oliveira, cirurgiã-dentista, radiologista, portadora de uma mente muito aberta, como poucas vistas até então pela comunidade odontológica, não resumiu o seu campo de ação à Odontologia, à Radiologia ou à Odontopediatria. Trata-se de uma líder nata! Levou o seu estado, o Maranhão, a ser reconhecido como uma das maiores referências no ensino na Saúde quando a temática é inovação e tecnologia. Criou sistemas, desenvolveu softwares e capacitou profissionais de todo o Brasil. Ensinou a rede UNA-SUS a como fazer uma boa gestão de recursos, de pessoas, de projetos e do seu precioso tempo. Com uma produção intelectual no mínimo diferente, questiono-me “como ela conseguiu fazer tudo isso?”. Ela criou, implementou, avaliou e colocou a tecnologia como ferramenta de educação na rotina do cirurgião-dentista. Incrível!

Apresentadas as mentoras desta obra, fica fácil entender o quanto esse e-book impactará na saúde geral da população, não somente na infância, mas também ao longo da vida!

A Teoria Desenvolvimentista da Saúde e das Doenças – DOHaD (do inglês, The Developmental Origins of Health and Disease) se baseia nas exposições ambientais que agem no início da vida e aumentam a susceptibilidade ao desenvolvimento de doenças não transmissíveis (DNT) no futuro. Assim, os primeiros mil dias de vida (270 dias da gestação + 365 dias do primeiro ano + 365 dias do segundo ano) são o período de maior sensibilidade do desenvolvimento humano, representando uma janela de oportunidades para prevenção de DNT. A atuação dos profissionais de saúde à luz da Teoria DOHaD pode ter repercussão ao longo do ciclo vital do indivíduo. Dentro de uma abordagem odontológica contemporânea, referendada pelas mais robustas evidências científicas, o cirurgião-dentista é elemento essencial como profissional da Equipe da Estratégia de Saúde da Família em contato direto com os pacientes nos primeiros mil dias de vida. Esse período torna-se propício para a prevenção de DNT, aconselhando a gestante e as mães no puerpério para a importância de escolhas alimentares mais saudáveis para si, para sua família e seus bebês, o que trará repercussões positivas para sua saúde, para a gestação e para a saúde da criança a longo prazo, visto que o consumo de açúcar de adição não é restrito somente na infância, mas ao longo da vida, sendo um fator de risco para muitas doenças crônicas em adultos e idosos.

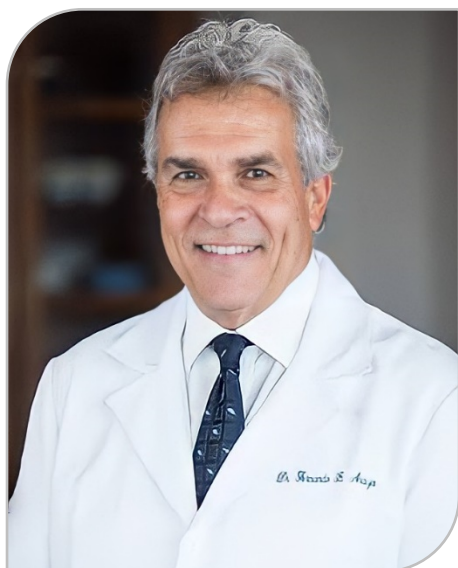
Neste livro em formato digital, as autoras trabalharam em consonância com as ações estratégicas dos Objetivos de Desenvolvimento Sustentável, no eixo Promoção de Saúde, ao propor este recurso instrucional em vista da ação “Formar e qualificar profissionais de saúde e sociedade civil para desenho e implantação de cidades/territórios inteligentes, saudáveis e sustentáveis; e, no eixo Atenção Integral à Saúde, apresentando evidências que dão suporte à ação “Ampliar o acesso ao pré-natal odontológico com o objetivo de reduzir a ocorrência de cárie e doença periodontal”.

À luz da teoria DOHaD, os primeiros mil dias de vida foram apresentados como um “intervalo de ouro” para a prevenção integrada das DNT, incluindo as bucais e sistêmicas de maior mortalidade no futuro. Destacamos como estratégia para prevenção primordial para DNT manter-se longe dos fatores de risco nesta etapa da vida. Nesse sentido, ressaltamos a importância do aleitamento materno exclusivo até os seis meses, além de evidências para o apoio irrestrito à sua continuidade até os dois anos de idade ou mais, o qual deve ser complementado por uma dieta saudável, baseada em alimentos in natura ou minimamente processados. Além disso, as autoras propõem uma abordagem integrada da cárie e da doença periodontal, com proposição de medidas de prevenção e/ou intervenção direcionadas para seus fatores de risco comuns para uma redução mais efetiva da carga de

doenças bucais crônicas, as quais devem começar precocemente no ciclo vital do indivíduo, ou seja, nos primeiros mil dias de vida.

As DNT bucais antecedem e predizem décadas antes o aparecimento de DNT de maior mortalidade. Por essa razão, no contexto da atuação multidisciplinar na Estratégia de Saúde da Família, o cirurgião-dentista deve assumir um papel de protagonismo na prevenção integral da saúde da mulher durante a gestação e da saúde do bebê nos primeiros mil dias de vida, identificando exposições de risco e sinais precoces de DNT, e orientando as famílias sobre seus fatores de risco comuns.

Mas para que isso venha a ser colocado em prática, há a necessidade das pessoas que compõem as famílias das comunidades envolvidas serem devidamente informadas. O presente e-book busca atualizar e capacitar o cirurgião-dentista, importante membro da Equipe Multidisciplinar de Saúde, a difundir ações para um impacto positivo na saúde bucal e geral das gestantes e das crianças, contribuindo para a redução da carga de DNT no futuro na prole, para seja um profissional essencial nas ações de modo a atingir os Objetivos de Desenvolvimento Sustentável nas próximas décadas. E, para tal, as autoras constroem de forma ímpar, com sustentação e competência, uma obra que será referência na Odontopediatria Contemporânea.



Finalizo recomendando fortemente a leitura desse livro aos profissionais da área da saúde e leigos, com impacto direto na prevenção das DNT, provendo uma prática odontológica realista e racional para todos, satisfazendo, assim, as demandas das nossas crianças e futuros adultos. A Odontopediatria brasileira agradece!

Fernando Borba de Araújo

Odontopediatra
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SUMÁRIO

INTRODUÇÃO	13
OS PRIMEIROS MIL DIAS DE VIDA	16
TEORIA DOHAD E A ODONTOLOGIA.....	19
A cárie e a doença periodontal são doenças não transmissíveis e estão associadas entre si.....	22
Alimentos ultraprocessados e açúcares de adição são fatores de risco para DNT bucais e sistêmicas.....	23
Microbioma humano em equilíbrio.....	24
Amamentação como proteção contra DNT	25
ATENÇÃO À SAÚDE DURANTE A GESTAÇÃO.....	26
Rede Cegonha.....	27
Atuação do cirurgião-dentista no pré-natal odontológico.....	28
Orientação sobre alimentação saudável para gestantes.....	30
ESTRESSORES AMBIENTAIS DURANTE A GESTAÇÃO	31
Bebidas alcoólicas e tabagismo	32
Uso de antibióticos na gestação.....	33
Consumo de açúcares de adição na gestação.....	34
Obesidade.....	35
Hipertensão arterial	36
Diabetes	36
Doenças bucais crônicas	37
ATENÇÃO À SAÚDE DURANTE OS DOIS PRIMEIROS ANOS DE VIDA	41
Aleitamento materno.....	42
Introdução alimentar complementar	45
Higiene oral do bebê	48
ESTRESSORES AMBIENTAIS DURANTE OS PRIMEIROS DOIS ANOS.....	49
Cesariana.....	50
Mamadeiras e chupetas	51
Açúcares de adição	52
Alterações no desenvolvimento da criança.....	53
Asma.....	53
Excesso de peso	54
Doenças bucais crônicas	54
OS PRIMEIROS MIL DIAS NA AGENDA DE ENFRENTAMENTO DAS DNT	55
PROGRAMA PREVINE BRASIL E OS INDICADORES DE DESEMPENHO DA ASSISTÊNCIA DURANTE OS PRIMEIROS MIL DIAS.....	58
CONSIDERAÇÕES FINAIS	61
REFERÊNCIAS.....	63

APRESENTAÇÃO

A Teoria das Origens Desenvolvimentistas da Saúde e da Doença, do inglês DOHaD, estuda como o ambiente na vida precoce pode repercutir no risco de desenvolver doenças não transmissíveis (DNT) no futuro.

Neste material, sob a ótica da Teoria DOHaD, vamos apontar as premissas que suportam a Odontologia nessa perspectiva e especialmente discutir as ações do cirurgião-dentista no acompanhamento das gestantes, no puerpério e atenção integral à saúde da criança nos Primeiros Mil Dias de Vida.

À luz do conhecimento de que as DNT bucais ocorrem décadas antes de outras DNT de maior mortalidade, apontaremos o papel de protagonismo do cirurgião-dentista na atuação multidisciplinar na Estratégia de Saúde da Família, identificando exposições de risco e sinais precoces de DNT e orientando as famílias neste processo, além da elaboração de políticas públicas para enfrentamento das DNT.

O agrupamento da cárie e da doença periodontal com outras DNT sistêmicas e de maior mortalidade na vida adulta, especialmente nas populações mais vulneráveis, exige um enfrentamento integrado, voltado para seus fatores de risco comuns, que deve começar em fases mais precoces do ciclo vital.

No Brasil, o Ministério da Saúde, em alinhamento com os Objetivos de Desenvolvimento Sustentável (ODS) 2021-2030, apresentou o Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas e Agravos Não Transmissíveis (2021-2030), com metas e ações direcionadas a estas doenças. Entre as metas, estão a redução das taxas de obesidade de crianças e a redução do consumo de alimentos ultraprocessados e de bebidas adoçadas. Dentre as estratégias, destacamos, para a Odontologia, a de “Ampliar o acesso ao pré-natal odontológico com o objetivo de reduzir a ocorrência de cárie e da doença periodontal”.

É neste panorama que apresentamos este livro em formato digital “Os primeiros mil dias de vida: a Odontologia na perspectiva DOHaD”. Esperamos que este material, preparado com muito carinho, amplie sua visão e seja útil a você!

Boa leitura!



INTRODUÇÃO

INTRODUÇÃO

O enfrentamento das Doenças Não Transmissíveis (DNT), ou apenas doenças crônicas, é o maior desafio em saúde pública do século XXI.¹ As DNT mais mortais, doenças cardiovasculares, diabetes tipo 2, doenças respiratórias e cânceres, são responsáveis por 71% de todas as mortes no mundo. Dessas mortes, mais de 85% são precoces, ocorrendo entre 30 a 69 anos de idade, afetando especialmente países de baixa e média renda, como o Brasil.^{1,2}

Mesmo no contexto da pandemia da covid-19, uma maior mortalidade devido a complicações da infecção por SARS-CoV-2 tem sido observada em grupos populacionais acometidos por DNT.³

Determinantes sociais e econômicos, como pobreza, exclusão social e baixo nível de escolaridade, são reconhecidamente fatores de risco para DNT, uma vez que essas doenças se agrupam e são mais prevalentes em países de baixa e média renda ou em grupos populacionais com maior vulnerabilidade social nos países de alta renda.^{1,2}

Além dos determinantes sociais, a Organização Mundial da Saúde (OMS) aponta quatro principais fatores de risco comportamentais e modificáveis para todas as DNT, a saber: tabagismo, inatividade física, dieta não saudável e uso nocivo de álcool. As exposições a esses comportamentos de risco resultam em alterações metabólicas, como pressão arterial elevada, sobrepeso/obesidade, níveis elevados de glicose no sangue (hiperglicemia) e níveis elevados de gordura no sangue (hiperlipidemia).²

A cárie e a periodontite são também doenças crônicas, sendo as DNT mais prevalentes no mundo. Ainda que não diretamente relacionadas à mortalidade, essas



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doenças bucais estão associadas à asma, inclusive em crianças e adolescentes⁴ e predizem o risco do diabetes e das doenças cardiovasculares décadas antes.^{5,6} Assim, temporalmente, as doenças bucais ocorrem antes que outras DNT de maior mortalidade na vida adulta.

É nesse contexto que o Comitê de Saúde Bucal da OMS⁷ preconiza estratégias direcionadas às DNT bucais e sistêmicas, com base em seus fatores de risco comuns. Ações direcionadas aos fatores de risco comuns visam à prevenção integrada das DNT bucais e sistêmicas, sendo que as intervenções precoces são as mais efetivas para reduzir as DNT no futuro.

A maior plasticidade do fenótipo dá suporte para ações de prevenção nos períodos mais sensíveis do desenvolvimento humano. A Teoria Desenvolvimentista da Saúde e das Doenças - DOHaD (do inglês, The Developmental Origins of Health and Disease) se baseia nas exposições ambientais que agem no início da vida e aumentam a susceptibilidade ao desenvolvimento de DNT no futuro. Assim, os primeiros mil dias de vida (270 dias da gestação + 365 dias do primeiro ano + 365 dias do segundo ano) são o período de maior sensibilidade do desenvolvimento humano, representando uma janela de oportunidades para

prevenção de DNT.^{8,9}

A atuação dos profissionais de saúde à luz da Teoria DOHaD pode ter repercussão ao longo do ciclo vital do indivíduo. O cirurgião-dentista é um dos profissionais da equipe da Estratégia de Saúde da Família com contato direto com os pacientes nos primeiros mil dias de vida. Esse período torna-se propício para a prevenção de DNT, aconselhando a gestante e as mães no puerpério sobre a importância de escolhas alimentares mais saudáveis para si, para sua família e

seus bebês, o que pode trazer repercussões positivas para sua saúde, para a gestação e para a saúde da criança a longo prazo.



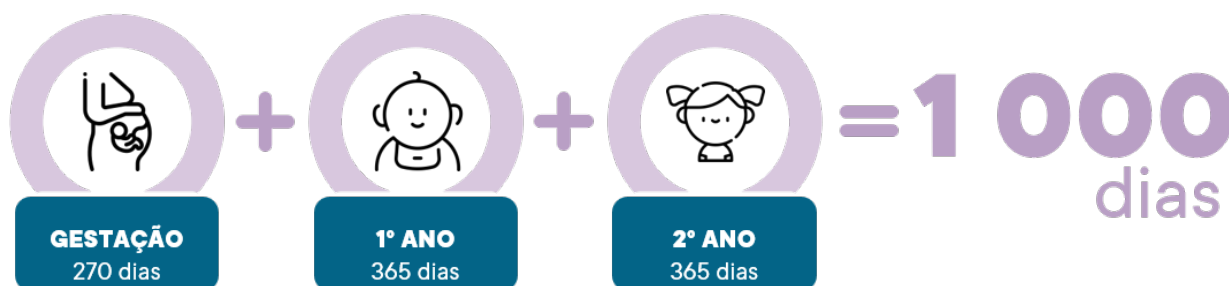
OS PRIMEIROS MIL DIAS DE VIDA

Capítulo 1

OS PRIMEIROS MIL DIAS DE VIDA

Os primeiros mil dias de vida, da gestação até os dois anos da criança, têm fortes repercussões no desenvolvimento cognitivo, emocional e sociocomportamental da criança. Uma dieta equilibrada e saudável, acesso a serviços de saúde, educação e saneamento básico, bem como o estímulo, a interação adequada e a proteção da criança de situações de violência ou de negligência são fundamentais para a promoção do crescimento e do desenvolvimento integral na primeira infância.

OS MIL DIAS DA CRIANÇA



O INTERVALO DE OURO

Esse é o período no qual as rápidas mudanças fisiológicas e a plasticidade do fenótipo da criança podem ter efeitos na saúde do indivíduo ao longo da vida, não apenas em termos biológicos (crescimento e desenvolvimento), mas também em questões intelectuais e sociais.

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Essa fase corresponde a uma “janela de oportunidades” para prevenir uma programação metabólica desfavorável e/ou alterá-la, melhorando os indicadores de saúde da gestante, fetal, do nascimento, da infância e até mesmo reduzindo o risco de a criança desenvolver DNT no futuro.

A gravidez é acompanhada de alterações fisiológicas bioquímicas, metabólicas e endócrinas no corpo da gestante para atender às necessidades do desenvolvimento do complexo materno-fetal. Estressores ambientais agindo no período gestacional, tais como alimentação não saudável, exposição ao álcool e ao fumo, têm impactos negativos na saúde

Foto: Ignacio Campo
Unsplash.com



da gestante, resultando em ganho de peso excessivo, hipertensão arterial, diabetes gestacional, doença periodontal, dentre outras DNT.¹⁰⁻¹² Esses comportamentos de risco também podem resultar em efeitos adversos no final da gestação, tais como nascimento pré-termo (< 37 semanas), bebês grandes para a idade gestacional (≥ 4000 g) ou podem, ainda, desencadear efeitos na sua prole a curto prazo, como asma, atraso no desenvolvimento neuropsicomotor e aumento da susceptibilidade à cárie dentária, além de DNT na prole a longo prazo.^{13,14}

Os estressores ambientais agindo nos primeiros dois anos de vida da criança, como aleitamento artificial e exposição precoce aos açúcares de adição, também podem causar impactos na primeira infância e ao longo da vida da criança.¹⁴⁻¹⁸

Dessa forma, o cirurgião-dentista tem papel fundamental na orientação das gestantes para adoção de um estilo de vida mais saudável. As atitudes e os comportamentos saudáveis nos primeiros mil dias de vida são determinantes para uma gestação mais saudável, com impacto na saúde da gestante e do bebê, inclusive a longo prazo.

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TEORIA DOHaD E A ODONTOLOGIA

Capítulo 2

TEORIA DOHaD E A ODONTOLOGIA

A Teoria DOHaD investiga como o ambiente, nos primeiros mil dias de vida, pode repercutir no risco de desenvolvimento de DNT, desde a infância até a idade adulta, analisando os mecanismos envolvidos nesses processos.^{9,19}

Essa ideia foi introduzida a partir dos estudos de David Barker²⁰ em 1961, que observou que os bebês gerados em condições de privação nutricional intraútero tinham maior risco de desenvolverem doenças cardiovasculares quando adultos. Os estudos de Barker vêm sendo aprofundados e expandidos. Atualmente, diversos grupos de pesquisa tentam entender como as condições adversas dos primeiros mil dias de vida da criança impactam a saúde futura.

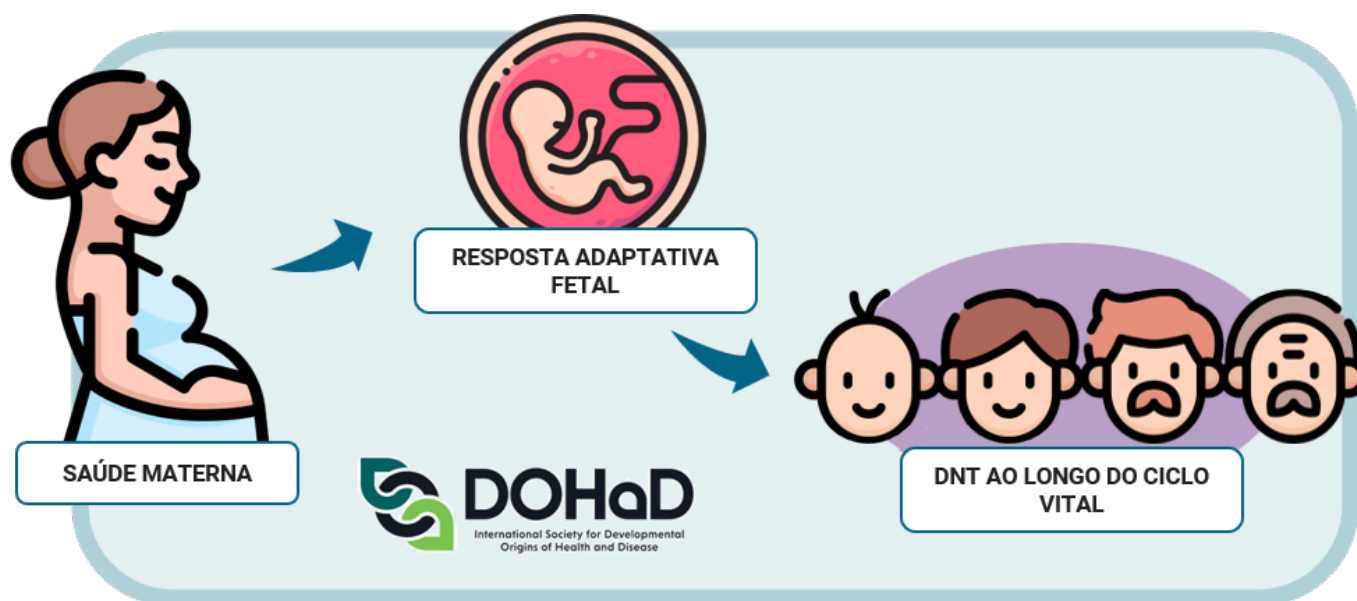
Ainda que o código genético seja predeterminado, estudos mostram que os fatores externos ou epigenéticos podem modificar a expressão dos genes humanos ao longo da vida.¹⁹ Os estímulos do meio ambiente são fundamentais para o equilíbrio saúde/doenças ao longo das gerações.^{9,21} Os estudos

DOHaD se concentram na prevenção de ambientes adversos na origem da vida, sendo um modelo integrador que explica como influências ambientais (meio ambiente, família, hábitos, condições socioeconômicas e estresse tóxico) podem afetar a programação biológica/herança genética, resultando em fenótipos que manifestam alterações imediatas (nascimento pré-termo, baixo peso ao nascer e anemia) ou tardias (obesidade, diabetes, hipertensão arterial e asma).¹⁴⁻¹⁶

A Teoria DOHaD propõe que um risco aumentado de doenças de longo prazo é inicialmente induzido por respostas adaptativas do bebê, a partir das condições de saúde e do estado físico da gestante. As respostas fetais ou perinatais podem incluir alterações no metabolismo, produção e sensibilidade endócrinas que, por sua vez, podem levar à quebra da homeostase fisiológica.²¹



Foto: Federico Giampieri
Unsplash.com



Fonte: GLUCKMAN *et al.*, 2010. Imagem criada com recursos do Flaticon.com

A Teoria DOHaD dá suporte à prerrogativa de que o melhor momento para promover intervenções preventivas para DNT, com redução substancial de risco, são os períodos de maior desenvolvimento: **vida intrauterina, infância** e, em como uma segunda janela de oportunidade, ainda que de menor efeito, a **adolescência**.^{22,23}

Agora, você deve estar se perguntando, como a Odontologia se insere nos estudos da Teoria DOHaD? Vamos, a seguir, apresentar as quatro premissas que suportam a visão da Odontologia na perspectiva DOHaD:

1. A cárie e a doença periodontal são DNT, sendo as mais prevalentes, e que antecedem temporalmente, inclusive, capazes de predizer outras DNT de maior mortalidade no futuro;
2. O consumo de uma dieta não saudável, especialmente rica em alimentos ultraprocessados e açúcares de adição, é um dos fatores de risco para DNT bucais e sistêmicas;
3. O equilíbrio do microbioma humano é fator primordial à saúde, e a quebra da sua homeostase resulta em alterações da diversidade microbiana (disbiose), a qual tem implicações na saúde bucal e geral do indivíduo;
4. A amamentação é importante para o crescimento e desenvolvimento dos bebês e para a prevenção DNT. A Odontologia deve apoiar as práticas de amamentação, de acordo com a recomendação da OMS.

Vamos, agora, apresentar evidências científicas para dar suporte às quatro premissas destacadas acima, que colocam a Odontologia na perspectiva DOHaD.

1 A CÁRIE E A DOENÇA PERIODONTAL SÃO DOENÇAS NÃO TRANSMISSÍVEIS E ESTÃO ASSOCIADAS ENTRE SI

A cárie e a doença periodontal são as DNT mais prevalentes ao redor de todo o mundo.²⁴ Segundo o Global Burden of Diseases Study, as cavidades de cárie na dentição permanente foram uma das condições mais prevalentes, com uma ocorrência global de 35% para todas as idades combinadas.²⁵ A periodontite afeta globalmente 45-50% da população adulta em sua forma mais branda e 9-11% da população adulta na forma mais grave.^{26,27} Ainda que as duas doenças bucais não tenham relação direta com o aumento do número de óbitos, elas estão associadas às DNT mais mortais. A cárie e a doença periodontal estão associadas à obesidade,²⁸ à asma^{4,29} e à depressão³⁰⁻³² e parecem prever outras DNT de maior mortalidade no futuro, como as doenças cardiovasculares e o diabetes.^{5,6,33-36}



Imagem criada com recursos do FlatIcon.com

A cárie é uma doença biofilme-açúcar dependente que afeta o tecido mineralizado dos dentes, enquanto a doença periodontal é uma doença desencadeada por acúmulo do biofilme oral, que resulta em resposta inflamatória no hospedeiro (gengivite) e pode evoluir para destruição dos tecidos de sustentação dos dentes (periodontite).³⁷ A cárie tem sua causa claramente ligada ao frequente e excessivo consumo dos açúcares de adição.^{7,38} A maior frequência e concentração do consumo de carboidratos altamente fermentáveis no biofilme dental, especialmente da sacarose, resulta em produção de ácido e na menor diversidade bacteriana (disbiose) representada, principalmente, por bactérias acidogênicas e acidúricas e pela desmineralização dos tecidos duros do dente.³⁹ A periodontite é desencadeada pela disbiose do biofilme subgengival em indivíduos com desregulação do sistema imunológico, com quebra da homeostase entre micro-organismo/hospedeiro,³⁹ o que pode resultar em danos aos tecidos periodontais, a saber: perda da inserção clínica e reabsorção óssea alveolar.⁴⁰

Ainda que essas doenças bucais tenham etiopatogenias completamente distintas, com a cárie afetando os tecidos mineralizados dos dentes^{38,39} e a doença periodontal afetando os tecidos de suporte,³⁷ ambas são desencadeadas pela presença de biofilme.³⁹ Evidências emergentes também apontam para o consumo de açúcares de adição como um

fator de risco comum para as duas doenças.^{17,18,41-43} Além disso, os indicadores da cárie e da doença periodontal estão associados entre si, formando um fenômeno denominado de Carga de Doenças Bucais Crônicas, que, na primeira infância, agrupa lesões como cárie e gengivite⁴³ e, nos adolescentes, profundidade de sondagem clínica, sangramento à sondagem, CPOD e Índice PUFA (gravidade de cárie).¹⁸

Assim, é importante destacar que o fenômeno Carga de Doenças Bucais Crônicas não deve ser compreendido apenas como indicador clínico de diagnóstico, mas como uma forma de oportunizar o planejamento de medidas de prevenção integrada das duas doenças, com ações preventivas e/ou intervencionais direcionadas para seus fatores de risco comuns. Ou seja, compreendendo a cárie e a doença periodontal como um conteúdo transdisciplinar, que ainda permanecem abordados como conteúdos completamente separados nos cursos de graduação em Odontologia.

2 ALIMENTOS ULTRAPROCESSADOS E AÇÚCARES DE ADIÇÃO SÃO FATORES DE RISCO PARA DNT BUCAIS E SISTÊMICAS

Os alimentos ultraprocessados são formulações produzidas por diversas técnicas de processamento e levam inúmeros ingredientes, muitos deles de uso industrial exclusivo, como óleos modificados e aditivos alimentares (corantes artificiais, conservantes, aromatizantes, emulsificantes, realçadores de sabor etc.), com pouca ou nenhuma quantidade de alimentos in natura.⁴⁴ Esses tipos de produto também apresentam, em sua composição, os açúcares de adição, que, por sua vez, estão presentes em vários alimentos do consumo diário, tendo sido adicionados (por isso o nome “açúcares de adição”) a alimentos processados, ultraprocessados ou preparações culinárias para melhorar o gosto desses produtos.^{45,46} Nesse contexto, as bebidas ricas em açúcares de adição representam a maior fonte de calorias discredionárias (densas em energia, mas sem valor nutricional) da dieta, estando associadas ao maior ganho de peso na gestação, o que pode desencadear hipertensão e diabetes gestacional, doenças bucais crônicas (cárie dentária e doença periodontal) e até mesmo o nascimento pré-termo da criança e o desenvolvimento de sintomas de asma na prole.^{10,14,41} A forma como esses açúcares serão identificados será descrita no Capítulo 4.



O papel crucial dos açúcares de adição na etiologia da cárie é inquestionável.^{7,38,47} Evidências recentes em estudos epidemiológicos de base-populacional também apontam para a associação entre os açúcares de adição e a gengivite em crianças, e a doença periodontal em adolescentes, gestantes e adultos.^{17,18,41,42}

Revisões sistemáticas e estudos de coortes têm mostrado que o maior consumo de bebidas ricas em açúcares de adição está associado ao excesso de peso (inclusive em crianças), obesidade, síndrome metabólica, esteatose hepática não alcoólica, hipertensão arterial, doenças cardiovasculares, resistência insulínica, menor memória episódica e marcadores da doença de Alzheimer.⁴⁸⁻⁵³

3 MICROBIOMA HUMANO EM EQUILÍBRIO

O corpo humano é ricamente colonizado por cerca de 100 trilhões de bactérias fundamentais para a homeostase do organismo, tendo profunda influência na fisiologia e nutrição do indivíduo.^{54,55} Ao nascer, o microbioma intestinal começa a se desenvolver intensamente, influenciado por diversos fatores externos.

Os primeiros dois anos de vida são considerados o principal período de desenvolvimento do microbioma humano, o qual ainda é menos resiliente, nesse intervalo, e muito mais responsivo aos fatores externos e ambientais do que o microbioma observado no adulto.⁵⁶

Dentre os fatores que interferem negativamente na composição do microbioma humano neste período, podem ser citados: nascer de cesariana, aleitamento artificial, uso de antibióticos e consumo de açúcares de adição na dieta complementar antes do segundo ano de vida.⁵⁷ Alterações na diversidade do microbioma intestinal (disbiose intestinal) podem repercutir no crescimento da criança, na resposta imune e no seu desenvolvimento neuropsicomotor e ósseo.⁵⁷⁻⁵⁹ Como vimos anteriormente, as doenças bucais crônicas também estão ligadas à disbiose do biofilme, que pode ter sua homeostase quebrada pelo consumo dos açúcares de adição.³⁹



Imagem criada com recursos do FlatIcon.com



VOCÊ SABIA?

O leite materno contém oligossacarídeos, carboidratos de cadeias curtas não digeríveis e não absorvidos pelo intestino, que têm um papel essencial na microbiota da criança. Esses oligossacarídeos funcionam como prebióticos, sendo metabolizados por bactérias benéficas para a homeostase do microbioma, como as bifidobactérias e as bacteroides. Além disso, parecem ser capazes de modular a resposta imune e servir como barreira intestinal para o bebê.

4 AMAMENTAÇÃO COMO PROTEÇÃO CONTRA DNT

A Organização Mundial da Saúde e o Ministério da Saúde do Brasil recomendam o aleitamento materno exclusivo nos primeiros seis meses de vida e que a amamentação se estenda até os dois anos ou mais.^{60,61} A amamentação é um fator de proteção para mortes infantis, diarreias, infecções infantis e respiratórias, alergias, aumenta a capacidade cognitiva/inteligência, reduz má oclusão e diminui as chances de sobrepeso, obesidade, hipertensão arterial, colesterol alto e diabetes; além de melhorar a nutrição da criança. Para

as mulheres que amamentam, o aleitamento protege contra o câncer de mama, de ovário, de útero, o diabetes tipo 2, hipercolesterolemia, hipertensão arterial, doença coronariana, obesidade, osteoporose, artrite reumatoide, depressão pós-parto; e diminuição do risco de recaída de esclerose múltipla pós-parto.^{15,62-64}



Imagem criada com recursos do Flaticon.com

Paradoxalmente, alguns estudos apontam para uma associação entre aleitamento materno e cárie na primeira

infância.⁶⁵ Entretanto, a melhor evidência disponível de revisão sistemática apontou que a amamentação por um tempo menor ou igual a 24 meses de vida não aumentou do risco de cárie na primeira infância e sugeriu que o maior tempo de aleitamento estaria associado à cárie em crianças, mas concluindo que as evidências são de baixa qualidade.⁶⁶ Além disso, o leite humano não tem potencial para resultar em produção ácida no biofilme dental com capacidade de desmineralizar o esmalte, enquanto só a sacarose tem este potencial.⁶⁷ Nesse mesmo sentido, a exposição ao leite humano intercalada à sacarose pode tornar o biofilme mais cariogênico, capaz de metabolizar também a lactose,⁶⁸ mostrando que a sacarose é a verdadeira vilã na etiologia da cárie.

Por fim, não há nenhuma evidência que mostre que a redução das práticas de amamentação ou do seu tempo tenha algum efeito de proteção para cárie na primeira infância. Alertamos que esse tipo de recomendação pode resultar na diminuição do tempo de amamentação e, conseqüentemente, na redução dos inúmeros benefícios para a saúde da criança, inclusive a longo prazo. O cirurgião-dentista deve unir esforços com a equipe da Atenção Primária à Saúde para proteger e promover a amamentação.

ATENÇÃO À SAÚDE DURANTE A GESTAÇÃO

Capítulo 3

ATENÇÃO À SAÚDE DURANTE A GESTAÇÃO

REDE CEGONHA

A Rede Cegonha é a estratégia do Ministério da Saúde, através do Serviço Único de Saúde, que tem por objetivo implementar uma rede de cuidados para assegurar o planejamento familiar às mulheres, a atenção humanizada no período da gravidez, durante o parto e puerpério, bem como assegurar às crianças o direito ao nascimento seguro e ao crescimento e desenvolvimento saudáveis. Esses cuidados estão organizados em quatro componentes que estruturam a Rede.⁶⁹ Conheça os quatro componentes da Rede Cegonha:

ESTRUTURA DA REDE CEGONHA



PRÉ-NATAL

- Captação das gestantes
- Acolhimento
- Vinculação da gestante ao local de parto
- Consultas de pré-natais médico e odontológico
- Exames pré-natais



PARTO E NASCIMENTO

- Presença de acompanhante
- Visita hospitalar da equipe de saúde
- Centro de parto normal
- Agendamento da consulta após o nascimento



PUERPÉRIO E ATENÇÃO À CRIANÇA

- Visitas domiciliares após o parto
- Incentivo e apoio ao aleitamento materno
- Busca ativa de crianças vulneráveis
- Apoio à alimentação complementar saudável
- Acompanhamento do calendário vacinal
- Prevenção de hábitos bucais deletérios



SISTEMA LOGÍSTICO

- Acesso aos serviços em tempo hábil
- Classificação de risco da gestante
- Acesso a toda a rede de unidade de saúde
- Acolhimento e responsabilização pela gestante





Como mencionado, a Rede Cegonha é uma importante ferramenta do SUS para a implementação de cuidados em saúde durante os primeiros mil dias. Desta forma, destacamos a atuação da equipe de saúde bucal no pré-natal odontológico, bem como no diagnóstico de doenças bucais crônicas na gestante e no bebê, além da orientação acerca do aleitamento materno e da dieta saudável, com vistas à prevenção de DNT bucais e sistêmicas.

ATUAÇÃO DO CIRURGIÃO-DENTISTA NO PRÉ-NATAL ODONTOLÓGICO

Todos os profissionais envolvidos na Estratégia Saúde da Família devem estar engajados para garantir um pré-natal de baixo risco. O cirurgião-dentista participa da estratégia conjunta ao realizar ações de atenção odontológica e de promoção da educação em saúde, de prevenção de agravos e de escuta qualificada das necessidades das usuárias em todas as ações, proporcionando um atendimento humanizado e viabilizando o estabelecimento do vínculo com as gestantes.⁷⁰

As atribuições do cirurgião-dentista descritas pelo Ministério da Saúde para a garantia do pré-natal de baixo risco podem refletir na prevenção de DNT para a mãe e para o bebê. Conheça as atribuições do cirurgião-dentista nesta fase:



ATRIBUIÇÕES DO CIRURGIÃO-DENTISTA PARA O PRÉ-NATAL DE BAIXO RISCO

1. Orientar as mulheres e suas famílias sobre a importância do pré-natal e da amamentação.
2. Realizar a consulta odontológica de pré-natal de gestação de baixo risco.
3. Orientar a mulher e seu companheiro sobre hábitos alimentares saudáveis e de higiene bucal.
4. Realizar condutas odontológicas preventivas, garantindo conforto à gestante e a continuidade do tratamento após a gravidez.
5. Identificar as gestantes de alto risco e encaminhá-las ao serviço de referência.
6. Desenvolver atividades educativas e de apoio à gestante e aos seus familiares.
7. Acompanhar o processo de aleitamento materno e os cuidados com o futuro bebê.
8. Realizar a avaliação geral da gestante, observando o período de gravidez.

Fonte: BRASIL, 2013. Imagem criada com recursos do Flaticon.com

As gestantes têm uma maior receptividade ao pré-natal odontológico e, apesar de reconhecerem sua importância, é observada uma baixa frequência a esse serviço da Rede Cegonha.⁷¹ Muitas gestantes mostraram disposição ao uso de mamadeiras e chupetas, o que pode levar ao desmame precoce. A educação em saúde durante a gestação é um importante vetor de propagação de hábitos saudáveis para a prole. Nesse sentido, o cirurgião-dentista deve estar preparado para atuar em parceria com a equipe multidisciplinar na linha de cuidados e orientações.^{72,73}

ORIENTAÇÃO SOBRE ALIMENTAÇÃO SAUDÁVEL PARA GESTANTES

No contexto da Estratégia Saúde da Família, o cirurgião-dentista deve ser capaz de protagonizar ações de orientação à gestante quanto à dieta adequada e saudável, sensibilizando sobre a adoção de hábitos alimentares saudáveis para repercussões positivas sobre a criança no futuro.

Nesse sentido, o Ministério da Saúde recomenda os “Dez passos para uma alimentação saudável para gestantes”,⁷⁰ subsidiando a orientação profissional para o ganho de peso saudável durante a gestação.



DEZ PASSOS PARA UMA ALIMENTAÇÃO SAUDÁVEL PARA GESTANTES

1. Faça pelo menos três refeições (café da manhã, almoço e jantar) e dois lanches saudáveis por dia e beba pelo menos 2 litros de água (6 a 8 copos) por dia.
2. Dê preferência aos alimentos na sua forma mais natural, pois são boas fontes de fibras, vitaminas e minerais.
3. Procure consumir diariamente pelo menos três porções de legumes e verduras como parte das refeições e três porções ou mais de frutas nas sobremesas e lanches.
4. Coma feijão com arroz todos os dias ou, pelo menos, cinco vezes por semana.
5. Consuma diariamente três porções de leite e derivados e uma porção de carnes, aves, peixes ou ovos. Retire a gordura aparente das carnes e a pele das aves antes da preparação.
6. Diminua o consumo de gorduras. Consuma, no máximo, uma porção diária de óleos vegetais, azeite, manteiga ou margarina.
7. Evite refrigerantes e sucos industrializados, biscoitos recheados e outras guloseimas no seu dia a dia.
8. Diminua a quantidade de sal na comida. Evite consumir alimentos industrializados, como hambúrguer, salsicha, linguiça, presunto, salgadinhos, sopas prontas e temperos prontos.
9. Consuma alimentos fontes de ferro, como: carnes, vísceras, feijão, soja, folhas verde-escuras, grãos integrais e outros. Consuma junto desses alimentos as fontes de vitamina C.
10. Mantenha o ganho de peso gestacional dentro de limites saudáveis. Pratique atividade física sob orientação de um profissional e evite bebidas alcoólicas e o fumo.

ESTRESSORES AMBIENTAIS DURANTE A GESTAÇÃO

Capítulo 4



ESTRESSORES AMBIENTAIS DURANTE A GESTAÇÃO

Como vimos até aqui, os primeiros mil dias de vida são uma janela de oportunidades para prevenção de DNT. Diante disso, estressores ambientais agindo nesse período podem levar a desfechos negativos na saúde da gestante, alterações no desenvolvimento fetal; em desfechos desfavoráveis na gestação e na saúde do bebê, tanto de forma imediata quanto ao longo de toda a sua vida. Assim, o cirurgião-dentista deve reconhecer esses fatores de risco durante a gravidez e suas repercussões, bem como saber como atuar na comunidade de modo a planejar e a executar estratégias de prevenção efetivas.

BEBIDAS ALCOÓLICAS E TABAGISMO

Na gestação, estressores ambientais, como o tabaco e o álcool, podem impactar o desenvolvimento do feto e levar à morte perinatal ou neonatal. O consumo de álcool durante a gestação aumenta o risco de malformação fetal, aborto espontâneo, nascimento pré-termo e baixo peso ao nascer.^{74,75} Esse conjunto de complicações para o bebê, acarretado pela exposição ao álcool durante a gestação, é conhecido como **Síndrome Alcoólica Fetal**, como vemos a seguir:



Imagem criada com recursos do Flaticon.com



SÍNDROME ALCOÓLICA FETAL

Essa condição leva a complicações como: anomalia facial, restrição de crescimento fetal, deficiências congênitas nos órgãos e anomalias relacionadas ao aprendizado, por exemplo, o desenvolvimento do transtorno do déficit de atenção e hiperatividade.

Fonte: MAY et al., 2016. Imagem criada com recursos do Flaticon.com



O hábito de fumar durante a gestação está associado à redução das dimensões do feto. Além disso, fumar durante a gestação está relacionado à natimortalidade, morte neonatal e morte perinatal por hemorragia materna e consequente asfixia do feto, decorrente do descolamento da placenta. Esses riscos aumentam com a quantidade de cigarros fumados pela mãe, contudo, seus efeitos podem ser minimizados se as mães interromperem ou minimizarem o hábito durante a gravidez.^{11,76} Até mesmo a exposição passiva à fumaça do cigarro está associada à restrição de crescimento fetal e ao nascimento pré-termo.¹¹

USO DE ANTIBIÓTICOS NA GESTAÇÃO

O uso de antibióticos no período da gestação pode aumentar o risco de asma na primeira infância, bem como está associado ao aumento do risco de epilepsia e obesidade infantil.⁷⁷ A tetraciclina tem sido associada à malformação congênita e à alteração do desenvolvimento dos dentes e dos ossos, portanto, deve ser evitada durante a gravidez.⁷⁸ Estudos em animais sugerem que a amoxicilina seria capaz de causar defeitos de desenvolvimento no esmalte dentário, se usada durante a gestação⁷⁹⁻⁸¹. Apesar disso, as infecções durante a gravidez apresentam riscos maiores e devem ser tratadas com antibióticos de baixa toxicidade, como os derivados da penicilina, sobretudo, a amoxicilina e a ampicilina.⁸² Assim, o cirurgião-dentista deve sempre avaliar criteriosamente a real necessidade de prescrição de antibióticos para cada caso durante o tratamento odontológico das gestantes.



CONSUMO DE AÇÚCARES DE ADIÇÃO NA GESTAÇÃO

Os açúcares de adição estão presentes em vários alimentos consumidos diariamente, como refrigerantes, biscoitos, energéticos, sucos industrializados, achocolatados, barras de cereais, iogurtes e guloseimas em geral.⁴⁵ Neste sentido, o Instituto Nacional do Câncer alerta para as informações presentes nas embalagens dos produtos industrializados, pois os açúcares de adição podem ser apresentados com diversos nomes diferentes.⁸³ No quadro abaixo, temos exemplos disso:



Imagem criada com recursos do Flaticon.com



APRESENTAÇÃO DOS AÇÚCARES EM RÓTULOS DE PRODUTOS INDUSTRIALIZADOS

Açúcar
Açúcar invertido
Açúcar turbinado
Dextrose

Dextrina
Frutose
Glicose
Glucose

Maltose
Maltodextrina
Oligossacarídeos
Sacarose

Xarope glucose-frutose
Xarope de milho

Fonte: BRASIL, 2021. Imagem criada com recursos do Flaticon.com

Evitar o consumo de açúcares de adição é uma das importantes orientações que devem ser transmitidas para as gestantes durante as consultas odontológicas. Nessa fase, o consumo de alimentos ricos em açúcares de adição, sobretudo, as bebidas industrializadas, está associado a desfechos negativos para a saúde, tanto na mãe quanto no bebê. A seguir, você vai estudar alguns agravos relacionados ao consumo de açúcares de adição durante a gestação.

OBESIDADE

A obesidade é o acúmulo excessivo de gordura corporal, sendo considerada mundialmente um sério problema de saúde e um fator de risco metabólico para as DNT, como as doenças cardiovasculares, doenças respiratórias, diabetes e doenças bucais crônicas.^{10,84–86}

A obesidade na gestação afeta a saúde da prole ao longo do seu ciclo vital. A obesidade na gestante está associada à hipertensão gestacional, diabetes gestacional e indicação de cesariana. Para o bebê, a obesidade gestacional está relacionada à macrosomia e ao parto pré-termo.^{87,88}

O consumo de bebidas ricas em açúcares de adição e de alimentos industrializados tem sido relacionado à obesidade ao redor do mundo, devendo ser prevenida durante a gestação, seguindo os “Dez passos para uma alimentação saudável para gestantes”, como vimos no Capítulo 3. Quando identificada a obesidade nesta fase, a gestante deve ser encaminhada aos cuidados médicos e nutricionais.

O ganho de peso recomendado durante a gravidez deve manter proporção com o crescimento e desenvolvimento do feto.⁸⁹ Para isso, o Instituto de Medicina (EUA), endossado por instituições brasileiras, recomenda:^{90,91}



RECOMENDAÇÕES PARA GANHO DE PESO TOTAL DURANTE A GRAVIDEZ ÚNICA

IMC ANTES DA GRAVIDEZ	GANHO DE PESO TOTAL
Baixo peso < 18,5 kg/m ²	12,5 a 18 Kg
Peso normal 18,5 a 24,9 kg/m ²	11,5 a 16 Kg
Excesso de peso 25 a 29,9 kg/m ²	7 a 11,5 Kg
Obesa ≥ 30 kg/m ²	5 a 9 Kg

IMC: Índice de Massa Corporal; Fonte: Institute of Medicine, 2009.
Imagem criada com recursos do Flaticon.com

HIPERTENSÃO ARTERIAL

A hipertensão arterial na gravidez é diagnosticada quando os níveis pressóricos são iguais ou maiores a 140/90 mmHg.⁹² Nesse sentido, pode ocorrer na gestação a **Síndrome Hipertensiva da Gestação**, que pode ser classificada, então, em quatro formas diferentes:⁹³



SÍNDROME HIPERTENSIVA DA GESTAÇÃO	
Eclâmpsia	- Hipertensão arterial identificada após 20 semanas de gestação - Associada à proteinúria
Hipertensão crônica	- Identificada antes da gestação ou antes de 20 semanas de gestação - Associada a qualquer causa
Pré-eclâmpsia sobreposta à hipertensão crônica	- Gestante previamente hipertensa - Desenvolvimento de proteinúria após 20 semanas de gestação
Hipertensão gestacional	- Hipertensão arterial identificada após 20 semanas de gestação

Fonte: MOURA et al., 2011. Imagem criada com recursos do Flaticon.com

O maior consumo de bebidas ricas em açúcares parece ser um fator de risco direto para hipertensão arterial na gestação, sugerindo que o alto consumo dessas bebidas deve ser desencorajado durante a gravidez.⁹⁴ Ademais, a hipertensão arterial nessa fase é a maior causa de morte materna no Brasil, sendo responsável por cerca de 35% dos óbitos. Com relação ao feto, tem sido apontada como precursora do parto pré-termo, sofrimento fetal e crescimento fetal restrito, principais causas de morte fetal.^{92,93}

DIABETES

O diabetes gestacional ocorre quando a gestante desenvolve intolerância à glicose durante a gravidez e pode se estender após o período da gestação.⁹⁵ A obesidade e o consumo de bebidas e alimentos ricos em açúcar durante a gestação têm sido associados a diabetes gestacional.⁹⁶

Mulheres com essa doença têm maior probabilidade de desenvolver hipertensão gestacional e pré-eclâmpsia, além de terem risco aumentado para diabetes tipo 2, obesidade e doenças cardiovasculares a longo prazo. Com relação à prole, o diabetes durante a gestação está associado a recém-nascidos grandes para a idade gestacional e

macrossomia, parto pré-termo e indicação de cesariana. Essas complicações na gravidez e neonatais foram associadas ao retardo do início da amamentação, a menores taxas de amamentação e menor duração da amamentação em mulheres com diabetes gestacional.^{96,97}

DOENÇAS BUCAIS CRÔNICAS

Durante a gestação, ocorrem alterações metabólicas, bioquímicas e hormonais para atender às necessidades do desenvolvimento do complexo materno-fetal. Além disso, enjoos e náuseas matinais são comuns no primeiro trimestre da gestação, resultando em menos práticas de higiene oral e no acúmulo de biofilme dental, o que pode contribuir com o aumento da cárie e da doença periodontal.



A maior incidência de cárie também sido observada na gestação.^{98,99} Além das mudanças nas práticas de higiene, possivelmente ocasionadas pelos enjoos matinais, outra razão para o aumento do risco de novas lesões de cárie na gestação pode estar associada a maior frequência e quantidade do consumo de alimentos ricos em açúcares durante a gestação.¹⁰⁰ Nesse contexto, gestantes podem ter alterações no seu paladar e menor percepção do sabor da sacarose.¹⁰¹

Também tem sido observado um aumento da prevalência e da gravidade da inflamação gengival durante a gestação,¹⁰² o que tem sido atribuído às

alterações hormonais na gravidez, que resultam em mudanças na microbiota subgengival e podem exacerbar a resposta inflamatória nos tecidos periodontais.^{102,103} O granuloma piogênico, a gengivite e a periodontite são as alterações

periodontais mais frequentes nas gestantes.⁹⁸ Além disso, a maior frequência de consumo de refrigerantes durante a gravidez foi associada à periodontite nas gestantes.⁴¹

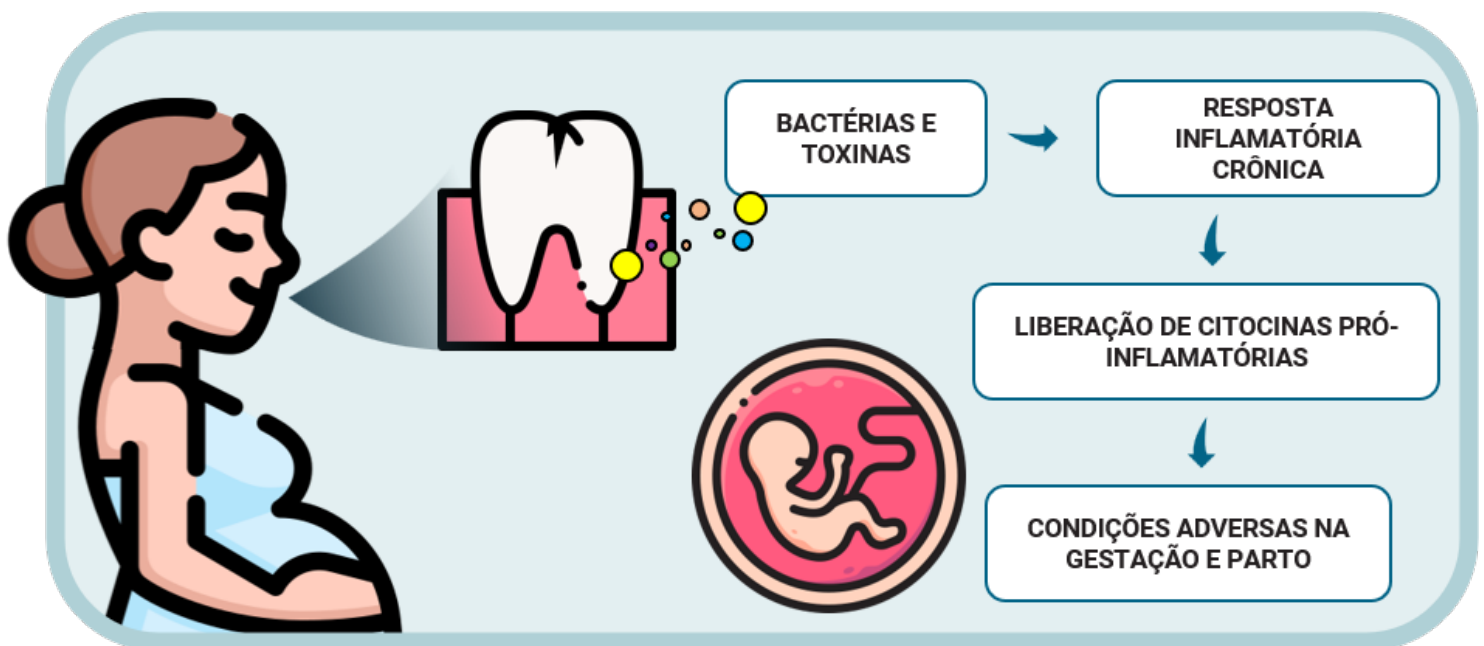


VOCÊ SABIA?

A doença periodontal na gestação está associada com alterações na saúde da gestante como pré-eclâmpsia e com desfechos adversos na gravidez: morte fetal espontânea/aborto (< 20 semanas) e natimorto (20-36 semanas), nascimento pré-termo, baixo peso ao nascer e muito baixo peso ao nascer (<1500 g), pré-eclâmpsia (hipertensão materna + proteinúria após a 20ª semana de gestação).

Fonte: KORNMAN, 2013; FIGUERO *et al.*, 2020. Imagem criada com recursos do Flaticon.com

Como explicações para a associação entre doença periodontal na gestante e esses desfechos desfavoráveis, seria possível que os patógenos periodontais e seus metabólitos atravessassem a barreira placentária, resultando em resposta imunoinflamatória no complexo feto-placentário.^{104,105}



Fonte: SILK *et al.*, 2008. Imagem criada com recursos do Flaticon.com

A Academia Americana de Periodontia e a Federação Europeia de Periodontia elaboraram um documento de consenso sobre essa temática, concluindo que a associação entre doença periodontite e desfechos desfavoráveis na gestação é modesta, variando conforme a classificação da doença periodontal empregada e também nas diferentes

populações.¹⁰⁴ Nesse documento, as entidades concluem que a terapia periodontal em gestantes é segura, resultando na melhora clínica dos parâmetros periodontais.¹⁰⁴ Entretanto, a terapia periodontal não parece ter efeito na redução das taxas de nascimento pré-termo e do baixo peso ao nascer, o que fragiliza a ideia de que os patógenos presentes na doença periodontal causariam diretamente os desfechos negativos para o feto,¹⁰⁴ pesando contra uma relação de natureza causal, pois a remoção de uma “provável causa” não parece interferir na ocorrência do desfecho.



VOCÊ SABIA?

A periodontite apical nas gestantes (infecção endodôntica) tem associação positiva com os desfechos adversos na gestação.

Cárie em gestantes já foi associada com pré-eclâmpsia e parto pré-termo.

Gestantes com lesões de cárie não tratadas tiveram um risco aumentado de dar à luz bebês grandes para a idade gestacional.

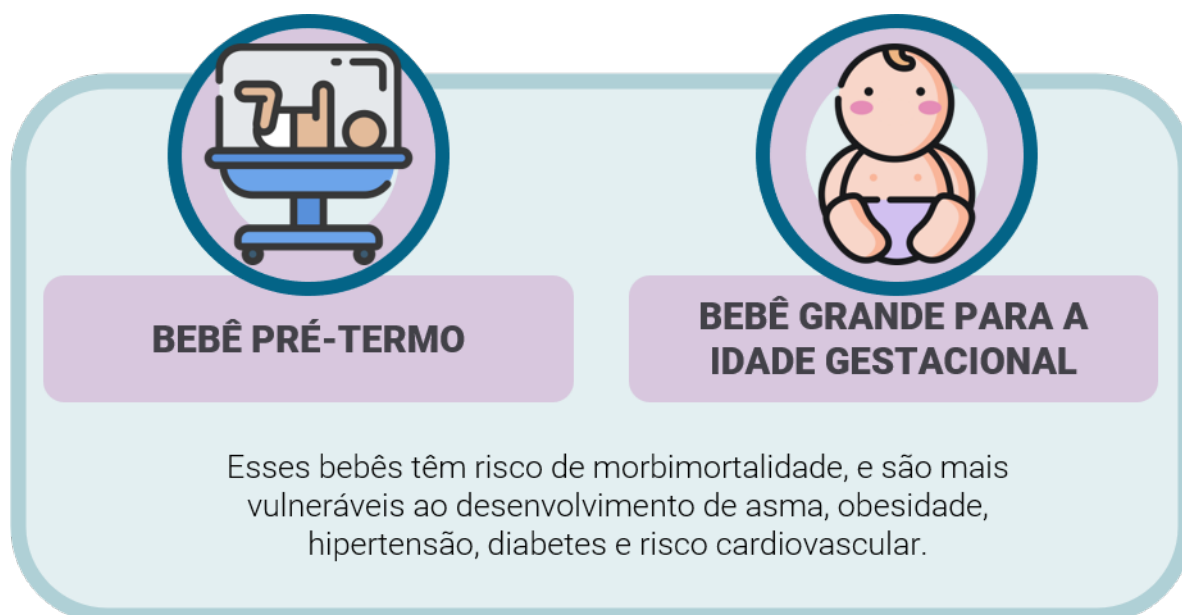
Fonte: JAKOVLJEVIC *et al.*, 2021; CHO *et al.*, 2020. Imagem criada com recursos do Flaticon.com

A cárie e a doença periodontal podem servir de alerta para o risco de desfechos negativos para a mãe e o bebê,^{106,107} e evidenciam a importância do pré-natal odontológico e da necessidade de cuidados odontológicos para gestantes com doenças bucais crônicas.

O consumo excessivo de bebidas ricas em açúcares de adição tem sido relacionado ao ganho de peso excessivo na gestante,¹⁰⁸ e ao diabetes gestacional, pré-eclâmpsia, hipertensão gestacional,^{94,108} nascimento pré-termo,^{109,110} bebês grandes para idade gestacional¹¹¹ e ao aumento do risco de asma na infância.¹⁴ Nesse contexto, o nascimento pré-termo e bebês grandes para a idade gestacional já foram associados à maior mortalidade, ao desenvolvimento de hipertensão, diabetes, asma, obesidade e doenças cardiovasculares ao longo da vida.^{112–116}

Além disso, a obesidade materna no início da gestação e o consumo de açúcar pela gestante podem explicar obesidade, alta exposição ao açúcar e cárie precoce na infância.¹¹⁷

A obesidade é um importante fator de risco metabólico para todas as DNT² e está associada tanto à cárie quanto à doença periodontal, inclusive em crianças.¹¹⁸⁻¹²⁰



Fonte: WHINCUP *et al.*, 2008; YU *et al.*, 2011; SIPOLA-LEPPÄNEN *et al.*, 2014; SONNENSCHNEIN-VAN der VOORT *et al.*, 2014; KUCIENE; DULSKIENE; MEDZIONIENE, 2018. Imagem criada com recursos do Flaticon.com

Interpretados em conjunto em uma perspectiva DOHaD, esses achados alertam para a necessidade das ações de prevenção integral das doenças crônicas na gestante, bucais e sistêmicas, serem direcionadas aos fatores de risco comuns. Por exemplo, ações voltadas para uma alimentação adequada e saudável e o aconselhamento para evitar alimentos ultraprocessados e açúcares de adição teriam impacto na saúde da gestante, prevenindo obesidade, hipertensão, diabetes, além de reduzir a carga de doenças bucais crônicas e de atenuar o risco de desfechos adversos da gravidez. Essas ações também têm reflexos sobre os impactos positivos na saúde da prole, reduzindo a cárie, a gengivite e o risco de DNT de maior mortalidade no futuro.

ATENÇÃO À SAÚDE DURANTE OS DOIS PRIMEIROS ANOS DE VIDA

Capítulo 5



ATENÇÃO À SAÚDE DURANTE OS DOIS PRIMEIROS ANOS DE VIDA

Como já discutimos anteriormente, todos os profissionais da saúde têm um importante papel na Rede Cegonha. No puerpério e até os dois anos da criança, o cirurgião-dentista deve conhecer as orientações necessárias para a promoção, proteção e apoio ao aleitamento materno e a introdução alimentar adequada, além de orientar e estimular práticas de higiene oral.

ALEITAMENTO MATERNO

O aleitamento materno é um dos momentos mais importantes para o estabelecimento e fortalecimento de vínculo entre a mãe e o bebê, com impactos na nutrição da criança, no seu estado imunológico, no funcionamento do seu organismo, no desenvolvimento emocional e cognitivo e na sua condição de saúde a longo prazo. Um estudo de coorte que acompanhou crianças durante os seis meses de idade e após oito anos de vida mostrou que crianças que mamaram por seis meses ou mais tiveram melhor desempenho na avaliação intelectual geral.⁶⁴ Além disso, o ato de amamentar repercute na saúde física e psíquica da mãe.⁶⁰ Para as mulheres que amamentam, a amamentação protege contra o câncer de mama e aumenta o espaçamento entre os partos, além de ser um fator de proteção contra câncer de ovário e diabetes tipo 2.⁶²

O leite materno é produzido de acordo com as necessidades do bebê e assume diferentes composições de acordo com o estágio da lactação.



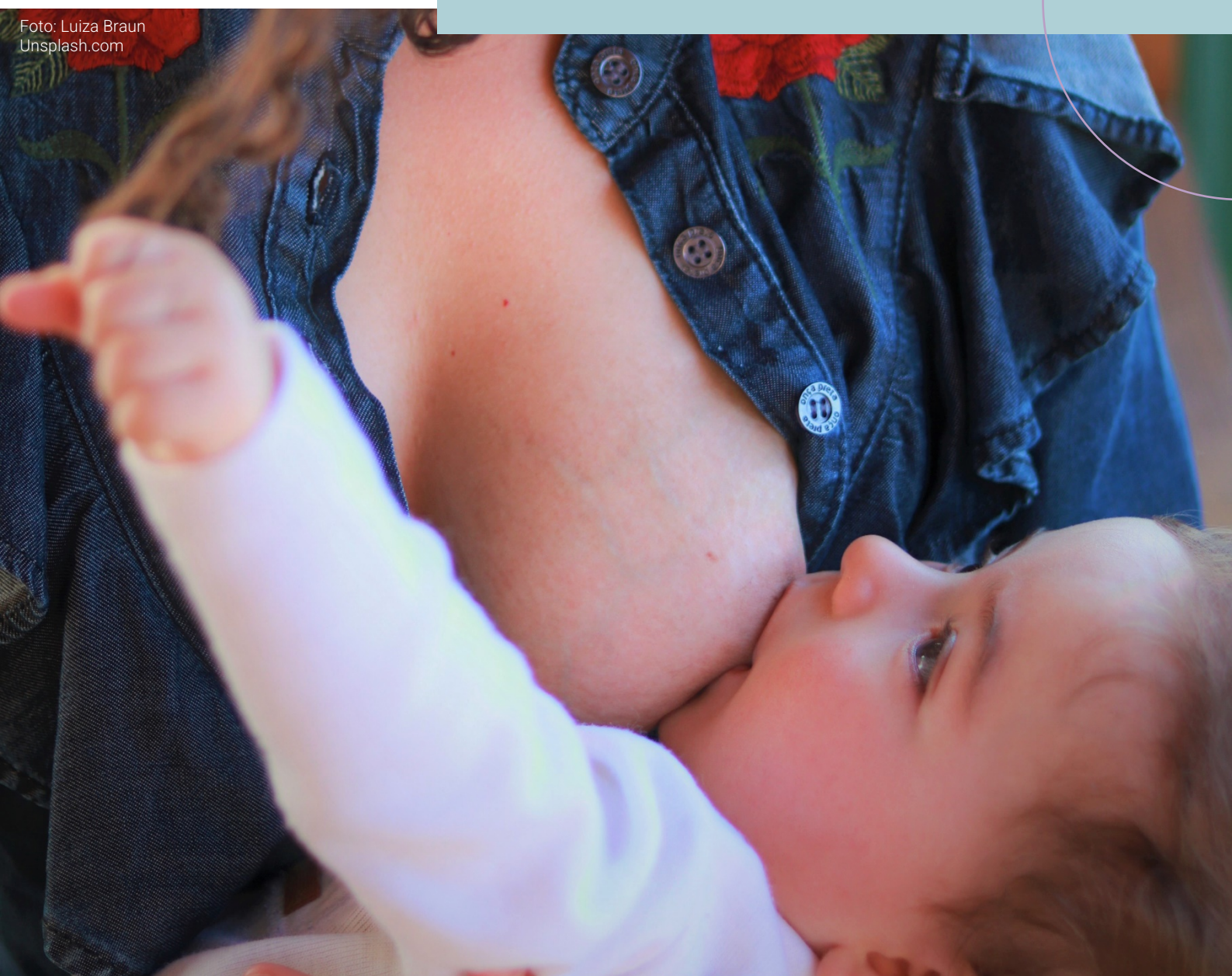
Foto: Luiza Braun
Unsplash.com



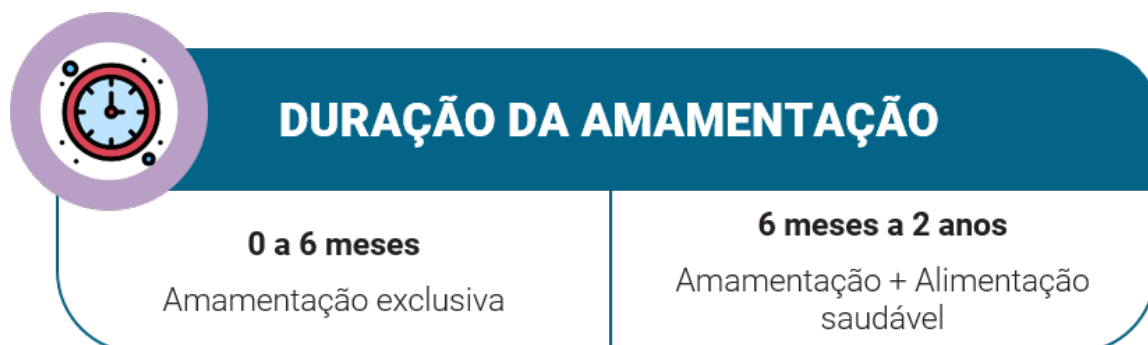
Foto: Junior Reis
Unsplash.com

Inicialmente, é produzido o colostro, que tem aspecto viscoso e é rico em proteínas, minerais e vitaminas A e E, apresentando imunoglobulinas e agentes antimicrobianos, substâncias imunomoduladoras, leucócitos e compostos anti-inflamatórios, dentre os quais se destacam os fatores de crescimento. Em seguida, o leite de transição é produzido até o que conhecemos como leite maduro. Neste período de transição, o leite não apresenta composição constante. Após o décimo quinto dia pós-parto, o leite materno é considerado maduro, rico em proteínas, algumas delas envolvidas no sistema de proteção, como a lactoferrina, a lisozima e as imunoglobulinas, especialmente a IgA secretória.¹²¹

Foto: Luiza Braun
Unsplash.com



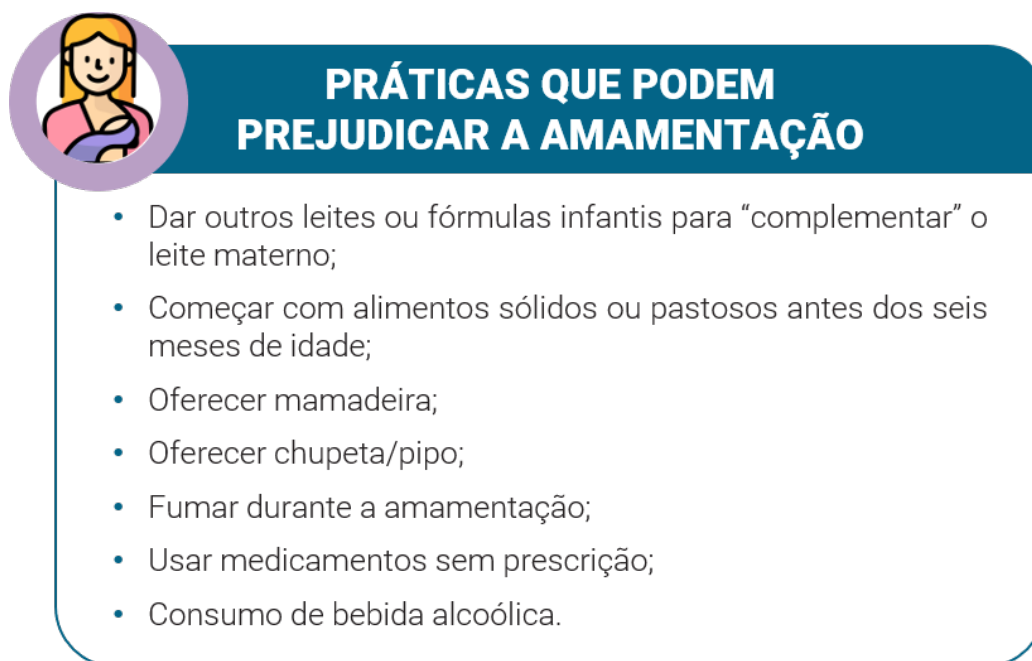
A Organização Mundial da Saúde e o Ministério da Saúde recomendam o aleitamento materno por dois anos ou mais, sendo exclusivo nos primeiros seis meses de vida, ou seja, sem a oferta de outro tipo de alimento para a criança: nem líquidos, nem mesmo a água, nem qualquer outro alimento, como frutas, verduras, papinha e mingau.



Fonte: BRASIL, 2015. Imagem criada com recursos do Flaticon.com

A introdução à alimentação complementar precoce (antes dos seis meses) não apresenta vantagens nutricionais e está associada a desfechos negativos à saúde da criança, como episódios de diarreia; aumento da frequência de hospitalizações por doença respiratória; menor absorção de nutrientes, como o ferro e o zinco; interrupção precoce do aleitamento materno; entre outros.^{60,61}

Durante as consultas pré-natais, o cirurgião-dentista deve agir visando à proteção e à promoção da amamentação. O Ministério da Saúde alerta para práticas que podem prejudicar a amamentação e fazer com que este período termine mais cedo do que deveria. Veja abaixo:



Fonte: BRASIL, 2019. Imagem criada com recursos do Flaticon.com

INTRODUÇÃO ALIMENTAR COMPLEMENTAR

Após os primeiros seis meses, é recomendada a introdução alimentar complementar saudável simultânea à amamentação, até os dois anos ou mais. Sabendo que o nutricionista nem sempre está disponível a todos no contexto do SUS, é importante que a equipe de saúde, inclusive o cirurgião-dentista, saiba orientar acerca da alimentação saudável nessa fase. A alimentação complementar da criança deve ser a mesma consumida pela mãe e por outros membros da família, constituída de alimentos in natura ou minimamente processados.^{122,123}

Os alimentos in natura descritos pelo “Guia Alimentar para a População Brasileira” ([Link](#)) são aqueles obtidos diretamente das plantas ou dos animais e que não são alterados após deixarem a natureza. Já os chamados minimamente processados sofrem apenas processos de limpeza, remoção de partes indesejáveis, moagem, secagem, congelamento, sem a adição de qualquer substância em relação ao alimento original.¹²³

Alimentos *in natura* ou minimamente processados



Obtidos diretamente das plantas ou dos animais e não são alterados após deixar a natureza, sofrendo apenas processos de limpeza, remoção de partes indesejáveis, moagem, secagem, congelamento, sem a adição de nenhuma substância em relação ao alimento original.

Ingredientes culinários processados



Produtos fabricados pela indústria usados para preparar as refeições, como sal de cozinha, açúcar, melado, mel, vinagres, manteiga e óleos. Devem ser usados com moderação.

Alimentos processados



Elaborados a partir de alimentos *in natura*, adicionados de sal ou açúcar. Ex.: conservas de legumes, carnes salgadas, peixe enlatado, queijos, pães, entre outros. Devem ser evitados.

Alimentos ultraprocessados



Formulações produzidas industrialmente por diversas técnicas de processamento e inúmeros ingredientes, muitos deles de uso industrial exclusivo, como açúcares de adição, óleos modificados e aditivos alimentares (corantes artificiais, conservantes, adoçantes, aromatizantes, emulsificantes, realçadores de sabor).

Fonte: BRASIL, 2014. Imagem criada com recursos do Flaticon.com

Na classificação de alimentos, podemos destacar as seguintes indicações para compor a alimentação complementar da criança e sua família¹²²:

- **Grupo dos feijões**

Feijão (branco, carioca, feijão-de-corda, feijão-fava, fradinho, mulatinho, preto, rajado, roxinho, vermelho), ervilha, grão-de-bico e soja.

- **Grupo dos cereais**

Arroz, arroz integral, aveia, centeio, milho, trigo, trigoilho, fubá, flocão e amido de milho.

- **Grupo das raízes e tubérculos**

Batata-baroa (mandioquinha, batata-salsa ou cenourinha-amarela), batata-doce, batata-inglesa, inhame, mandioca, farinha de mandioca, fécula de batata e polvilho.

- **Grupo dos legumes e verduras**

Abóbora (ou jerimum), abobrinha, berinjela, beterraba, cenoura, chuchu, maxixe, pepino, quiabo, tomate e vagem. Também acelga, agrião, alface, brócolis, cebola, chicória, couve, couve-flor, espinafre, jambu, repolho e taioba.

- **Grupo das frutas**

Abacate, abacaxi, açaí, acerola, ameixa, amora, banana, cajá, caju, caqui, carambola, cereja, cupuaçu, figo, goiaba, graviola, jaca, laranja, tangerina, lima, maçã, manga, mamão, melancia, melão, morango, pequi, pera e uva.

- **Grupo das carnes**

Carnes bovina, suína, cabrito, cordeiro, búfalo, aves, pescados, frutos do mar e ovos. Inclui vísceras ou miúdos de animais.

- **Grupo dos leites**

Leite materno, leite de outros animais, coalhadas e iogurtes naturais sem açúcar.

- **Grupo dos amendoins e castanhas**

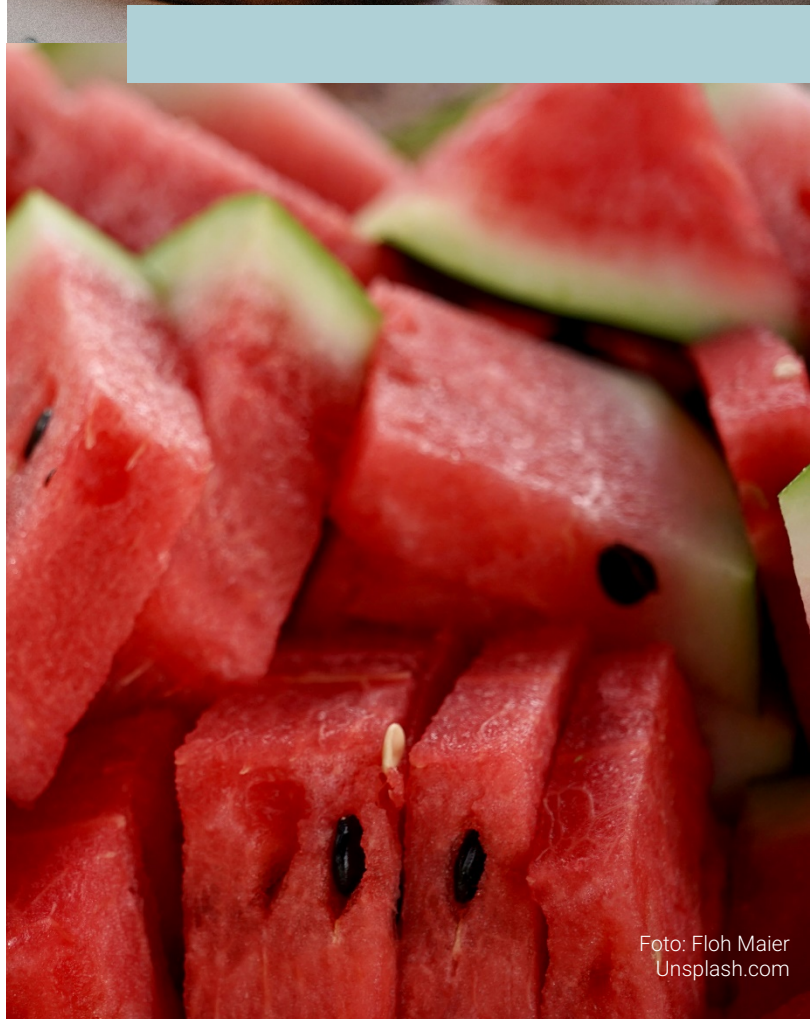
Amêndoas, amendoim, castanha-de-caju, castanha-do-Pará, castanha-de-baru e noz-pecã.

- **Grupo dos condimentos e temperos**

Alecrim, açafrão-da-terra (cúrcuma), canela, cebolinha, cheiro-verde, coentro, cominho, cravo, gengibre, louro, manjericão, orégano, salsa, sálvia e tomilho.

- **Água**

Após os seis meses de idade, oferecer um pouco de água natural potável no copo (sem bico), no intervalo entre as refeições.



Considerando essas recomendações, o Ministério da Saúde, em 2019,¹²² propôs o “Guia Alimentar para Crianças Brasileiras Menores de 2 anos” ([Link](#)), com destaque para “Os Doze Passos para uma Alimentação Saudável”.



DOZE PASSOS PARA UMA ALIMENTAÇÃO SAUDÁVEL

1. Amamentar até dois anos ou mais, oferecendo somente o leite materno até seis meses.
2. Oferecer alimentos *in natura* ou minimamente processados, além do leite materno, a partir dos seis meses.
3. Oferecer água própria para o consumo à criança em vez de sucos, refrigerantes e outras bebidas açucaradas.
4. Oferecer alimentos de consistência espessa quando a criança começar a introdução alimentar.
5. Não oferecer açúcar nem preparações ou produtos que contenham açúcar à criança até dois anos de idade.
6. Não oferecer alimentos ultraprocessados para a criança.
7. Cozinhar a mesma comida para a criança e para a família.
8. Zelar para que a hora da alimentação da criança seja um momento de experiências positivas.
9. Prestar atenção aos sinais de fome e saciedade da criança.
10. Cuidar da higiene em todas as etapas da alimentação da criança e da família.
11. Oferecer à criança alimentação adequada e saudável também fora de casa.
12. Proteger a criança da publicidade de alimentos.



Foto: Tim Bish
Unsplash.com

HIGIENE ORAL DO BEBÊ

As doenças bucais crônicas, cárie e gengivite, só ocorrem na presença do elemento dental,^{37,47} assim, não há recomendação para práticas de higiene da cavidade bucal antes da irrupção dos primeiros dentes, sendo este o posicionamento da Associação Brasileira de Odontopediatria.¹²⁴ Além disso, a microbiota do trato gastrointestinal (incluindo a boca) está em uma fase de adaptação através do leite materno exclusivo,⁵⁷ e remover a flora bacteriana que está se consolidando na boca não resulta em benefícios para o bebê.

Após o aparecimento do primeiro dente, os cuidadores devem escovar os dentes do bebê duas vezes por dia, utilizando escova com cerdas macias e dentifrício fluoretado contendo 1000-1500 ppm de flúor, para proteção contra a cárie dentária. Inicialmente, deve-se usar o equivalente a um “grão de arroz cru” e com o aumento do número de dentes decíduos irrompidos, a quantidade pode ir aumentando até o tamanho de uma “ervilha”. Essas quantidades são seguras contra a fluorose.^{125,126}



Imagem criada com recursos do Flaticon.com



ESTRESSORES AMBIENTAIS DURANTE OS PRIMEIROS DOIS ANOS

Capítulo 6

ESTRESSORES AMBIENTAIS DURANTE OS PRIMEIROS DOIS ANOS

Nos dois primeiros anos de vida da criança, fatores ambientais, como a cesariana, o aleitamento artificial e a exposição precoce aos açúcares de adição, podem levar a desfechos desfavoráveis (sistêmicos e bucais) na infância e perdurar ao longo da vida.

CESARIANA

A Organização Mundial da Saúde recomenda que a cesariana seja realizada apenas em condições em que a saúde ou a vida da mãe e/ou do recém-nascido estejam ameaçadas. No entanto, a frequência desse tipo de parto aumentou em todo o mundo,^{127,128} e está muito acima dos níveis preconizados pela OMS, que é de 10 a 15%.^{129,130}

Nascer de cesariana, de forma eletiva ou de urgência, tem sido associado ao desenvolvimento de alterações imunológicas e metabólicas durante a infância, como: asma, alergia alimentar, diabetes tipo I e obesidade.¹³¹

Por isso, é importante que na consulta pré-natal haja incentivo ao parto vaginal e que sejam mencionados os riscos a longo prazo da cesariana para a prole.

Observe a seguir alguns fatores relacionados à decisão pela cesariana:



Imagem criada com recursos do Flaticon.com



FATORES ASSOCIADOS À DECISÃO PELA CESARIANA

- Insegurança materna;
- Medo do parto;
- Medo da dor durante o parto;
- Predisposição da equipe de saúde pela cirurgia cesariana.

Fonte: MAGNE et al., 2017. Imagem criada com recursos do Flaticon.com



MAMADEIRAS E CHUPETAS

A maneira que o bebê suga o peito da mãe é diferente da forma de sugar a mamadeira, independentemente do tipo de bico utilizado. Sugar em uma mamadeira pode confundir a criança, causando a “confusão de bicos”. O fluxo da mamadeira é mais abundante que o peito materno, o que faz com que o bebê se frustre ao empenhar maior esforço durante a mamada.¹³²

Além disso, o conteúdo das mamadeiras normalmente é rico em açúcares, podendo prejudicar a habilidade de regulação do apetite da criança e ocasionar predisposição à obesidade e às DNT (mais adiante, ainda neste capítulo, veremos os efeitos dos açúcares de adição na saúde do bebê). Em acréscimo, o bico da mamadeira faz com que o movimento e a posição da língua afetem o desenvolvimento da deglutição, mastigação e fala. Em contrapartida, a alimentação complementar com o auxílio de copos aumenta a extensão e a duração da amamentação, em detrimento ao uso de mamadeiras, mesmo em bebês pré-termos.¹³³

O uso de chupeta está relacionado à diminuição do tempo de mamada e ao desmame precoce.^{60,134} A amamentação é um importante fator de proteção para maloclusões, tais como: mordida cruzada anterior, mordida cruzada posterior, classe II esquelética, distoclusão e apinhamento na dentadura decídua e mista.¹³⁵

A chupeta também está associada ao aumento das chances de a criança desenvolver infecções orais, sobretudo candidíase.¹³⁶ Enquanto a remoção da chupeta após 12 meses melhorou a distância intercanina (superior e inferior), os aspectos relacionados à pressão dos dentes durante a mastigação, bem como os indicadores do desenvolvimento da fala e respiração.¹³⁷

AÇÚCARES DE ADIÇÃO

A exposição **precoce** aos açúcares de adição, em especial às bebidas ricas em açúcares de adição, vem sendo relacionada a desfechos adversos na infância, tais como obesidade, asma, cárie e gengivite, além de aumentar o risco às DNT no futuro, como as doenças cardiovasculares (DCV).^{14,18,138,139}

Evidências dos efeitos nocivos do consumo de açúcares levaram a Associação Americana do Coração a publicar diretrizes que visam à redução do consumo de açúcares, limitado a 25 gramas diárias para crianças e adolescentes, com a recomendação de **que crianças menores de dois anos não devam consumir açúcares de adição**.¹⁴⁰ Essa recomendação também é endossada pelo Ministério de Saúde do Brasil, por meio do Guia Alimentar para Crianças Brasileiras Menores de dois anos, de 2019.¹²²

A Organização Mundial da Saúde (OMS) publicou diretrizes pautadas na redução do consumo de açúcares para a prevenção da obesidade e da cárie, de modo que o consumo de açúcares livres não ultrapasse 10% da quantidade total das calorias ingeridas diariamente. Além disso, há a recomendação adicional para uma redução no consumo destes açúcares para menos que 5% das calorias totais ingeridas diariamente.⁷



Imagem criada com recursos do Flaticon.com

Ingestão de açúcares **não deve ultrapassar 25 g diárias** para adolescentes e crianças maiores de dois anos. Equivalente a seis colheres de chá de açúcar.

Associação Americana do Coração®

CRIANÇAS MENORES DE DOIS ANOS DE IDADE NÃO DEVEM CONSUMIR AÇÚCARES DE ADIÇÃO

Fonte: VOS et al., 2017. Imagem criada com recursos do Flaticon.com

Vamos estudar a seguir alguns agravos relacionados à exposição precoce aos açúcares de adição, ou seja, ao consumo destes alimentos ricos em açúcares antes dos dois anos de vida da criança.

ALTERAÇÕES NO DESENVOLVIMENTO DA CRIANÇA

Estudos recentes sugerem que a exposição precoce às bebidas ricas em açúcares de adição estaria relacionada ao risco de desenvolver transtorno de déficit de atenção e hiperatividade, indicando que a quantidade do consumo é um fator importante nesta associação. Ao passo que uma dieta saudável, com alto consumo de frutas e vegetais, parece proteger dessas alterações.^{141–143}



ASMA

A asma é uma doença que afeta as vias respiratórias inferiores, acometendo indivíduos de todas as idades, mas normalmente começa durante a infância, com sintomas de chiado, tosse ou angina (aperto no peito).¹⁴⁴

A OMS descreve a asma como uma DNT associada à inflamação, causando estreitamento das vias aéreas, e sua presença representa risco para todas as outras DNT no futuro, como o diabetes e as doenças cardiovasculares.¹⁴⁵

Estudos mostram que o consumo de bebidas ricas em açúcares de adição está associado ao risco de asma na infância.^{14,146} Enquanto isso, a amamentação exclusiva tem sido apontada como fator de proteção contra infecções respiratórias na infância.¹¹ Há evidências de que o maior tempo de amamentação também seria uma forma de proteção contra a asma na infância.^{14,147}



EXCESSO DE PESO

O consumo de açúcar pela gestante e a obesidade materna pré-gestacional podem explicar a obesidade, a alta exposição ao açúcar e a cárie precoce na infância nos seus filhos.¹¹⁷ O consumo de açúcares de adição está associado ao sobrepeso e à obesidade na infância. Crianças obesas são mais propensas a desenvolverem doenças crônicas não transmissíveis ao longo da vida.¹⁴⁷

DOENÇAS BUCAIS CRÔNICAS

Estima-se que aproximadamente 600 milhões de bebês no mundo ainda sejam acometidos pela cárie dentária na primeira infância, o que pode gerar quadros de dor e dificuldade para mastigar, afetando a qualidade de vida das crianças e suas famílias, sendo de difícil tratamento.^{61,148}

Os açúcares têm papel inquestionável na etiologia da cárie^{7,38}. Evidências epidemiológicas emergentes também apontam para uma consistente associação do consumo de açúcares com o aumento da carga de doenças bucais crônicas na primeira infância.^{17,41-43} Crianças que consomem bebidas adoçadas, como sucos industrializados, achocolatados e refrigerantes, apresentam aumento da inflamação gengival, aumento de citocinas pró-inflamatórias e maior número de lesões de cárie.^{118,119,149}



Fonte: Acervo dos autores



OS PRIMEIROS MIL DIAS NA AGENDA DE ENFRENTAMENTO DAS DNT

Capítulo 7

OS PRIMEIROS MIL DIAS NA AGENDA DE ENFRENTAMENTO DAS DNT

Os Objetivos de Desenvolvimento Sustentável da Organização das Nações Unidas (ONU) visam enfrentar as desigualdades, proteger o meio ambiente, promover o desenvolvimento econômico e social, restaurar a paz, a saúde e a prosperidade entre os povos.¹⁵⁰ Veja quais são os 17 objetivos a serem alcançados até 2030:

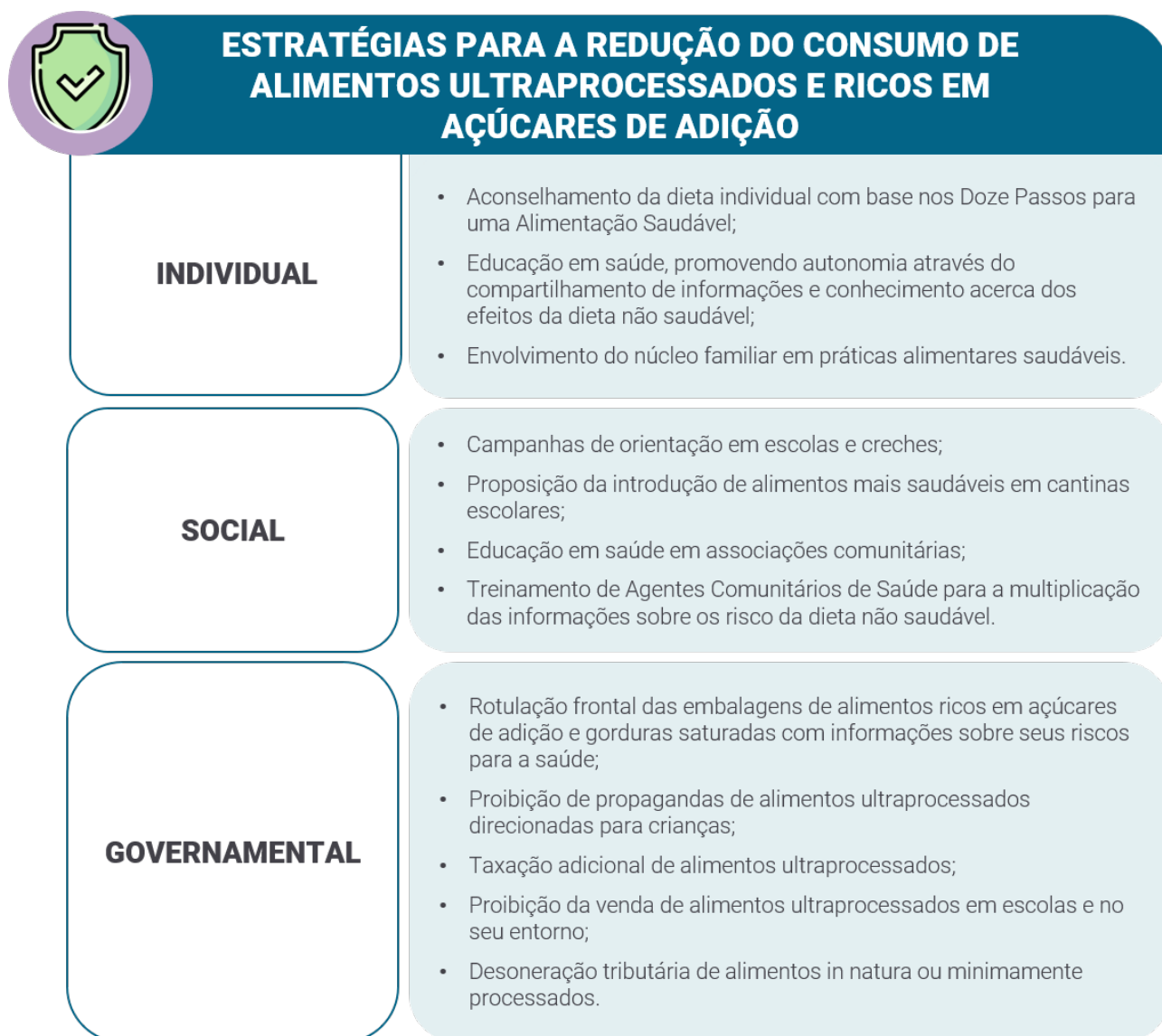


Fonte: ONU, 2015.

Na agenda dos Objetivos de Desenvolvimento Sustentável (ODS3), o Ministério da Saúde do Brasil apresentou o Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas e Agravos Não Transmissíveis: 2021-2030 ([Link](#)), com metas e ações propostas para enfrentamento das DNT. Como um eixo norteador na elaboração do documento, o “Desenvolvimento Saudável nos Ciclos da Vida” destacou a importância da atenção à saúde da criança, especialmente nos primeiros mil dias de vida, na perspectiva da promoção da saúde e da prevenção de doenças no futuro. Dentre as metas estabelecidas no documento para o enfrentamento dos fatores de risco para as DNT até o ano de 2030, estão:

1. Redução em 2% das taxas de obesidade em crianças e adolescentes;
2. Aumentar em 30% o consumo de frutas e hortaliças;
3. Reduzir o consumo de alimentos ultraprocessados;
4. Reduzir em 30% o consumo regular de bebidas adoçadas.

Para auxiliar na elaboração de ações para redução do consumo de bebidas ricas em açúcares de adição e de alimentos ultraprocessados, foram agrupados três níveis de ações estratégicas.



Fonte: PEREIRA *et al.*, 2021. Imagem criada com recursos do Flaticon.com

A close-up photograph of a person's hands, likely a pregnant woman, holding a medical ultrasound printout against their pregnant belly. The hands are positioned on either side of the printout, which is held flat against the skin. The printout shows various ultrasound images, including a fetal profile and a cross-section of the fetus. The text on the printout is partially legible, showing patient information and technical details. The background is a blue, textured fabric, possibly a hospital gown or a blanket. The overall tone of the image is clinical and focused on prenatal care.

PROGRAMA PREVINE BRASIL E OS INDICADORES DE DESEMPENHO DA ASSISTÊNCIA DURANTE OS PRIMEIROS MIL DIAS

PROGRAMA PREVINE BRASIL E OS INDICADORES DE DESEMPENHO DA ASSISTÊNCIA DURANTE OS PRIMEIROS MIL DIAS

O **Programa Previne Brasil** é o novo modelo de financiamento da Atenção Primária à Saúde (APS) do SUS instituído pela Portaria n.º 2.979/GM/MS, de 12 de novembro de 2019. Antes, o custeio da APS era baseado no tamanho da população do município e na oferta dos serviços de saúde. Com o Previne Brasil, o financiamento federal será baseado em três princípios: a captação ponderada, o pagamento por desempenho e o incentivo por ações estratégicas. Conheça melhor no quadro abaixo¹⁵¹:



PRINCÍPIOS DO CUSTEIO DA ATENÇÃO PRIMÁRIA À SAÚDE

CAPTAÇÃO PONDERADA	Calculada considerando: - A população cadastrada por equipe de Saúde da Família e equipe de Atenção Primária; - Os indicadores de vulnerabilidade socioeconômica da população; - O perfil demográfico por faixa etária; - A classificação geográfica definida pelo IBGE.
PAGAMENTO POR DESEMPENHO	- Calculado a partir do cumprimento de meta para cada indicador definido pelo Ministério da Saúde.
INCENTIVO POR AÇÕES ESTRATÉGICAS	- Calculado a partir das ações estratégicas, considerando as especificidades, os aspectos estruturais das equipes e a produção realizada por essas estratégias em saúde; - O incentivo contemplará o custeio de ações, programas e estratégias, como Programa Saúde na Hora, Equipe de Saúde Bucal, Unidade Odontológica Móvel; Centro de Especialidades Odontológicas, Equipe de Consultório na Rua, Unidade Básica de Saúde Fluvial, entre outros.

Fonte: BRASIL, 2019. Imagem criada com recursos do Flaticon.com

Com relação ao princípio do pagamento por desempenho, o Ministério da Saúde tem estabelecido metas específicas para indicadores em saúde relacionados à assistência pré-natal, o que reflete diretamente nos primeiros mil dias de vida da criança.

Especificamente, os indicadores 1 e 3 servem como incentivadores para o atendimento pré-natal, como prevenção de DNT durante os primeiros mil dias. Veja quais são esses indicadores:^{152,153}



FICHA DE ATENDIMENTO ODONTOLÓGICO INDIVIDUAL

DIGITADO POR: _____

CONFERIDO POR: _____

DATA: ____/____/____

FOLHA Nº: ____

CNS DO PROFISSIONAL* _____

CBO* _____

CNES* _____

CNES _____

INE* _____

INE _____

DATA* ____/____/____

Sexo* (F) Feminino (M) Masculino		(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)
Local de atendimento* (ver legenda)		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Paciente com necessidades especiais		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Gestante		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Tipo atendimento*			(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)	(O)
	Demanda espontânea																
	Consulta agendada		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Escuta inicial/Orientação		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Consulta no dia		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Atendimento de urgência		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Procedimentos (quantidade realizada)			(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)	(U)
	Acesso à polpa dentária e medicação (por dente)		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Adaptação de prótese dentária		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Aplicação de cariotático (por dente)		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Aplicação de selante (por dente)		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Aplicação tópica de flúor (individual por sessão)		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Capeamento pulpar		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Cimentação de prótese dentária		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Curativo de demora c/ ou s/ preparo biomecânico		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Drenagem de abscesso		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Evidenciação de placa bacteriana		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Exodontia de dente decíduo		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
	Exodontia de dente permanente		☐	☐	☐												



CONSIDERAÇÕES FINAIS

CONSIDERAÇÕES FINAIS

Neste livro em formato digital, trabalhamos em consonância com as ações estratégicas dos Objetivos de Desenvolvimento Sustentável, no eixo **Promoção de Saúde**, ao propor este recurso instrucional em vista da ação “Formar e qualificar profissionais de saúde e sociedade civil para desenho e implantação de cidades/territórios inteligentes, saudáveis e sustentáveis; e, no eixo **Atenção Integral à Saúde**, apresentando evidências que dão suporte à ação “Ampliar o acesso ao pré-natal odontológico com objetivo de reduzir a ocorrência de cárie e doença periodontal”.

À luz da Teoria DOHaD, apresentamos os primeiros mil dias de vida como um “intervalo de ouro” para a prevenção integrada das DNT, incluindo as bucais e sistêmicas de maior mortalidade no futuro. Destacamos estratégias para a prevenção primordial das DNT, ou seja, manter-se longe dos fatores de risco, nesta etapa da vida. Nesse sentido, ressaltamos a importância do aleitamento materno exclusivo até os seis meses, além de evidências para o apoio irrestrito a sua continuidade até os dois anos de idade ou mais, o qual deve ser complementado por uma dieta adequada e saudável, baseada em alimentos in natura ou minimamente processados. Além disso, propomos uma abordagem integrada da cárie e da doença periodontal, com a proposição de medidas de prevenção e/ou intervenção direcionadas para seus fatores de risco comuns para a redução mais efetiva da carga de Doenças Bucais Crônicas, as quais devem começar precocemente no ciclo vital do indivíduo, ou seja, nos primeiros mil dias de vida.

As DNT bucais antecedem e predizem décadas antes o aparecimento de DNT de maior mortalidade. Por essa razão, no contexto da atuação multidisciplinar na Estratégia de Saúde da Família, o cirurgião-dentista deve assumir um papel de protagonismo na prevenção integral da saúde da mulher durante a gestação e da saúde do bebê nos primeiros mil dias de vida, identificando exposições de risco e sinais precoces de DNT e orientando as famílias sobre seus fatores de risco comuns.

O cirurgião-dentista deve, também, apoiar e propor políticas voltadas para rotulação, taxação e regulação de alimentos ultraprocessados e ricos em açúcares, bem como endossar políticas de incentivo ao consumo de alimentos mais saudáveis, que podem ter um amplo impacto na saúde bucal e geral das gestantes e das crianças, contribuindo com a redução da carga de DNT no futuro na prole, ou seja, este é um profissional essencial nas ações para atingir os Objetivos de Desenvolvimento Sustentável nas próximas décadas.

Até a próxima!

REFERÊNCIAS

1. WORLD HEALTH ORGANIZATION. Noncommunicable Diseases Progress Monitor 2022. Geneva: 2022.
2. WORLD HEALTH ORGANIZATION. Noncommunicable disease. World Health Organization. 2021.
3. WORLD HEALTH ORGANIZATION. The impact of the COVID-19 pandemic on noncommunicable disease resources and services: results of a rapid assessment. Geneva: 2020.
4. ALAVALIKKO, S.; JAAKKOLA, M. S.; TJADERHANE, L.; JAAKKOLA, J. J. K. Asthma and Caries: a Systematic Review and Meta-Analysis. *American Journal of Epidemiology*. 2011;174:631–41. doi: <https://doi.org/10.1093/aje/kwr129>.
5. VAN DYKE, T. E.; KHOLY, K. E. L.; ISHAI, A.; TAKX, R. A. P.; MEZUE, K.; ABOHASHEM, S. M. *et al*. Inflammation of the periodontium associates with risk of future cardiovascular events. *Journal of Periodontology*. 2021;92:348–58. doi: <https://doi.org/10.1002/JPER.19-0441>.
6. MAJBAUDDIN, A.; TANIMURA, C.; AOTO, H.; OTANI, S.; PARRENAS, M. C. E.; KOBAYASHI, N. *et al*. Association between dental caries indicators and serum glycated hemoglobin-levels among patients with type 2 diabetes mellitus. *Journal of Oral Science*. 2019;61:335–42. doi: <https://doi.org/10.2334/josnusd.18-0156>.
7. WORLD HEALTH ORGANIZATION. Guideline: sugars intake for adults and children. Geneva: 2015.
8. Subcomisión DOHaD. Concepto de Developmental Origins of Health and Disease: El ambiente en los primeros mil días de vida y su asociación con las enfermedades no transmisibles. *Archivos Argentinos de Pediatría*. 2020; 118:118–29. doi: <https://doi.org/10.5546/aap.2020.s118>.
9. SUZUKI, K. The developing world of DOHaD. *Journal of Developmental Origins of Health and Disease*. 2018; 9:266–9. doi: <https://doi.org/10.1017/S2040174417000691>.
10. PIETROBELLI, A.; AGOSTI, M. Nutrition in the First 1000 Days: Ten Practices to Minimize Obesity Emerging from Published Science. *International Journal of Environmental Research and Public Health*. 2017; 14:1491. doi: <https://doi.org/10.3390/ijerph14121491>.
11. ABRAHAM, M.; ALRAMADHAN, S.; INIGUEZ, C.; DUIJTS, L.; JADDOE, V. W. V.; DEN DEKKER, H. T. *et al*. A systematic review of maternal smoking during pregnancy and fetal measurements with meta-analysis. *PLOS ONE*. 2017; 12:e0170946. doi: <https://doi.org/10.1371/journal.pone.0170946>.
12. MAY, P. A.; HASKEN, J. M.; BLANKENSHIP, J.; MARAIS, A-S.; JOUBERT, B.; CLOETE, M. *et al*. Breastfeeding and maternal alcohol use: Prevalence and effects on child outcomes and fetal alcohol spectrum disorders. *Reproductive Toxicology*. 2016; 63:13–21. doi: <https://doi.org/10.1016/j.reprotox.2016.05.002>.
13. GUSTAVSON, K.; YSTROM, E.; STOLTENBERG, C.; SUSSER, E.; SURÉN, P.; MAGNUS, P. *et al*. Smoking in Pregnancy and Child ADHD. *Pediatrics*. 2017; 139: e20162509. doi: <https://doi.org/10.1542/peds.2016-2509>.
14. NASCIMENTO, J. X. P. T.; RIBEIRO, C. C. C.; BATISTA, R. F. L.; DE BRITTO ALVES, M. T. S. S.; SIMÕES, V. M. F.; PADILHA, L. L. *et al*. The First 1000 Days of Life Factors Associated with “Childhood Asthma Symptoms”: Brisa Cohort, Brazil. *Scientific Reports*. 2017; 7:16028. doi: <https://doi.org/10.1038/s41598-017-16295-4>.
15. VICTORA, C.G.; ADAIR, L.; FALL, C.; HALLAL, P. C.; MARTORELL, R.; RICHTER, L. *et al*. Maternal and child undernutrition: consequences for adult health and human capital. *The Lancet*. 2008;371: 340–57. doi: [https://doi.org/10.1016/S0140-6736\(07\)61692-4](https://doi.org/10.1016/S0140-6736(07)61692-4).
16. BHUTTA, Z. A.; AHMED, T.; BLACK, R. E.; COUSENS, S.; DEWEY, K.; GIUGLIANI, E. *et al*. What works? Interventions for maternal and child undernutrition and survival. *The Lancet*. 2008; 371:417–40. doi: [https://doi.org/10.1016/S0140-6736\(07\)61693-6](https://doi.org/10.1016/S0140-6736(07)61693-6).

17. LULA, E. C.; RIBEIRO, C. C.; HUGO, F. N.; ALVES, C. M.; SILVA, A. A. Added sugars and periodontal disease in young adults: an analysis of NHANES III data. *The American Journal of Clinical Nutrition*. 2014; 100:1182–7. doi: <https://doi.org/10.3945/ajcn.114.089656>.
18. CARMO, C. D. S.; RIBEIRO, M. R. C.; TEIXEIRA, J. X. P.; ALVES, C. M. C.; FRANCO, M. M.; FRANÇA, A. K. T. C. *et al.* Added Sugar Consumption and Chronic Oral Disease Burden among Adolescents in Brazil. *Journal of Dental Research*. 2018; 97:508–14. doi: <https://doi.org/10.1177/0022034517745326>.
19. BIANCO-MIOTTO, T.; CRAIG, J. M.; GASSER, Y. P.; VAN DIJK, S. J.; OZANNE, S. E. Epigenetics and DOHaD: from basics to birth and beyond. *Journal of Developmental Origins of Health and Disease*. 2017; 8:513–9. doi: <https://doi.org/10.1017/S2040174417000733>.
20. BARKER, D. Infant Mortality, Childhood Nutrition, and Ischaemic Heart Disease in England and Wales. *The Lancet*. 1986; 327:1077–81. doi: [https://doi.org/10.1016/S0140-6736\(86\)91340-1](https://doi.org/10.1016/S0140-6736(86)91340-1).
21. GLUCKMAN, P. D.; HANSON, M. A.; BUKLIJAS, T. A conceptual framework for the developmental origins of health and disease. *Journal of Developmental Origins of Health and Disease*. 2010; 1:6–18. doi: <https://doi.org/10.1017/S2040174409990171>.
22. BARKER, D. J. P. Developmental origins of chronic disease. *Public Health*. 2012; 126:185–9. doi: <https://doi.org/10.1016/j.puhe.2011.11.014>.
23. BARKER, D. J. P. The Developmental Origins of Adult Disease. *J Am Coll Nutr*. 2004; 23:588S-595S. doi: <https://doi.org/10.1080/07315724.2004.10719428>.
24. INSTITUTE FOR HEALTH METRICS AND EVALUATION. Global Burden of Disease Study 2019. Periodontal diseases – Level 4 cause. 2019.
25. MARCENES, W.; KASSEBAUM, N. J.; BERNABÉ, E.; FLAXMAN, A.; NAGHAVI, M.; LOPEZ, A. *et al.* Global burden of oral conditions in 1990–2010: a systematic analysis. *J Dent Res*. 2013; 92:592–7. doi: <https://doi.org/10.1177/0022034513490168>.
26. EKE, P. I.; PAGE, R. C.; WEI, L.; THORNTON-EVANS, G.; GENCO, R. J. Update of the Case Definitions for Population-Based Surveillance of Periodontitis. *Journal of Periodontology*. 2012; 83:1449–54. doi: <https://doi.org/10.1902/jop.2012.110664>.
27. KASSEBAUM, N. J.; BERNABÉ, E.; DAHIYA, M.; BHANDARI, B.; MURRAY, C. J. L.; MARCENES, W. Global burden of severe periodontitis in 1990–2010: a systematic review and meta-regression. *J Dent Res*. 2014; 93:1045–53. doi: <https://doi.org/10.1177/0022034514552491>.
28. SALAMONOWICZ, M.; ZALEWSKA, A.; MACIEJCZYK, M. Oral consequences of obesity and metabolic syndrome in children and adolescents. *Dental and Medical Problems*. 2019; 56:97–104. doi: <https://doi.org/10.17219/dmp/102620>.
29. FERREIRA, M. K. M.; FERREIRA, R. DE O.; CASTRO, M. M. L.; MAGNO, M. B.; ALMEIDA, A. P. C. P. S. C.; FAGUNDES, N. C. F. *et al.* Is there an association between asthma and periodontal disease among adults? Systematic review and meta-analysis. *Life Sciences*. 2019; 223:74–87. doi: <https://doi.org/10.1016/j.lfs.2019.03.005>.
30. HWANG, S. H.; PARK, S. G. The relationship between depression and periodontal diseases. *Community Dental Health*. 2018; 35:23–9. doi: https://doi.org/10.1922/CDH_4150Hwang07.
31. HUGO, F. N.; HILGERT, J. B.; DE SOUSA, M. D. L. R.; CURY, J. A. Depressive Symptoms and Untreated Dental Caries in Older Independently Living South Brazilians. *Caries Research*. 2012; 46:376–84. doi: <https://doi.org/10.1159/000338382>.
32. CADEMARTORI, M. G.; GASTAL, M. T.; NASCIMENTO, G. G. DEMARCO, F. F.; CORRÊA, M. B. Is depression associated with oral health outcomes in adults and elders? A systematic review and meta-analysis. *Clinical Oral Investigations*. 2018; 22:2685–702. doi: <https://doi.org/10.1007/s00784-018-2611-y>.

33. GENCO, R. J.; BORGNACKE, W. S. Diabetes as a potential risk for periodontitis: association studies. *Periodontol* 2000. 2020; 83:40–5. doi: <https://doi.org/10.1111/prd.12270>.
34. DIETRICH, T.; WEBB, I.; STENHOUSE, L.; PATTONI, A.; READY, D.; WANYONYI, K. L. *et al.* Evidence summary: the relationship between oral and cardiovascular disease. *British Dental Journal*. 2017; 222:381–5. doi: <https://doi.org/10.1038/sj.bdj.2017.224>.
35. LICCARDO, D.; CANNAVO, A.; SPAGNUOLO, G.; FERRARA, N.; CITTADINI, A.; RENGO, C. *et al.* Periodontal Disease: A Risk Factor for Diabetes and Cardiovascular Disease. *International Journal of Molecular Sciences*. 2019; 20:1414. doi: <https://doi.org/10.3390/ijms20061414>.
36. GLODNY, B.; NASSERI, P.; CRISMANI, A.; SCHOENHERR, E.; LUGER, A.; BERTL, K. *et al.* The occurrence of dental caries is associated with atherosclerosis. *Clinics*. 2013; 68:946–53. doi: [https://doi.org/10.6061/clinics/2013\(07\)10](https://doi.org/10.6061/clinics/2013(07)10).
37. European Federation of Periodontology. What is periodontitis? European Federation of Periodontology. 2021.
38. SHEIHAM, A.; JAMES, W. P. T. Diet and Dental Caries. *Journal of Dental Research*. 2015; 94:1341–7. doi: <https://doi.org/10.1177/0022034515590377>.
39. NYVAD, B.; TAKAHASHI, N. Integrated hypothesis of dental caries and periodontal diseases. *Journal of Oral Microbiology*. 2020;12. doi: <https://doi.org/10.1080/20002297.2019.1710953>.
40. CHAPPLE, I. L. C.; BOUCHARD, P.; CAGETTI, M. G.; CAMPUS, G.; CARRA, M-C.; COCCO, F. *et al.* Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. *Journal of Clinical Periodontology*. 2017;44:S39–51. doi: <https://doi.org/10.1111/jcpe.12685>.
41. MENEZES, C. C.; RIBEIRO, C. C. C.; ALVES, C. M. C.; THOMAZ, E. B. A. F.; FRANCO, M. M.; BATISTA, R. F. L. *et al.* Soft drink consumption and periodontal status in pregnant women. *Journal of Periodontology*. 2019; 90:159–66. doi: <https://doi.org/10.1002/JPER.16-0388>.
42. MOREIRA, A. R.O.; BATISTA, R. F. L.; LADEIRA, L. L. C.; THOMAZ, E. B. A. F.; ALVES, C. M. C.; SARAIVA, M. C. *et al.* Higher sugar intake is associated with periodontal disease in adolescents. *Clinical Oral Investigations*. 2021; 25:983–91. doi: <https://doi.org/10.1007/s00784-020-03387-1>.
43. ARAÚJO, S. M. P.; DA SILVA, G. Q. T. L.; COSTA, E. L.; NUNES, A. M. M.; RIBEIRO, C. C. C. Pathways in the association between added sugar consumption, obesity in mother-child dyads, and chronic oral disease burden in early childhood. *European Journal of Oral Sciences*. 2022;130. doi: <https://doi.org/10.1111/eos.12847>.
44. MONTEIRO, C. A.; CANNON, G.; LEVY, R. B.; MOUBARAC, J. C.; LOUZADA, M. L. C.; RAUBER, F. *et al.* Ultra-processed foods: What they are and how to identify them. *Public Health Nutrition*. 2019;22:936–41. doi: <https://doi.org/10.1017/S1368980018003762>.
45. U.S. Department of Agriculture, U.S. Department of Health and Human Services. Dietary guidelines for Americans, 2020-2025 2020.
46. DINICOLANTONIO, J. J.; O'KEEFE, J. H.; WILSON, W. L. Sugar addiction: is it real? A narrative review. *British Journal of Sports Medicine*. 2018;52:910–3. doi: <https://doi.org/10.1136/bjsports-2017-097971>.
47. MACHIULSKIENE, V.; CAMPUS, G.; CARVALHO, J. C.; DIGE, I.; EKSTRAND, K. R.; JABLONSKI-MOMENI, A. *et al.* Terminology of Dental Caries and Dental Caries Management: Consensus Report of a Workshop Organized by ORCA and Cariology Research Group of IADR. *Caries Research*. 2020;54:7–14. doi: <https://doi.org/10.1159/000503309>.

48. MALIK, V. S.; PAN, A.; WILLETT, W. C.; HU, F. B. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *The American Journal of Clinical Nutrition*. 2013;98:1084–102. doi: <https://doi.org/10.3945/ajcn.113.058362>.
49. KIM, Y.; JE, Y. Prospective association of sugar-sweetened and artificially sweetened beverage intake with risk of hypertension. *Archives of Cardiovascular Diseases*. 2016;109:242–53. doi: <https://doi.org/10.1016/j.acvd.2015.10.005>.
50. DEKKER, M. J.; SU, Q.; BAKER, C.; RUTLEDGE, A. C.; ADELI, K. Fructose: a highly lipogenic nutrient implicated in insulin resistance, hepatic steatosis, and the metabolic syndrome. *American Journal of Physiology-Endocrinology and Metabolism*. 2010;299:E685–94. doi: <https://doi.org/10.1152/ajpendo.00283.2010>.
51. PASE, M. P.; HIMALI, J. J.; BEISER, A. S.; APARICIO, H. J.; SATIZABAL, C. L.; VASAN, R. S. *et al.* Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia. *Stroke*. 2017;48:1139–46. doi: <https://doi.org/10.1161/STROKEAHA.116.016027>.
52. HUANG, C.; HUANG, J.; TIAN, Y.; YANG, X.; GU, D. Sugar sweetened beverages consumption and risk of coronary heart disease: A meta-analysis of prospective studies. *Atherosclerosis*. 2014;234:11–6. doi: <https://doi.org/10.1016/j.atherosclerosis.2014.01.037>.
53. BRAY, G. A.; POPKIN, B. M. Calorie-sweetened beverages and fructose: what have we learned 10 years later. *Pediatr Obes*. 2013; 8:242–8. doi: <https://doi.org/10.1111/j.2047-6310.2013.00171.x>.
54. LEY, R. E.; PETERSON, D. A.; GORDON, J. I. Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell*. 2006;124:837–48. doi: <https://doi.org/10.1016/j.cell.2006.02.017>.
55. QIN, J.; LI, R.; RAES, J.; ARUMUGAM, M.; BURGDORF, K. S.; MANICHANH, C. *et al.* A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*. 2010;464:59–65. doi: <https://doi.org/10.1038/nature08821>.
56. LAURSEN, M. F.; BAHL, M. I.; LICHT, T. R. Settlers of our inner surface – factors shaping the gut microbiota from birth to toddlerhood. *FEMS Microbiology Reviews*. 2021;45. doi: <https://doi.org/10.1093/femsre/fuab001>.
57. LAURSEN, M.F. Gut Microbiota Development: Influence of Diet from Infancy to Toddlerhood. *Annals of Nutrition and Metabolism*. 2021;77:1–14. doi: <https://doi.org/10.1159/000517912>.
58. CHENG, Y-J.; YEUNG, C-Y. Recent advance in infant nutrition: Human milk oligosaccharides. *Pediatrics & Neonatology*. 2021;62:347–53. doi: <https://doi.org/10.1016/j.pedneo.2020.12.013>.
59. BODE, L. Human milk oligosaccharides: Every baby needs a sugar mama. *Glycobiology*. 2012; 22:1147–62. doi: <https://doi.org/10.1093/glycob/cws074>.
60. BRASIL. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Saúde da criança: aleitamento materno e alimentação complementar. vol. 23. 2nd ed. Brasília: Ministério da Saúde; 2015.
61. WORLD HEALTH ORGANIZATION. Ending childhood dental caries: WHO implementation manual. Geneva: 2019.
62. VICTORA, C. G.; BAHL, R.; BARROS, A. J. D.; FRANÇA, G. V. A.; HORTON, S.; KRASEVEC, J. *et al.* Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet*. 2016; 387:475–90. doi: [https://doi.org/10.1016/S0140-6736\(15\)01024-7](https://doi.org/10.1016/S0140-6736(15)01024-7).
63. THOMAZ, E. B. A. F.; ALVES, C. M. C.; GOMES E SILVA, L. F.; RIBEIRO DE ALMEIDA, C. C. C.; SOARES DE BRITTO E ALVES, M. T. S.; HILGERT, J. B. *et al.* Breastfeeding Versus Bottle Feeding on Malocclusion in Children: A Meta-Analysis Study. *Journal of Human Lactation*. 2018;34:089033441875568. doi: <https://doi.org/10.1177/0890334418755689>.

64. FONSECA, A. L. M.; ALBERNAZ, E. P.; KAUFMANN, C. C.; NEVES, I. H.; DE FIGUEIREDO, V. L. M. Impact of breastfeeding on the intelligence quotient of eight-year-old children. *Jornal de Pediatria*. 2013; 89:346–53. doi: <https://doi.org/10.1016/j.jped.2012.12.010>.
65. FELDENS, C. A.; RODRIGUES, P. H.; DE ANASTÁCIO, G.; VÍTOLO, M. R.; CHAFFEE, B. W. Feeding frequency in infancy and dental caries in childhood: a prospective cohort study. *International Dental Journal*. 2018;68:113–21. doi: <https://doi.org/10.1111/idj.12333>.
66. MOYNIHAN, P.; TANNER, L. M.; HOLMES, R. D.; HILLIER-BROWN, F.; MASHAYEKHI, A.; KELLY, S. A. M. *et al.* Systematic Review of Evidence Pertaining to Factors That Modify Risk of Early Childhood Caries. *JDR Clinical & Translational Research*. 2019; 4:202–16. doi: <https://doi.org/10.1177/2380084418824262>.
67. NEVES, P. A. M.; RIBEIRO, C. C.; TENUTA, L. M. A.; LEITÃO, T. J.; MONTEIRO-NETO, V.; NUNES, A. M. M. *et al.* Breastfeeding, Dental Biofilm Acidogenicity, and Early Childhood Caries. *Caries Research*. 2016; 50:319–24. doi: <https://doi.org/10.1159/000445910>.
68. CAMPOS VIEIRA, J.; CURY, J. A.; RICOMINI FILHO, A. P. Combination Effect of Diurnal Exposure to Sucrose and Nocturnal Exposure to Lactose on Enamel Demineralization. *Caries Research*. 2022; 56:47–54. doi: <https://doi.org/10.1159/000520590>.
69. BRASIL. Ministério da Saúde. Portaria de Consolidação n.º 03, de 28 de setembro de 2017. Consolidação das normas sobre as redes do Sistema Único de Saúde. Anexo II. Rede Cegonha. Brasil: 2017.
70. BRASIL. Ministério da Saúde. Atenção ao pré-natal de baixo risco. Cadernos de Atenção Básica, n.º 32; 2013.
71. FERREIRA, S. M. S. P.; SILVA, J. F.; SILVA, R. V.; PINHEIRO, É. S.; BATISTA, L. D.; FERNANDES, C. G. Conhecimento em Saúde Bucal do Bebê e Expectativa Relativa ao Pré-Natal Odontológico: Retrato de Um Município Baiano de Grande Porte. *Rev Faculdade Odontol Lins*. 2015; 25:19–30. doi: <https://doi.org/10.15600/2238-1236/fol.v25n2p19-30>.
72. BERNARDI, C.; MASIEIRO, A. V.; OLIVEIRA, J. B. Assistência odontológica à gestante: conhecimento e prática de dentistas da rede pública e seu papel na rede cegonha. *Arquivos Em Odontologia*. 2019;55. doi: <https://doi.org/10.7308/aodontol/2019.55.e18>.
73. REIS, D. M.; PITTA, D. R.; FERREIRA, H. M. B.; JESUS, M. C. P. D. E. *et al.* Educação em saúde como estratégia de promoção de saúde bucal em gestantes. *Ciência & Saúde Coletiva*. 2010; 15:269–76. doi: <https://doi.org/10.1590/S1413-81232010000100032>.
74. SUNDERMANN, A. C.; ZHAO, S.; YOUNG, C. L.; LAM, L.; JONES, S. H.; VELEZ EDWARDS, D. R. *et al.* Alcohol Use in Pregnancy and Miscarriage: A Systematic Review and Meta-Analysis. *Alcoholism: Clinical and Experimental Research*. 2019;43:1606–16. doi: <https://doi.org/10.1111/acer.14124>.
75. HENDERSON, J.; GRAY, R.; BROCKLEHURST, P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2007;114:243–52. doi: <https://doi.org/10.1111/j.1471-0528.2006.01163.x>.
76. PINELES, B. L.; HSU, S.; PARK, E.; SAMET, J. M. Systematic Review and Meta-Analyses of Perinatal Death and Maternal Exposure to Tobacco Smoke During Pregnancy. *American Journal of Epidemiology*. 2016;184:87–97. doi: <https://doi.org/10.1093/aje/kwv301>.
77. KUPERMAN, A. A.; KOREN, O. Antibiotic use during pregnancy: how bad is it? *BMC Medicine*. 2016;14:91. doi: <https://doi.org/10.1186/s12916-016-0636-0>.
78. SMILACK, J. D. The Tetracyclines. *Mayo Clinic Proceedings*. 1999;74:727–9. doi: <https://doi.org/10.4065/74.7.727>.

79. CIARROCCHI, I.; MASCI, C.; SPADARO, A.; CARAMIA, G.; MONACO, A. Dental enamel, fluorosis and amoxicillin. *La Pediatria Medica e Chirurgica*. 2012; 34:148–54. doi: <https://doi.org/10.4081/pmc.2012.84>.
80. SOUZA, J. F.; JEREMIAS, F.; ALALUUSUA, S.; SAHLBERG, C.; SANTOS-PINTO, L.; JERNVALL, J. *et al.* The effect of amoxicillin on dental enamel development in vivo. *Brazilian Oral Research*. 2020;34:1–9. doi: <https://doi.org/10.1590/1807-3107bor-2020.vol34.0116>.
81. GOTTBORG, B.; BERNE, J.; QUINONEZ, B.; SOLORZANO, E. Prenatal effects by exposing to amoxicillin on dental enamel in Wistar rats. *Medicina Oral Patología Oral y Cirugía Bucal*. 2014;19:e38–43. doi: <https://doi.org/10.4317/medoral.18807>.
82. VASCONCELOS, R. G.; VASCONCELOS, M. G.; MAFRA, R. P.; ALVES JÚNIOR, L. C.; QUEIROZ, L. M. G.; BARBOZA, C. A. G. Atendimento odontológico a pacientes gestantes: como proceder com segurança. *Rev Bras Odontol*. 2012;69.
83. BRASIL. Ministério da Saúde. Instituto Nacional do Câncer. Saiba como identificar o açúcar escondido nos alimentos 2021.
84. GENCO, R. J.; GROSSI, S. G.; HO, A.; NISHIMURA, F.; MURAYAMA, Y. A Proposed Model Linking Inflammation to Obesity, Diabetes, and Periodontal Infections. *Journal of Periodontology*. 2005;76:2075–84. doi: <https://doi.org/10.1902/jop.2005.76.11-S.2075>.
85. SALTIEL, A. R.; OLEFSKY, J. M. Inflammatory mechanisms linking obesity and metabolic disease. *Journal of Clinical Investigation*. 2017;127:1–4. doi: <https://doi.org/10.1172/JCI92035>.
86. ECKEL, R. H.; KAHN, S. E.; FERRANNINI, E.; GOLDFINE, A. B.; NATHAN, D. M.; SCHWARTZ, M. W. *et al.* Obesity and Type 2 Diabetes: What Can Be Unified and What Needs to Be Individualized? *Diabetes Care*. 2011; 34:1424–30. doi: <https://doi.org/10.2337/dc11-0447>.
87. DAI, R.; HE, X-J.; HU, C-L. Maternal pre-pregnancy obesity and the risk of macrosomia: a meta-analysis. *Archives of Gynecology and Obstetrics*. 2018;297:139–45. doi: <https://doi.org/10.1007/s00404-017-4573-8>.
88. HOWELL, K. R.; POWELL, T. L. Effects of maternal obesity on placental function and fetal development. *Reproduction*. 2017;153:R97–108. doi: <https://doi.org/10.1530/REP-16-0495>.
89. RASMUSSEN, L.; POULSEN, C. W.; KAMPMANN, U.; SMEDEGAARD, S. B.; OVESEN, P. G.; FUGLSANG, J. Diet and healthy lifestyle in the management of gestational diabetes mellitus. *Nutrients*. 2020; 12:1–24. doi: <https://doi.org/10.3390/nu12103050>.
90. AMARANTE, S. Alimentação durante a gravidez: o que devo saber. Instituto Nacional de Saúde Da Mulher, Da Criança e Do Adolescente Fernandes Figueira. 2017.
91. INSTITUTE OF MEDICINE. National Research Council. Weight Gain During Pregnancy. Washington, D.C.: National Academies Press; 2009. doi: <https://doi.org/10.17226/12584>.
92. OLIVEIRA, C. A.; LINS, C. P.; SÁ, R. A. M.; NETTO, H. C.; BORNIA, R. G.; SILVA, N. R. *et al.* Síndromes hipertensivas da gestação e repercussões perinatais. *Revista Brasileira de Saúde Materno Infantil*. 2006; 6:93–8. doi: <https://doi.org/10.1590/S1519-38292006000100011>.
93. MOURA, M. D. R.; CASTRO, M. P.; MARGOTTO, P. R.; RUGOLO, L. M. S. Hipertensão Arterial na Gestação: importância do seguimento materno no desfecho neonatal. *Com Ciências Saúde*. 2011;22:S113–20.
94. BARBOSA, J. M. A.; SILVA, A. A. M.; KAC, G.; SIMÕES, V. M. F.; BETTIOL, H.; CAVALLI, R. C. *et al.* Is soft drink consumption associated with gestational hypertension? Results from the BRISA cohort. *Brazilian Journal of Medical and Biological Research*. 2021; 54:1–9. doi: <https://doi.org/10.1590/1414-431x202010162>.

95. REHDER, P. M.; BOROVAC-PINHEIRO, A.; DE ARAUJO, R. O. M. B.; DINIZ, J. A. P. M.; FERREIRA, N. L. C.; BRANCO, A. C. R. *et al.* Gestational Diabetes Mellitus and Obesity are Related to Persistent Hyperglycemia in the Postpartum Period. *Revista Brasileira de Ginecologia e Obstetrícia / RBGO Gynecology and Obstetrics*. 2021; 43:107–12. doi: <https://doi.org/10.1055/s-0040-1721356>.
96. BERGER, H.; GAGNON, R.; SERMER, M. Diabetes in Pregnancy. *Journal of Obstetrics and Gynaecology Canada*. 2016;38:667-679.e1. doi: <https://doi.org/10.1016/j.jogc.2016.04.002>.
97. MUSTAD, V. A.; HUYNH, D. T. T.; LÓPEZ-PEDROSA, J. M.; CAMPOY, C.; RUEDA, R. The role of dietary carbohydrates in gestational diabetes. *Nutrients*. 2020; 12:385. doi: <https://doi.org/10.3390/nu12020385>.
98. FIGUEIREDO, C. S. A.; ROSALEM, C. G. C.; CANTANHEDE, A. L. C.; THOMAZ, É. B. A. F.; CRUZ, M. C. F. N. Systemic alterations and their oral manifestations in pregnant women. *Journal of Obstetrics and Gynaecology Research*. 2017; 43:16–22. doi: <https://doi.org/10.1111/jog.13150>.
99. GONÇALVES, K. F. Cuidado Odontológico no pré-natal na atenção primária à saúde: dados do PMAQ-AB. 2016.
100. SALUJA, P. Comparative Evaluation of the Effect of Menstruation, Pregnancy and Menopause on Salivary Flow Rate, pH and Gustatory Function. *Journal of Clinical and Diagnostic Research*. 2014. doi: <https://doi.org/10.7860/JCDR/2014/9935.5071>.
101. BROWN, J. E.; TOMA, R. B. Taste changes during pregnancy. *The American Journal of Clinical Nutrition*. 1986;43:414–8. doi: <https://doi.org/10.1093/ajcn/43.3.414>.
102. WU, M.; CHEN, S-W.; JIANG, S-Y. Relationship between Gingival Inflammation and Pregnancy. *Mediators of Inflammation*. 2015;2015:1–11. doi: <https://doi.org/10.1155/2015/623427>.
103. ORTIZ-SÁNCHEZ, B. J.; LEGORRETA-HERRERA, M.; RODRIGUEZ-SOSA, M. Influence of Gestational Hormones on the Bacteria-Induced Cytokine Response in Periodontitis. *Mediators of Inflammation*. 2021;2021:1–12. doi: <https://doi.org/10.1155/2021/5834608>.
104. SANZ, M.; KORNMAN, K. Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology*. 2013;40:S164–9. doi: <https://doi.org/10.1111/jcpe.12083>.
105. FIGUERO, E.; HAN, Y. W.; FURUICHI, Y. Periodontal diseases and adverse pregnancy outcomes: Mechanisms. *Periodontol 2000*. 2020;83:175–88. doi: <https://doi.org/10.1111/prd.12295>.
106. JAKOVLJEVIC, A.; SLJIVANCANIN JAKOVLJEVIC, T.; DUNCAN, H. F.; NAGENDRABABU, V.; JACIMOVIC, J.; AMINOSHARIAE, A. *et al.* The association between apical periodontitis and adverse pregnancy outcomes: a systematic review. *International Endodontic Journal*. 2021;54:1527–37. doi: <https://doi.org/10.1111/iej.13538>.
107. CHO, G. J.; KIM, S.; LEE, H. C.; KIM, H. Y.; LEE, K-M.; HAN, S. W. *et al.* Association between dental caries and adverse pregnancy outcomes. *Scientific Reports*. 2020;10:5309. doi: <https://doi.org/10.1038/s41598-020-62306-2>.
108. CASAS, R.; CASTRO BARQUERO, S.; ESTRUCH, R. Impact of Sugary Food Consumption on Pregnancy: A Review. *Nutrients*. 2020;12:3574. doi: <https://doi.org/10.3390/nu12113574>.
109. ENGLUND-ÖGGE, L.; BRANTSÆTER, A. L.; HAUGEN, M.; SENGPIEL, V.; KHATIBI, A.; MYHRE, R. *et al.* Association between intake of artificially sweetened and sugar-sweetened beverages and preterm delivery: a large prospective cohort study. *The American Journal of Clinical Nutrition*. 2012;96:552–9. doi: <https://doi.org/10.3945/ajcn.111.031567>.
110. PETHERICK, E. S.; GORAN, M. I.; WRIGHT J. Relationship between artificially sweetened and sugar-sweetened cola beverage consumption during pregnancy and preterm delivery in a multi-ethnic cohort: analysis of the Born in Bradford cohort study. *European Journal of Clinical Nutrition*. 2014;68:404–7. doi: <https://doi.org/10.1038/ejcn.2013.267>.

111. GRUNDT, J. H.; NAKLING, J.; EIDE, G. E.; MARKESTAD, T. Possible relation between maternal consumption of added sugar and sugar-sweetened beverages and birth weight – time trends in a population. *BMC Public Health*. 2012;12:901. doi: <https://doi.org/10.1186/1471-2458-12-901>.
112. WHINCUP, P. H.; KAYE, S. J.; OWEN, C. G.; HUXLEY, R.; COOK, D. G.; ANAZAWA, S. *et al.* Birth weight and risk of type 2 diabetes: a systematic review. *JAMA*. 2008;300:2886–97. doi: <https://doi.org/10.1001/jama.2008.886>.
113. YU, Z. B.; HAN, S. P.; ZHU, G. Z.; ZHU, C.; WANG, X. J.; CAO, X. G. *et al.* Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. *Obesity Reviews*. 2011;12:525–42. doi: <https://doi.org/10.1111/j.1467-789X.2011.00867.x>.
114. SIPOLA-LEPPÄNEN, M.; VÄÄRÄSMÄKI, M.; TIKANMÄKI, M.; HOVI, P.; MIETTOLA, S.; RUOKONEN, A. *et al.* Cardiovascular Risk Factors in Adolescents Born Preterm. *Pediatrics*. 2014;134:e1072–81. doi: <https://doi.org/10.1542/peds.2013-4186>.
115. SONNENSCHNEIDER-VAN DER VOORT, A. M. M.; ARENDS, L. R.; DE JONGSTE, J. C.; ANNESI-MAESANO, I.; ARSHAD, S. H.; BARROS, H. *et al.* Preterm birth, infant weight gain, and childhood asthma risk: A meta-analysis of 147,000 European children. *Journal of Allergy and Clinical Immunology*. 2014;133:1317–29. doi: <https://doi.org/10.1016/j.jaci.2013.12.1082>.
116. KUCIENE, R.; DULSKIENE, V.; MEDZIONIENE, J. Associations between high birth weight, being large for gestational age, and high blood pressure among adolescents: a cross-sectional study. *European Journal of Nutrition*. 2018; 57:373–81. doi: <https://doi.org/10.1007/s00394-016-1372-0>.
117. PINTO, D. A. S.; NASCIMENTO, J. X. P. T.; PADILHA, L. L.; DA CONCEIÇÃO, S. I. O.; FRANÇA, A. K. T.; SIMÕES, V. M. F. *et al.* High sugar content and body mass index: modelling pathways around the first 1000 d of life, BRISA cohort. *Public Health Nutrition*. 2021; 24:4997–5005. doi: <https://doi.org/10.1017/S136898002000525X>.
118. COSTA, E. L.; COSTA, J. F.; SANTOS, M. P.; LADEIRA, L. L. C.; SILVA, R. A.; RIBEIRO, C. C. C. Streptococcus mutans in Mother-Child Dyads and Early Childhood Caries: Examining Factors Underlying Bacterial Colonization. *Caries Research*. 2017; 51:582–9. doi: <https://doi.org/10.1159/000479435>.
119. RIBEIRO, C. C. C.; PACHÊCO, C. DE J. B.; COSTA, E. L.; LADEIRA, L. L. C.; COSTA, J. F.; DA SILVA, R. A. *et al.* Proinflammatory cytokines in early childhood caries: Salivary analysis in the mother/children pair. *Cytokine*. 2018;107:113–7. doi: <https://doi.org/10.1016/j.cyto.2017.12.009>.
120. MARTENS, L.; DE SMET, S.; YUSOF, M. Y. P. M.; RAJASEKHARAN, S. Association between overweight/obesity and periodontal disease in children and adolescents: a systematic review and meta-analysis. *European Archives of Paediatric Dentistry*. 2017;18:69–82. doi: <https://doi.org/10.1007/s40368-017-0272-1>.
121. CALIL, V. M. L. T.; FALCÃO, M. C. Composição do leite humano: o alimento ideal. *Revista de Medicina*. 2003; 82:1–10. doi: <https://doi.org/10.11606/issn.1679-9836.v82i1-4p1-10>.
122. BRASIL. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Departamento de Promoção da Saúde. Guia alimentar para crianças brasileiras menores de 2 anos. Brasília: Ministério da Saúde; 2019.
123. BRASIL. Ministério da Saúde. Secretaria de Atenção à Saúde. Guia alimentar para a população brasileira. vol. 2. 2014.
124. RUIZ, D. R. Orientações ao pais sobre cuidados com a saúde bucal do bebê e das crianças. Associação Brasileira de Odontopediatria. 2021.
125. ELLWOOD, R. P.; CURY, J. A. How much toothpaste should a child under the age of 6 years use? *European Archives of Paediatric Dentistry*. 2009;10:168–74. doi: <https://doi.org/10.1007/BF03262679>.

126. BRASIL, Ministério da Saúde. Guia de recomendações para o uso de fluoretos no Brasil. Ministério Da Saúde. 2009.
127. BETRAN, A. P.; YE, J.; MOLLER, A-B.; SOUZA, J. P.; ZHANG, J. Trends and projections of caesarean section rates: global and regional estimates. *BMJ Global Health*. 2021;6: e005671. doi: <https://doi.org/10.1136/bmjgh-2021-005671>.
128. BETRAN, A. P.; TORLONI, M. R.; ZHANG, J. J.; GÜLMEZOGLU, A. M. WHO Working Group on Caesarean Section. WHO Statement on Caesarean Section Rates. *BJOG*. 2016;123:667–70. doi: <https://doi.org/10.1111/1471-0528.13526>.
129. WORLD HEALTH ORGANIZATION. Declaração da OMS sobre Taxas de Cesáreas. World Health Organization. 2015.
130. BETRAN, A. P.; TORLONI, M. R.; ZHANG, J.; YE, J.; MIKOLAJCZYK, R.; DENEUX-THARAUX, C. *et al*. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. *Reproductive Health*. 2015;12:57. doi: <https://doi.org/10.1186/s12978-015-0043-6>.
131. MAGNE, F.; PUCHI SILVA, A.; CARVAJAL, B.; GOTTELAND, M. The Elevated Rate of Cesarean Section and Its Contribution to Non-Communicable Chronic Diseases in Latin America: The Growing Involvement of the Microbiota. *Frontiers in Pediatrics*. 2017;5. doi: <https://doi.org/10.3389/fped.2017.00192>.
132. ZIMMERMAN, E.; THOMPSON, K. Clarifying nipple confusion. *J Perinatol*. 2015; 35:895–9. doi: <https://doi.org/10.1038/jp.2015.83>.
133. COLLINS, C. T.; GILLIS, J.; MCPHEE, A. J.; SUGANUMA, H.; MAKRIDES, M. Avoidance of bottles during the establishment of breast feeds in preterm infants. *Cochrane Database of Systematic Reviews*. 2016;2016. doi: <https://doi.org/10.1002/14651858.CD005252.pub4>.
134. TURKE, K. C.; DOS SANTOS, L. R.; MATSUMURA, L. S.; SARNI, R. O. S. Risk factors for the lack of adherence to breastfeeding. *Revista Da Associacao Medica Brasileira*. 2021; 67:107–14. doi: <https://doi.org/10.1590/1806-9282.67.01.20200510>.
135. SILVA JÚNIOR, A. C.; ALVES, C. M. C.; MARTINS, R. F. M.; RODRIGUES, V. P.; SOUZA, S. DE F. C.; RIBEIRO, C. C. C. *et al*. Adverse pregnancy outcomes and occlusal traits in the primary dentition: A prospective cohort (BRISA). *Orthodontics & Craniofacial Research*. 2022. doi: <https://doi.org/10.1111/ocr.12563>.
136. MATTOS-GRANER, R. O.; DE MORAES, A. B.; RONTANI, R. M.; BIRMAN, E. G. Relation of oral yeast infection in Brazilian infants and use of a pacifier. *ASDC J Dent Child*. 2001; 68:33–6, 10.
137. SCUDINE, K. G. DE O.; FREITAS, C. N.; NASCIMENTO DE MORAES, K. S. G.; BOMMARITO, S.; POSSOBON, R. DE F.; BONI, R. C. *et al*. Multidisciplinary Evaluation of Pacifier Removal on Oro-Dentofacial Structures: A Controlled Clinical Trial. *Frontiers in Pediatrics*. 2021;9. doi: <https://doi.org/10.3389/fped.2021.703695>.
138. NUNES, A. M. M.; DA SILVA, A. A. M.; ALVES, C. M. C.; HUGO, F. N.; RIBEIRO, C. C. C. Factors underlying the polarization of early childhood caries within a high-risk population. *BMC Public Health*. 2014;14:988. doi: <https://doi.org/10.1186/1471-2458-14-988>.
139. STEVENS, A.; HAMEL, C.; SINGH, K.; ANSARI, M. T.; MYERS, E.; ZIEGLER, P. *et al*. Do sugar-sweetened beverages cause adverse health outcomes in children? A systematic review protocol. *Systematic Reviews*. 2014;3:96. doi: <https://doi.org/10.1186/2046-4053-3-96>.
140. VOS, M. B.; KAAR, J. L.; WELSH, J. A.; VAN HORN, L. V.; FEIG, D. I.; ANDERSON, C. A; M. *et al*. Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. *Circulation*. 2017;135: e1017–34. doi: <https://doi.org/10.1161/CIR.0000000000000439>.

141. DEL-PONTE, B.; QUINTE, G. C.; CRUZ, S.; GRELLERT, M.; SANTOS, I. S. Dietary patterns and attention deficit/hyperactivity disorder (ADHD): A systematic review and meta-analysis. *Journal of Affective Disorders*. 2019;252:160–73. doi: <https://doi.org/10.1016/j.jad.2019.04.061>.
142. FARSAD-NAEIMI, A.; ASJODI, F.; OMIDIAN, M.; ASKARI, M.; NOURI, M.; PIZARRO, A. B. *et al.* Sugar consumption, sugar sweetened beverages and attention deficit hyperactivity disorder: A systematic review and meta-analysis. *Complementary Therapies in Medicine*. 2020;53. doi: <https://doi.org/10.1016/j.ctim.2020.102512>.
143. YU, C. J.; DU, J. C.; CHIOU, H. C.; FENG, C. C.; CHUNG, M. Y.; YANG, W. *et al.* Sugar-sweetened beverage consumption is adversely associated with childhood attention deficit/hyperactivity disorder. *International Journal of Environmental Research and Public Health*. 2016;13. doi: <https://doi.org/10.3390/ijerph13070678>.
144. NATIONAL HEARTH LUNG AND BLOOND INSTITUTE. Asthma 2020.
145. WORLD HEALTH ORGANIZATION. Asthma 2021.
146. PADILHA, L. L.; VIANNA, E. O.; VALE, A. T. M.; NASCIMENTO, J. X. P. T.; SILVA, A. A. M.; RIBEIRO, C. C. C. Pathways in the association between sugar sweetened beverages and child asthma traits in the 2nd year of life: Findings from the BRISA cohort. *Pediatric Allergy and Immunology*. 2020;31:480–8. doi: <https://doi.org/10.1111/pai.13243>.
147. NOUTSIOS, G.; FLOROS, J. Childhood asthma: causes, risks, and protective factors; a role of innate immunity. *Swiss Medical Weekly*. 2014;144. doi: <https://doi.org/10.4414/smw.2014.14036>.
148. Early Childhood Caries: IAPD Bangkok Declaration. *Int J Paediatr Dent*. 2019;29:384–6. doi: <https://doi.org/10.1111/ipd.12490>.
149. LIMA, G. Q. T.; BRONDANI, M. A.; SILVA, A. A. M.; DO CARMO, C. D. S.; SILVA, R. A.; RIBEIRO, C. C. C. Serum levels of proinflammatory cytokines are high in early childhood caries. *Cytokine*. 2018; 111:490–5. doi: <https://doi.org/10.1016/j.cyto.2018.05.031>.
150. ORGANIZAÇÃO DAS NAÇÕES UNIDAS. Objetivos de Desenvolvimento Sustentável 2015.
151. BRASIL. Ministério da Saúde. Portaria n.º 2.979, de 12 de novembro de 2019. Institui o Programa Previne Brasil, que estabelece novo modelo de financiamento de custeio da Atenção Primária à Saúde no âmbito do Sistema Único de Saúde, por meio da alteração da Portaria de Consolidação n.º 6/GM/MS, de 28 de setembro de 2017. Brasília: 2019.
152. BRASIL. Ministério da Saúde. Guia para qualificação dos indicadores da APS 2020.
153. BRASIL. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Departamento de Saúde da Família. Portaria GM/MS n.º 102, de 20 de janeiro de 2022. Altera a Portaria GM/MS n.º 3.222, de 10 de dezembro de 2019, que dispõe sobre os indicadores do pagamento por desempenho, no âmbito do Programa Previne Brasil. Brasil: DOU; 2022.

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THE FIRST THOUSAND DAYS OF LIFE

**A DOHaD perspective
to Dentistry**



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Silas Alves-Costa

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PREFACE

The first thousand days of life are a crucial period that significantly influences a child's health trajectory, establishing foundational elements for their future well-being. In "The First Thousand Days of Life: Dentistry from the DOHaD Perspective," the authors explore the complex relationship between early life experiences and oral health, highlighting the importance of understanding dental care within the framework of the Developmental Origins of Health and Disease (DOHaD). This perspective emphasizes that the choices made during this formative time can have lasting effects on a child's overall health, including the mouth, of course.

This book is a thoughtful contribution to the field of pediatric health, reflecting the dedication and collaborative efforts of its authors. Comprising professionals in pediatric dentistry, public health, and nutrition, the authors draw from their diverse experiences to address the challenges associated with oral health in early childhood. Their insights underscore the multifaceted nature of oral health and the various factors that influence it.

A key theme of this book is the understanding that while oral biofilm dysbiosis—an imbalance in the microbial communities within the mouth—plays a role in the development of oral diseases, it does not fully account for oral health issues. The authors bring the theory of multiple causation, which suggests that oral diseases, including dental caries and periodontal disease, arise from a combination of biological, environmental, and behavioral factors. This perspective acknowledges that no single factor can explain the prevalence of oral diseases; instead, it is the interplay of elements such as nutrition, socioeconomic status, and access to care that shapes health outcomes.

Throughout the book, the authors present practical strategies for prevention and intervention, aiming to support healthcare professionals, policymakers, and caregivers. They advocate for a proactive approach to oral health, emphasizing the importance of early interventions in preventing dental diseases. By addressing the underlying causes of dental caries and promoting healthy behaviors from an early age, we can help ensure that children have a solid foundation for their oral health. The authors provide guidance on implementing these strategies in various settings, making their insights accessible and actionable.

This book also serves as an invitation for collaboration among stakeholders at all levels, stressing the need to integrate oral health into broader health initiatives. The discussions within these pages enhance our understanding of the connections between early life experiences and oral health while offering practical tools for creating healthier

environments for children. The authors emphasize the value of cooperation among healthcare providers, educators, and families to promote a supportive framework that prioritizes oral health as an integral part of overall health.

Moreover, the importance of equitable access to healthcare resources cannot be overlooked. The disparities in oral health outcomes often reflect broader societal inequalities, where children from less advantaged backgrounds face significant barriers to accessing quality dental care. Addressing these disparities requires a collective commitment to ensuring that all children, regardless of their socioeconomic status, can receive the care they need. By recognizing and addressing the systemic factors that contribute to these inequities, we can work towards a more just healthcare system that prioritizes the health of all children.

As you read this book, you may find encouragement in the authors' commitment to improving the lives of children and promoting healthier futures. Their work serves as a reminder that investing in the health of our youngest human beings is essential for the well-being of our communities. By recognizing the multifactorial nature of oral conditions and the significance of the first thousand days, we can work together to promote a healthier future for all children.

In conclusion, "The First Thousand Days of Life: Dentistry from the DOHaD Perspective" is an essential discussion of pediatric health. It invites readers to reflect on the role of oral health in child development and to consider how we can collectively enhance health outcomes for future generations. This book encourages a comprehensive approach to oral health, recognizing the interconnectedness of various health aspects during these formative years and the need for a healthcare system that serves all members of society equitably.



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SUMÁRIO

INTRODUCTION	13
THE FIRST THOUSAND DAYS OF LIFE	16
DOHaD THEORY AND DENTISTRY	19
1 Caries and periodontal disease are non-communicable diseases and are interrelated	22
2 Ultra-processed foods and added sugars as risk factors for oral and systemic NCDs	23
3 Balanced human microbiome	24
4 Breastfeeding as protection against NCDs	25
PREGNANCY HEALTHCARE	27
Importance of prenatal dental visits	28
Nutritional guidance for pregnant women	30
ENVIRONMENTAL STRESSORS DURING PREGNANCY	31
Alcohol and tobacco use	32
Use of antibiotics during pregnancy	33
Added sugars	34
Obesity	35
Hypertension	36
Diabetes	37
Chronic oral diseases	37
HEALTHCARE DURING THE FIRST TWO YEARS OF LIFE	41
Breastfeeding	42
Introduction of complementary foods	45
Infant oral hygiene	48
ENVIRONMENTAL STRESSORS DURING THE FIRST TWO YEARS	49
Cesarean delivery	50
Bottles and pacifiers	51
Added sugars	52
Child development	53
Asthma	53
Overweight	54
Chronic oral diseases	54
THE FIRST THOUSAND DAYS IN THE AGENDA FOR TACKLING NCDs	55
FINAL CONSIDERATIONS	58
REFERENCES	60

PRESENTATION

The Developmental Origins of Health and Disease (DOHaD) theory examines how early life environments can influence the risk of developing non-communicable diseases (NCDs) later in life. In this material, based on the perspective of the DOHaD Theory, we will highlight the principles supporting Dentistry in this context and specifically discuss the dentist's role in monitoring pregnant women, postpartum care, and comprehensive child health care during the First Thousand Days of Life.

Recognizing that oral NCDs emerge decades before other high-mortality NCDs, we will emphasize the dentist's pivotal role in a multidisciplinary task force. This includes identifying risk exposures and early signs of oral NCDs, guiding families through this process, and developing public policies to address NCDs.

The grouping of caries and periodontal diseases with other high-mortality systemic NCDs in adulthood, particularly among vulnerable populations, requires an integrated approach focused on common risk factors that should begin in the earliest phases of the life cycle.

Among the Sustainable Development Goals (SDGs), the #3 Good Health and Well-Being, the target 3.1 "to reduce by one-third premature mortality from NCDs through prevention and treatment and promote mental health and well-being by 2030. Thus, the goals must include reducing child obesity rates and decreasing the consumption of ultra-processed foods and sugary beverages. For Dentistry, one highlighted strategy is to "Expand access to prenatal dental care and early prevention to reduce the occurrence of caries and periodontal diseases."

We present this digital book, "The First Thousand Days of Life: Dentistry from the DOHaD Perspective," within this framework. We hope this carefully prepared material broadens your perspective and proves useful to you.

Enjoy your reading!



INTRODUCTION

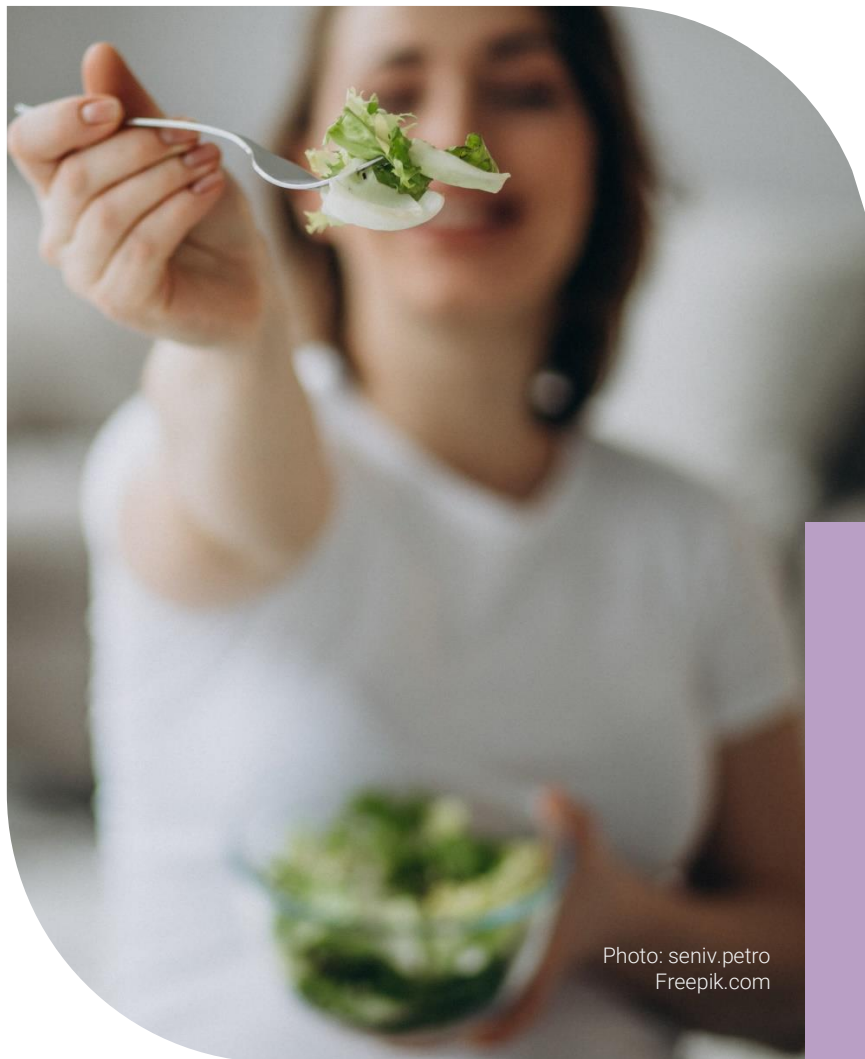
INTRODUCTION

Tackling Non-Communicable Diseases (NCDs), or chronic diseases, is the most significant public health challenge of the 21st century.¹ The most lethal NCDs — cardiovascular diseases, type 2 diabetes, respiratory diseases, and cancers — are responsible for 71% of all deaths worldwide. Of these deaths, over 85% are premature, occurring between the ages of 30 and 69, particularly affecting low- and middle-income countries.^{1,2}

Even in the context of the COVID-19 pandemic, higher mortality due to complications from SARS-CoV-2 infection has been observed in populations already affected by NCDs.³

Social and economic determinants, such as poverty and low educational levels, are well-known risk factors for NCDs. These diseases cluster and are more prevalent in low- and middle-income countries or socially vulnerable groups in high-income countries.^{1,2}

In addition to social determinants, the World Health Organization (WHO) identifies four main behavioral and modifiable risk factors for all NCDs: smoking, physical inactivity, unhealthy diet, and harmful use of alcohol. Exposure to these risk behaviors leads to metabolic changes such as high blood pressure,



overweight/obesity, elevated blood glucose levels (hyperglycemia), and elevated blood fat levels (hyperlipidemia).²

Caries and periodontitis are also chronic diseases and are the most prevalent NCDs globally. Although not directly linked to mortality, these oral diseases are associated with asthma, including in children and adolescents,⁴ and predict the risk of diabetes and cardiovascular diseases decades in advance.^{5,6} Thus, oral diseases occur earlier than other high-mortality NCDs in adulthood.

In this context, the WHO Oral Health Committee recommends strategies targeting oral and systemic NCDs based on their common risk factors.⁷ Actions targeting common risk factors aim to integrate the prevention of both oral and systemic NCDs, with early interventions being the most effective in reducing future NCDs.

The greater plasticity of the phenotype supports preventive actions during the most sensitive periods of human development. The DOHaD theory is based on environmental exposures early in life that increase susceptibility to developing NCDs in the future. Thus, the first thousand days of life (270 days of pregnancy + 365 days of the first year + 365 days of the second year) are the most critical period of human development, representing a window of opportunity for NCD prevention.^{8,9}

The work of health professionals in light of the DOHaD theory can have repercussions throughout an individual's life cycle. The dentist is one of the

professionals on the multidisciplinary healthcare team who is directly in contact with patients during the first thousand days of life. This period is conducive to NCD prevention, advising pregnant women and postpartum mothers on the importance of healthier dietary choices for themselves, their families, and their babies, which can positively impact their health, pregnancy, and child health in the long term.



THE FIRST THOUSAND DAYS OF LIFE

THE FIRST THOUSAND DAYS OF LIFE

The first thousand days of life, from pregnancy to a child's second birthday, have significant impacts on a child's cognitive, emotional, and socio-behavioral development. A balanced and healthy diet, access to healthcare services, education, basic sanitation, proper stimulation, interaction, and protection from violence or neglect are essential for promoting comprehensive growth and development in early childhood.

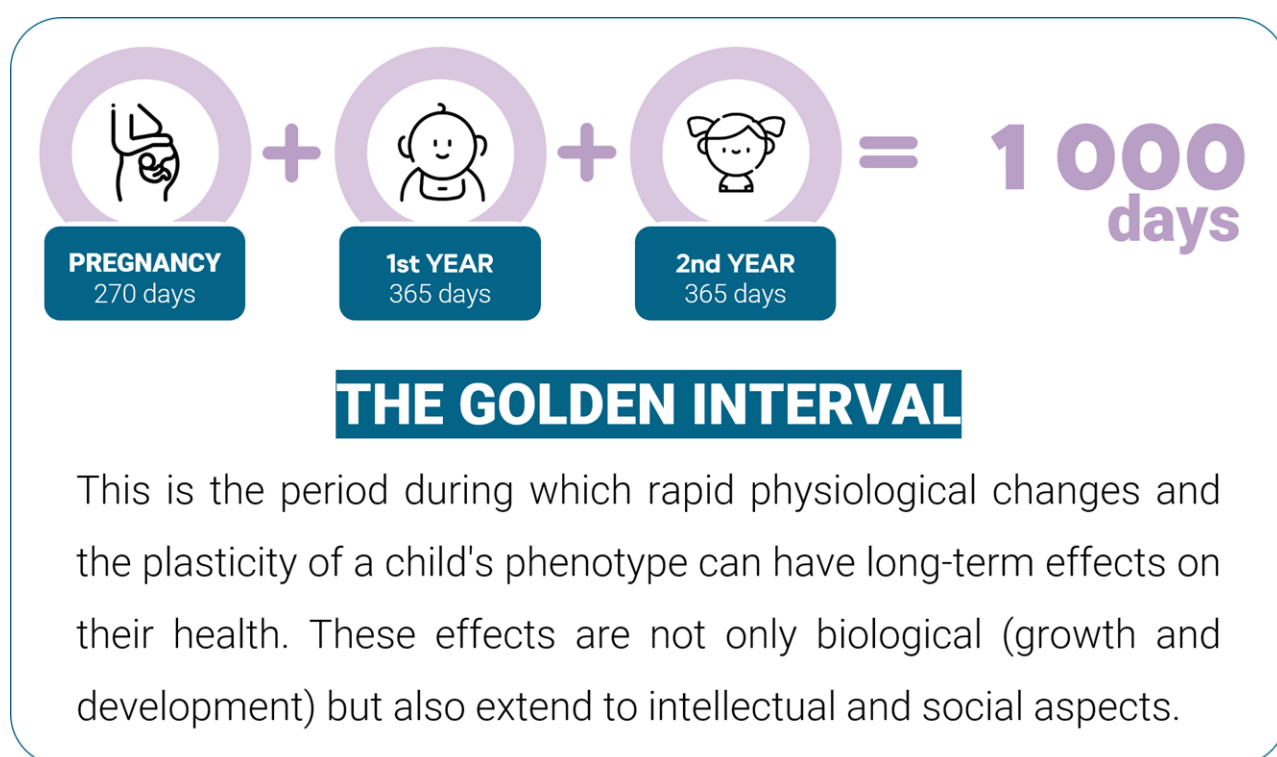


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This period represents a unique "window of opportunity" to prevent or modify unfavorable metabolic programming. Doing so can improve health indicators for the mother, fetus, newborn, and child and even reduce the risk of developing NCDs later in life.

Pregnancy induces a series of physiological, biochemical, metabolic, and endocrine changes in a woman's body to accommodate the needs of maternal-fetal complex development. Environmental stressors during pregnancy, such as an



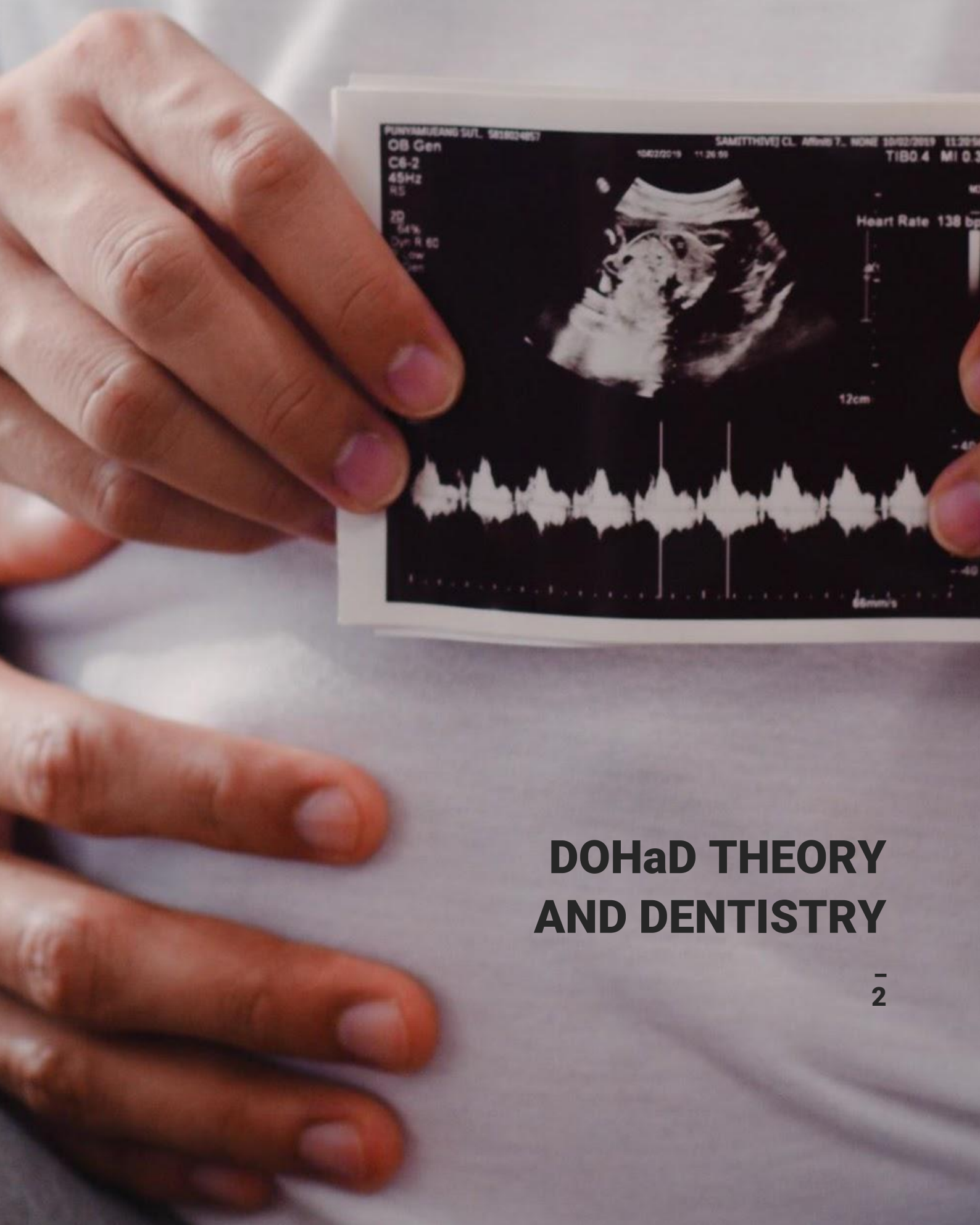
unhealthy diet, alcohol consumption, and tobacco exposure, can have detrimental effects on maternal health. These impacts include excessive weight gain, hypertension, gestational diabetes, dental caries, periodontal disease, and other NCDs.^{10–12} Furthermore, these behavioral risks can result in adverse pregnancy outcomes, such as preterm birth (< 37 weeks) and large-for-gestational-age babies (≥ 4000 g). They may also trigger short-term effects in offspring, including asthma, allergies, neurodevelopmental delay, and increased susceptibility to dental caries. Additionally, these behaviors can lead to long-term health issues, predisposing children to NCDs in their later years.^{13,14}



Environmental stressors in the first two years of a child's life, such as artificial feeding and early exposure to added sugars, can also have lasting impacts. These stressors can affect a child's development and health in early

childhood and throughout their entire life. For instance, poor dietary practices in infancy can set the stage for childhood obesity, which in turn increases the risk of diabetes, cardiovascular diseases, and other NCDs in adulthood.^{14–18}

Therefore, the dentist plays a crucial role in guiding pregnant women toward adopting healthier lifestyles. By providing education and support, dentists can help expectant mothers understand the importance of nutritious diets, regular dental check-ups, and the avoidance of harmful substances like tobacco and alcohol. These healthy attitudes and behaviors during the first thousand days of life are pivotal for ensuring a healthier pregnancy and have a significant impact on the long-term health of both the mother and the baby.



DOHaD THEORY AND DENTISTRY

DOHaD THEORY AND DENTISTRY

The DOHaD theory explores how the environment during the first thousand days of life can influence the risk of developing NCDs from childhood through adulthood. This theory examines the mechanisms involved in these processes.^{9,19}

The concept was introduced through the studies of David Barker²⁰ in 1961, who observed that babies born under conditions of intrauterine nutritional deprivation had a higher risk of developing cardiovascular diseases as adults. Barker's studies have since been deepened and expanded. Currently, numerous research groups are striving to understand how adverse conditions during a child's first thousand days impact future health.

Although the genetic code is predetermined, studies indicate that external or epigenetic factors can modify the expression of human genes throughout life.¹⁹ Environmental stimuli are crucial for the balance of health and disease across generations.^{9,21} DOHaD studies focus on preventing adverse environments at the origin of life, offering an integrative model that explains how environmental influences (including family, habits, socioeconomic conditions, and toxic stress) can affect biological programming and genetic inheritance. This results in phenotypes that manifest immediate changes (such as preterm birth, low birth weight, and anemia) or delayed effects (such as obesity, diabetes, hypertension, and asthma).¹⁴⁻¹⁶

The DOHaD theory suggests that an increased risk of long-term diseases is initially induced by the adaptive responses of the baby to the health conditions and physical state of the mother. Fetal or perinatal responses may include changes in



metabolism, endocrine function, and sensitivity, which can disrupt physiological homeostasis.²¹

The DOHaD theory supports the idea that the best times to implement preventive interventions for NCDs, significantly reducing risk, are during key developmental periods: **intrauterine life**, **childhood**, and, as a second, albeit less impactful, window of opportunity, **adolescence**.^{22,23}

Now, you may wonder how Dentistry fits into the DOHaD Theory studies. Let's explore the four premises that support Dentistry's perspective within the DOHaD framework:

- 1.** Caries and periodontal disease are NCDs, being the most prevalent, and they precede and can even predict other higher-mortality NCDs in the future;
- 2.** Eating an unhealthy diet, especially one high in ultra-processed foods and added sugars, is a risk factor for both oral and systemic NCDs;
- 3.** The balance of the human microbiome is crucial for health, and its dysregulation (dysbiosis) leads to changes in microbial diversity, which impacts oral and general health.
- 4.** Breastfeeding is important for babies' growth and development and for NCD prevention. According to WHO recommendations, dentistry should support breastfeeding practices

Let's present scientific evidence to support the four premises highlighted above, which position Dentistry within the DOHaD perspective.

1 CARIES AND PERIODONTAL DISEASE ARE NON-COMMUNICABLE DISEASES AND ARE INTERRELATED



Caries and periodontal disease are among the most prevalent NCDs worldwide.²⁴ According to the Global Burden of Diseases Study, dental caries in permanent teeth affects approximately 35% of people globally.²⁵ Periodontitis affects 45-50% of the adult population in its milder form and 9-11% in its severe form.^{26,27} While these oral diseases do not directly increase mortality rates, they are associated with more severe NCDs. Caries and periodontal disease have been linked to conditions such as obesity,²⁸ asthma^{4,29} and depression,³⁰⁻³² they may predict the development of more lethal NCDs, including cardiovascular diseases and diabetes.^{5,6,33-36}

Caries is a disease dependent on the presence of biofilm and sugar, affecting the mineralized tissues of the teeth. Periodontal disease is multifactorial, with the accumulation of oral biofilm leading to an inflammatory response in the host (gingivitis) and potentially progressing to the destruction of the supporting tissues of the teeth (periodontitis).³⁷ Caries is closely linked to the frequent and excessive consumption of added sugars.^{7,38} The increased frequency and concentration of highly fermentable carbohydrates, mainly sucrose, in dental biofilm result in acid production and decreased bacterial diversity, leading to the demineralization of tooth hard tissues.³⁹ Gingivitis is associated with changes in the supragingival biofilm, while periodontitis is linked to dysbiosis in the subgingival environment.³⁹ Systemic changes related to an unhealthy diet can cause an imbalance in the immune system, low-grade inflammation, and a breakdown in microorganism/host homeostasis, resulting in dysbiosis⁴⁰ that can damage periodontal tissues, including clinical attachment loss and alveolar bone resorption.⁴¹

Despite their different etiopathogeneses—caries affecting the mineralized teeth tissues^{38,39} and periodontal disease affecting the supporting ones³⁷ — both are associated with the presence of biofilm.³⁹ Emerging evidence also points to the consumption of added sugars as a common risk factor for both diseases.^{17,18,42-45}

Indicators of caries and periodontal disease are interrelated, forming a phenomenon known as the **Chronic Oral Disease Burden**, which includes caries and gingivitis in early childhood^{44,46} and adolescence, as well as clinical probing depth, bleeding on probing, DMFT (Decayed, Missing, and Filled Teeth), and PUFA (severity of caries) Index.^{18,47} Among people over 50, caries indicators are grouped with severe periodontal probing depth and clinical attachment loss, as well as furcation involvement.⁴⁸

Thus, it is important to highlight that the **Chronic Oral Disease Burden** phenomenon should not be understood merely as a clinical diagnostic indicator but as an opportunity to plan integrated preventive measures for both diseases, with preventive and/or interventional actions targeting their common risk factors. This means understanding caries and periodontal disease as interconnected issues, although they are often taught as separate subjects in dental school curricula.

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2 ULTRA-PROCESSED FOODS AND ADDED SUGARS AS RISK FACTORS FOR ORAL AND SYSTEMIC NCDs

Ultra-processed foods are formulations produced using various processing techniques and numerous ingredients, many of which are exclusively for industrial use, such as modified oils and food additives (artificial colorings, preservatives, flavorings, emulsifiers, flavor enhancers, etc.), with little or no whole foods.⁴⁹ These products also contain added sugars, which are present in many everyday foods, having been added to processed, ultra-processed, or culinary preparations to improve their taste.^{50,51} In this context, sugar-sweetened beverages represent the largest source of discretionary calories (energy-dense but nutritionally poor) in the diet, being associated with greater weight gain during pregnancy,¹⁰ which can lead to hypertension⁵² and gestational diabetes,¹⁰ chronic oral diseases (dental caries and periodontal disease),^{42,46} and even preterm birth¹⁰ and the development of asthma symptoms¹⁴ and allergies⁵³ in offspring.

The crucial role of added sugars in the etiology of caries is indisputable. Recent evidence from population-based epidemiological studies also points to the association between added sugars and gingivitis in children and periodontal disease in adolescents, pregnant women, and adults.^{17,18,42,43}

Systematic reviews and cohort studies have shown that higher consumption of sugar-sweetened beverages is associated with excess weight (including in children), obesity, metabolic syndrome, non-alcoholic fatty liver disease, hypertension, cardiovascular diseases, insulin resistance, lower episodic memory, and markers of Alzheimer's disease.^{54–59}

3 BALANCED HUMAN MICROBIOME

The human body is richly colonized by approximately 100 trillion bacteria essential for homeostasis, profoundly influencing an individual's physiology and nutrition.^{60,61} At birth, the intestinal microbiome begins to develop intensely, influenced by various external factors. The first two years of life are considered the most critical period for microbiome development, during which it is less resilient and much more responsive to external and environmental factors than the adult microbiome.⁶²



Factors that negatively affect the composition of the human microbiome during this period include cesarean delivery, artificial feeding, antibiotic use, and the consumption of added sugars in complementary diets before the second year of life.⁶³ Reduction of intestinal microbiome diversity (intestinal dysbiosis) can affect a child's growth, immune response, and neuropsychomotor and bone development.^{63–65} As previously mentioned, chronic oral diseases are also linked to biofilm dysbiosis, which can have its homeostasis disrupted by the consumption of added sugars.³⁹

Breast milk contains oligosaccharides, which are short-chain carbohydrates that are not digestible or absorbed by the intestine. These oligosaccharides play an essential role in the child's microbiota. They function as prebiotics, being metabolized by beneficial bacteria such as bifidobacteria and bacteroides, which contribute to the homeostasis of the microbiome. Additionally, they appear to be capable of modulating the immune response and serving as an intestinal barrier for the baby.

Source: CHENG, YJ, YEUNG, CY, 2021; BODE L, 2012.

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4 BREASTFEEDING AS PROTECTION AGAINST NCDs

The WHO and various national health authorities recommend exclusive breastfeeding for the first six months of life, continuing up to two years or more.⁶⁶ Breastfeeding protects against infant mortality, diarrhea, childhood and respiratory infections, and allergies. It enhances cognitive

ability/intelligence, reduces malocclusion, and decreases the chances of obesity, hypertension, high cholesterol, and diabetes while improving child nutrition. For breastfeeding women, it protects against breast, ovarian, and uterine cancers, type 2 diabetes, hypercholesterolemia, hypertension, coronary heart disease, obesity, osteoporosis, rheumatoid arthritis, and postpartum depression, and reduces the risk of multiple sclerosis relapse after childbirth.^{15,67–69}

Paradoxically, some studies suggest an association between breastfeeding and early childhood caries.⁷⁰ However, the best available evidence from systematic reviews indicates that breastfeeding for up to 24 months does not increase the risk of early childhood caries and suggests that extended breastfeeding may be associated with caries in children, though the evidence is of low quality.⁷¹ Additionally, human milk does not have the potential to produce acid in dental biofilm capable of demineralizing enamel, whereas only sucrose has this potential.⁷² Furthermore, exposure to human milk interspersed with sucrose can make the biofilm more cariogenic, capable of

metabolizing lactose as well,⁷³ showing that sucrose is the true culprit in the etiology of caries.

Finally, there is no evidence suggesting that reducing breastfeeding practices or duration has any protective effect against early childhood caries. It is crucial to note that such recommendations may lead to shorter breastfeeding periods and, consequently, diminish the numerous health benefits for the child, both in the short and long term. Dentists should collaborate with the multidisciplinary healthcare team to protect and promote breastfeeding.

PREGNANCY HEALTHCARE

PREGNANCY HEALTHCARE

It is essential to prioritize comprehensive and compassionate healthcare for women during pregnancy, childbirth, and the postpartum period to ensure the safety and well-being of both mothers and their children. A well-functioning healthcare system should offer family planning services, secure childbirth, and support healthy growth and development. These goals can be achieved through a well-organized system of care that meets the specific needs of expectant mothers and their babies.^{74,75}

We emphasize the importance of the oral health team in providing prenatal dental care, diagnosing chronic oral diseases in pregnant women and babies, and offering guidance on breastfeeding and a healthy diet to prevent oral and systemic non-communicable diseases.

IMPORTANCE OF PRENATAL DENTAL VISITS

All healthcare professionals can work collaboratively to ensure low-risk pregnancies. Dentists play a vital role in this effort by providing dental care, promoting health education, preventing oral health issues, and addressing the specific needs of expectant mothers through personalized care and support. This approach fosters a humanized healthcare experience and strengthens the bond between healthcare providers and pregnant women.⁷⁶



Dentists' responsibilities during prenatal care can significantly contribute to preventing NCDs in both mothers and their babies. Here are some key responsibilities of dentists during this phase:

RESPONSIBILITIES OF THE DENTIST IN LOW-RISK PRENATAL CARE

- 1. Educate Women and Their Families:** Provide guidance on the importance of prenatal care and breastfeeding.
- 2. Conduct Prenatal Dental Consultations:** Offer dental care for women with low-risk pregnancies.
- 3. Promote Healthy Habits:** Advise women and their partners on healthy eating and oral hygiene practices.
- 4. Perform Preventive Dental Procedures:** Ensure the comfort of pregnant women and the continuation of treatment after pregnancy.
- 5. Identify High-Risk Pregnancies:** Recognize and refer high-risk pregnant women to specialized care services.
- 6. Develop Educational and Support Activities:** Create programs to support and educate pregnant women and their families.
- 7. Monitor Breastfeeding and Newborn Care:** Support the breastfeeding process and provide guidance on caring for the future baby.
- 8. Conduct General Health Evaluations:** Assess the overall health of pregnant women, taking into account their stage of pregnancy.

Pregnant women often recognize the importance of prenatal dental care but may not frequently attend these services.⁷⁷ Education on the significance of maintaining oral health during pregnancy is essential for encouraging regular dental visits. Additionally, addressing common practices, such as the use of bottles and pacifiers, which can lead to early weaning, is crucial. Health education during pregnancy can instill healthy habits that benefit both the mother and the child.^{78,79}

NUTRITIONAL GUIDANCE FOR PREGNANT WOMEN

Dentists should guide pregnant women in maintaining a healthy and balanced diet. Emphasizing the adoption of nutritious eating habits can have positive long-term effects on the child's health.

TEN STEPS TO HEALTHY EATING FOR PREGNANT WOMEN

1. Have at least three meals (breakfast, lunch, and dinner) and two healthy snacks each day. Drink at least 2 liters of water (6 to 8 cups) daily.
2. Prefer foods in their most natural form, as they are good sources of fiber, vitamins, and minerals.
3. Try to consume at least three servings of vegetables as part of your meals and three or more servings of fruit for desserts and snacks every day.
4. Eat beans with rice every day or at least five times a week. Consume three servings of dairy products and one serving of meat, poultry, fish, or eggs daily.
5. Remove visible fat from meats and skin from poultry before preparation.
6. Reduce your intake of fats. Consume no more than one daily serving of vegetable oils, olive oil, butter, or margarine.
7. Avoid sodas and industrialized juices, stuffed cookies, and other sweets in your daily diet.
8. Reduce the amount of salt in your food. Avoid consuming processed foods like hamburgers, sausages, hot dogs, ham, snacks, instant soups, and pre-made seasonings.
9. Eat iron-rich foods such as meat, organ meats, beans, soy, dark green leafy vegetables, whole grains, and others. Consume vitamin C-rich foods along with these.
10. Maintain gestational weight gain within healthy limits. Engage in physical activity under professional guidance and avoid alcoholic beverages and smoking.

To support this effort, healthcare providers often follow evidence-based guidelines, such as the **"Ten Steps to Healthy Eating for Pregnant Women"**,⁷⁶ which provide practical advice for achieving healthy weight gain during pregnancy and promoting overall maternal and fetal well-being.

ENVIRONMENTAL STRESSORS DURING PREGNANCY

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4



ENVIRONMENTAL STRESSORS DURING PREGNANCY

The first thousand days of life are a critical window for preventing NCDs. Environmental stressors during this period can negatively impact maternal health, fetal development, pregnancy outcomes, and the long-term health of the child. Healthcare professionals, including dentists, need to identify these risk factors and their consequences and collaborate with communities to develop and implement effective prevention strategies.

ALCOHOL AND TOBACCO USE

During pregnancy, environmental stressors such as tobacco and alcohol can impact the development of the fetus and lead to perinatal or neonatal death. Alcohol consumption during pregnancy increases the risk of fetal malformation, miscarriage, preterm birth, and low birth weight.^{80,81} This set of complications for the baby, caused by exposure to alcohol during pregnancy, is known as **Fetal Alcohol Syndrome**, as we'll see below:



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FETAL ALCOHOL SYNDROME

This condition leads to complications such as facial anomalies, fetal growth restriction, congenital organ deficiencies, and learning-related anomalies, such as the development of attention deficit hyperactivity disorder (ADHD).

Source: MAY et al., 2016.



Smoking during pregnancy is associated with reduced fetal dimensions. Additionally, smoking during pregnancy is linked to stillbirth, neonatal death, and perinatal death due to maternal hemorrhage and resulting fetal asphyxia from placental abruption. These risks increase with the number of cigarettes smoked by the mother; however, their effects can be minimized if mothers quit or reduce smoking during pregnancy.^{11,82} Even passive exposure to cigarette smoke is associated with fetal growth restriction and preterm birth.¹¹

USE OF ANTIBIOTICS DURING PREGNANCY

Antibiotic use during pregnancy can increase the risk of asthma in early childhood and is associated with a higher risk of epilepsy and childhood obesity.⁸³ Tetracycline, for instance, is linked to congenital malformations and altered dental and bone development and should be avoided.⁸⁴ Animal studies suggest that amoxicillin might cause dental enamel defects if used during pregnancy.^{85–87} Nonetheless, untreated infections during pregnancy pose greater risks and should be managed with low-toxicity antibiotics like penicillin derivatives, including amoxicillin and ampicillin.⁸⁸ Dentists should carefully evaluate the necessity of prescribing antibiotics to pregnant patients.



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ADDED SUGARS

Added sugars are prevalent in many everyday foods, such as sodas, cookies, energy drinks, industrialized juices, chocolate milk, cereal bars, yogurts, and sweets. Below are examples of the various names added sugars can be presented on the labels of industrialized products:



PRESENTATION OF SUGARS ON LABELS OF PROCESSED PRODUCTS

Sugar	Maltodextrin	Glucose
Inverted sugar	Oligosaccharides	Glucose-fructose syrup
Turbinado sugar	Sucrose	Corn syrup
Dextrose	Dextrin	
Maltose	Fructose	

It's important to advise pregnant women to avoid consuming added sugars during dental consultations. Eating foods high in added sugars, especially processed beverages, during this time can have harmful effects on both the mother and the baby. Next, we'll explore some of the adverse effects associated with consuming added sugars during pregnancy.

OBESITY

A obesidade é o acúmulo excessivo de gordura corporal, sendo considerada mundialmente um sério problema de saúde e um fator de risco metabólico para as DNT, como as doenças cardiovasculares, doenças respiratórias, diabetes e doenças bucais crônicas.^{10,89–91}

Obesity during pregnancy impacts the offspring's health throughout their life. Maternal obesity is associated with gestational hypertension, gestational diabetes, and an increased likelihood of cesarean delivery. For the baby, maternal obesity is linked to macrosomia and preterm birth.^{92,93}

The consumption of sugar-sweetened beverages and processed foods has been associated with obesity on a global scale. It is important to avoid these during pregnancy and adhere to general dietary guidelines for pregnant women. If obesity is identified during pregnancy, the woman should be referred for medical and nutritional care.

The recommended weight gain during pregnancy should be in proportion to the growth and development of the fetus.⁹⁴ For this purpose, the Institute of Medicine (USA) recommends:⁹⁵

RECOMMENDATIONS FOR TOTAL WEIGHT GAIN DURING A SINGLE PREGNANCY	
BMI BEFORE PREGNANCY	TOTAL WEIGHT GAIN
Underweight < 18.5 kg/m ²	12.5 to 18 kg
Normal weight 18.5 to 24.9 kg/m ²	11.5 to 16 kg
Overweight 25 to 29.9 kg/m ²	7 to 11.5 kg
Obesity ≥ 30 kg/m ²	5 to 9 kg

BMI: Body Mass Index; Source: Institute of Medicine, 2009.

HYPERTENSION

Hypertension during pregnancy is diagnosed when blood pressure (BP) levels are equal to or greater than 140/90 mmHg.⁹⁶ This condition can lead to different forms of **Hypertensive Disorders of Pregnancy**.⁹⁷

HYPERTENSIVE DISORDERS OF PREGNANCY	
Pre-pregnancy or before 20 weeks' gestation	
Chronic hypertension	- Hypertension pre-pregnancy or before 20 weeks' gestation
White coat hypertension	- BP $\geq$ 140/90 mm Hg in clinic, but BP <135/85 mm Hg with home or ambulatory BP monitoring
Masked hypertension	- BP <140/90 mm Hg in clinic, but BP $\geq$ 135/85 mm Hg outside clinic
20 weeks' gestation or more	
Gestational hypertension	- Hypertension de novo $\geq$ 20 weeks' gestation without proteinuria or other features suggestive of pre-eclampsia
Pre-eclampsia	- Gestational hypertension with $\geq$ 1 new onset conditions of organ or uteroplacental dysfunction
Superimposed pre-eclampsia on chronic hypertension	- Chronic hypertension with development of new proteinuria and/or organ or uteroplacental dysfunction(s) with the onset conditions

Source: WU *et al.*, 2023.

The increased consumption of beverages high in added sugars appears to be a direct risk factor for hypertension during pregnancy, suggesting that high intake of these beverages should be discouraged during this period.⁵² Additionally, hypertension during pregnancy is a leading cause of maternal mortality in many countries, contributing to ~31.6% of maternal deaths.⁹⁸ For the fetus, hypertension in the mother is a precursor to preterm birth, fetal distress, and restricted fetal growth, which are major causes of fetal mortality.^{96,97}

DIABETES

Gestational diabetes occurs when a pregnant woman develops glucose intolerance during pregnancy, which can sometimes persist after childbirth.⁹⁹ Obesity and the consumption of sugary foods and beverages during pregnancy have been linked to gestational diabetes.¹⁰⁰

Women with gestational diabetes are at a higher risk of developing gestational hypertension and preeclampsia. They also have an increased likelihood of developing type 2 diabetes, obesity, and cardiovascular diseases in the long term. For the baby, gestational diabetes is associated with being large for gestational age, preterm birth, and the need for a cesarean section. These complications have been linked to delayed initiation of breastfeeding, lower breastfeeding rates, and shorter breastfeeding duration in women with gestational diabetes.^{100,101}



CHRONIC ORAL DISEASES

During pregnancy, metabolic, biochemical, and hormonal changes occur to support the mother and the growing fetus. Morning sickness and nausea are common in the first trimester, which can result in reduced oral hygiene and the buildup of dental plaque. This can lead to an increased risk of dental caries and periodontal disease.

An increased incidence of caries has been observed during pregnancy.^{102,103} In addition to changes in hygiene practices due to morning sickness,

another reason for the increased risk of developing new cavities during pregnancy could be the higher frequency and amount of consumption of sugary foods.¹⁰⁴ Pregnant women may experience changes in their taste preferences and have a reduced ability to perceive the taste of sucrose.¹⁰⁵

There has also been an observed increase in the prevalence and severity of gingival inflammation during pregnancy,¹⁰² attributed to hormonal changes that result in shifts in the subgingival microbiota and can exacerbate the inflammatory response in periodontal tissues.^{106,107} Pyogenic granuloma, gingivitis, and periodontitis are the most common periodontal conditions in pregnant women.¹⁰² Additionally, a higher frequency of soda consumption during pregnancy has been associated with periodontitis in pregnant women.⁴²

Periodontal disease during pregnancy is associated with health issues for the pregnant woman, such as preeclampsia, and adverse pregnancy outcomes: spontaneous fetal death/miscarriage (< 20 weeks) and stillbirth (20-36 weeks), preterm birth, low birth weight, very low birth weight (<1500 g), and preeclampsia (maternal hypertension + proteinuria after the 20th week of gestation).

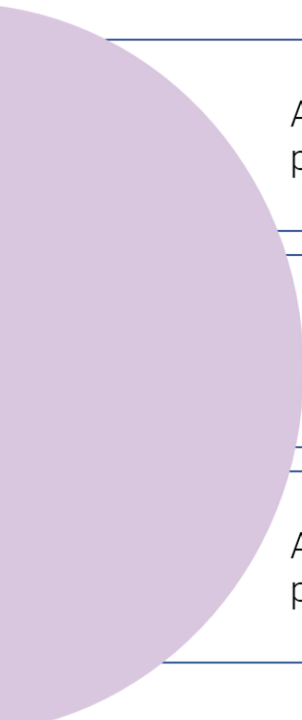
Source: KORNMAN, 2013; FIGUERO et al., 2020.

One possible explanation for the association between periodontal disease in pregnant women and adverse outcomes is that periodontal pathogens and their metabolites may cross the placental barrier, resulting in an immune-inflammatory response in the fetal-placental complex.^{108,109}

The American Academy of Periodontology and the European Federation of Periodontology have developed a consensus document on this topic, concluding that the association between periodontitis and adverse pregnancy outcomes is modest, varying depending on the classification of periodontal disease used and the populations studied.¹⁰⁸ This document concludes that periodontal therapy in pregnant women is safe, resulting in clinical improvement of periodontal parameters.¹⁰⁸ However, periodontal therapy does not appear to reduce preterm birth rates or low birth weight, challenging the idea that periodontal pathogens directly cause adverse

fetal outcomes,¹⁰⁸ as removing a "probable cause" does not seem to affect the occurrence of the outcome.

Caries and periodontal disease can serve as alerts for the risk of adverse outcomes in the mother and baby,^{110,111} highlighting the importance of prenatal dental care and the need for dental care for pregnant women with chronic oral diseases.



Apical periodontitis (endodontic infection) in pregnant women is positively associated with adverse pregnancy outcomes.

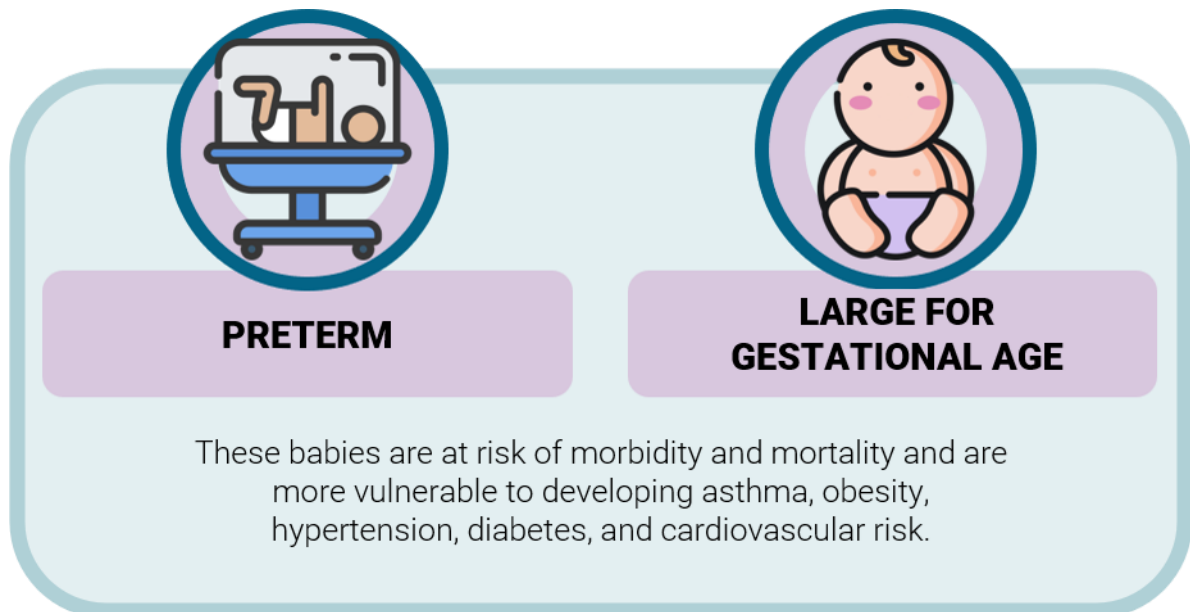
Apical periodontitis (endodontic infection) in pregnant women is positively associated with adverse pregnancy outcomes.

Apical periodontitis (endodontic infection) in pregnant women is positively associated with adverse pregnancy outcomes.

Source: JAKOVLJEVIC *et al.*, 2021; CHO *et al.*, 2020.

Excessive consumption of sugary beverages has been associated with excessive weight gain in pregnant women,¹¹² and with gestational diabetes, pre-eclampsia, gestational hypertension,^{52,112} preterm birth,^{113,114} large-for-gestational-age babies,¹¹⁵ and increased risk of childhood asthma.¹⁴ Preterm birth and large-for-gestational-age babies have been associated with higher mortality and development of hypertension, diabetes, asthma, obesity, and cardiovascular diseases throughout life.^{116–120}

Furthermore, maternal obesity at the beginning of pregnancy and sugar consumption by the pregnant woman can explain childhood obesity, high sugar exposure, and early childhood caries.¹²¹ Obesity is a significant metabolic risk factor for all NCDs² and is associated with both caries and periodontal disease, even in children.^{122–124}



Source: WHINCUP *et al.*, 2008; YU *et al.*, 2011; SIPOLA-LEPPÄNEN *et al.*, 2014; SONNENSCHN-EIN-VAN der VOORT *et al.*, 2014; KUCIENE; DULSKIENE; MEDZIONIENE, 2018. Image created with Flaticon.com

From a DOHaD perspective, these findings underscore the importance of comprehensive chronic disease prevention in pregnant women by addressing common risk factors. Promoting healthy eating and advising against ultra-processed foods and added sugars can prevent obesity, hypertension, diabetes, and chronic oral diseases, thereby reducing adverse pregnancy outcomes. These measures will also benefit offspring by decreasing the risk of caries, gingivitis, and high-mortality NCDs in the future.

HEALTHCARE DURING THE FIRST TWO YEARS OF LIFE

5



HEALTHCARE DURING THE FIRST TWO YEARS OF LIFE

As previously discussed, multidisciplinary healthcare teams play a crucial role in supporting maternal and child health. During the postpartum period and up to the child's second year, dental professionals should be knowledgeable about the necessary guidelines for promoting, protecting, and supporting breastfeeding and appropriate complementary feeding. Additionally, they should provide guidance and encourage proper oral hygiene practices.

BREASTFEEDING

Breastfeeding is one of the most critical moments for establishing and strengthening the bond between mother and baby, impacting the child's nutrition, immune status, bodily functions, emotional and cognitive development, and long-term health. A cohort study that followed children for six months and then again at eight years old showed that breastfed children had better performance in general intellectual evaluations.⁶⁹ Additionally, breastfeeding benefits the physical and psychological health of the mother.¹²⁵ For women who breastfeed, it provides protection against breast cancer, increases birth spacing, and offers protection against ovarian cancer and type 2 diabetes.⁶⁷

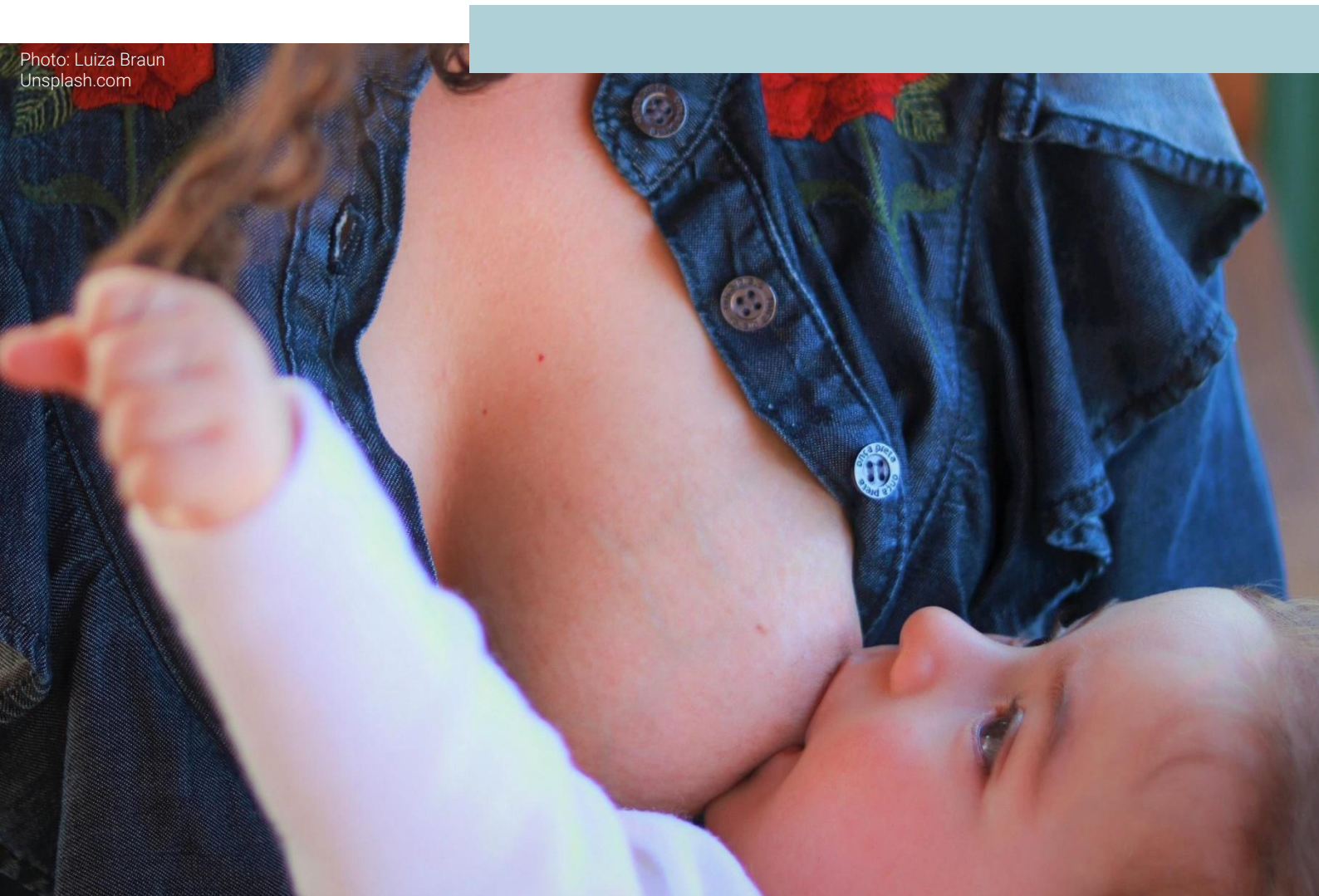


Photo: Luiza Braun
Unsplash.com



Photo: Junior Reis
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Breast milk is produced according to the baby's needs and changes composition according to the stage of lactation. Initially, colostrum is produced, which is viscous and rich in proteins, minerals, and vitamins A and E, containing immunoglobulins, antimicrobial agents, immunomodulatory substances, leukocytes, and anti-inflammatory compounds, including growth factors. Then, transitional milk is produced, leading to what is known as mature milk. During this transition, milk composition is not constant. After the fifteenth day postpartum, breast milk is considered mature and rich in proteins, some of which are involved in the protective system, such as lactoferrin, lysozyme, and immunoglobulins, especially secretory IgA.¹²⁶



The WHO recommends breastfeeding for two years or more, breastfeeding exclusively for the first six months of life, i.e., without giving the child any other type of food: not liquids, not even water, nor any other food, such as fruit, vegetables, porridge or baby food. The introduction of any foods before six months offers no nutritional advantages. It is associated with negative health outcomes for the child, such as episodes of diarrhea, increased frequency of hospitalizations due to respiratory illness, lower absorption of nutrients like iron and zinc, and premature cessation of breastfeeding.⁶⁶

DURATION OF BREASTFEEDING	
0 to 6 months Exclusive breastfeeding	6 months to 2 years Breastfeeding + healthy diet

Source: WHO, 2015.

During prenatal consultations, healthcare professionals should work to protect and promote breastfeeding. It's important to be aware of practices that can undermine breastfeeding and lead to its early termination. See below:

PRACTICES THAT COULD HARM BREASTFEEDING
• Providing other milks or infant formulas to "supplement" breast milk. • Starting solid or mashed foods before six months of age. • Offering a bottle. • Offering a pacifier/soother. • Smoking during breastfeeding. • Using medications without prescription. • Consuming alcoholic beverages.

Source: BRAZIL, 2019.

INTRODUCTION OF COMPLEMENTARY FOODS

After the first six months, it is recommended to introduce healthy complementary foods alongside breastfeeding, continuing until two years of age or beyond. Given that a nutritionist may not always be available to everyone, it is important for the healthcare team, including the dentist, to provide guidance on healthy eating during this phase. Complementary foods for the child should be the same as those consumed by the mother and other family members, consisting of natural or minimally processed foods.^{127,128}

Natural foods are those obtained directly from plants or animals and remain unaltered after leaving nature. Minimally processed foods undergo processes such as cleaning, removal of undesirable parts, grinding, drying, and freezing without the addition of any substances to the original food.¹²⁸



Whole or minimally processed foods

These are obtained directly from plants or animals and undergo minimal alteration after leaving nature. They undergo processes such as cleaning, removal of undesirable parts, grinding, drying, freezing, without the addition of any substances compared to the original food.



Processed culinary ingredients

These are products manufactured by the industry used in meal preparation, such as table salt, sugar, molasses, honey, vinegar, butter, and oils. They should be used in moderation.



Processed foods

These are made from whole foods with the addition of salt or sugar. Examples include canned vegetables, salted meats, canned fish, cheeses, breads, among others. They should be avoided.



Ultra-processed foods

These are formulations produced industrially using various processing techniques and numerous ingredients, many of which are exclusively used in the industry. They often contain added sugars, modified oils, and food additives (artificial colors, preservatives, sweeteners, flavor enhancers, emulsifiers).

Source: BRAZIL, 2014.

To compose complementary feeding for children and their families, the following food groups are recommended:¹²⁸

- **Beans Group**

Includes: white beans, carioca beans, black-eyed peas, fava beans, black beans, speckled beans, red beans, peas, chickpeas, and soybeans.

- **Cereals Group**

Includes: rice, brown rice, oats, rye, corn, wheat, bulgur, cornmeal, grits, and cornstarch.

- **Roots and Tubers Group**

Includes: parsnip, parsley potato, or yellow carrot), sweet potato, potato, yam, cassava, cassava flour, potato starch, and tapioca.

- **Vegetable Group**

Includes: pumpkin, zucchini, eggplant, beet, carrot, chayote, maxixe, cucumber, okra, tomato, green beans, Swiss chard, watercress, lettuce, broccoli, onion, chicory, kale, cauliflower, spinach, cabbage, etc.

- **Fruits Group**

Includes: avocado, pineapple, plum, blackberry, banana, cashew, persimmon, starfruit, cherry, guava, soursop, jackfruit, orange, tangerine, lime, apple, mango, papaya, watermelon, melon, strawberry, pear, and grape.

- **Meats Group**

Includes: beef, pork, goat, lamb, buffalo, poultry, fish, seafood, and eggs, including animal organs and offal.

- **Dairy Group**

Includes breast milk, milk from other animals, plain yogurt without sugar, and curdled milk.

- **Nuts and Seeds Group**

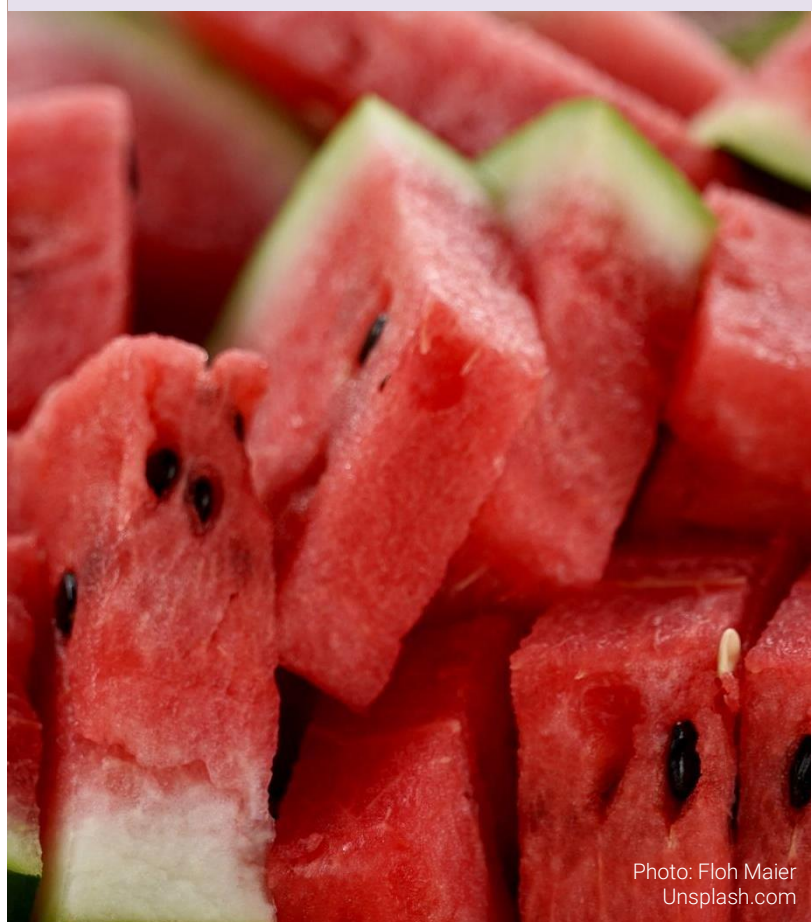
Includes almonds, peanuts, cashew nuts, Brazil nuts, and pecans.

- **Condiments and Spices Group**

Includes: rosemary, turmeric, cinnamon, chives, cilantro, coriander, cumin, cloves, ginger, bay leaf, basil, oregano, parsley, sage, and thyme.

- **Water**

From six months of age, offer small amounts of potable water in a cup (without a spout) between meals.



Considering these recommendations, the Brazilian Ministry of Health proposed the "Food Guide for Brazilian Children Under 2 Years" in 2019, highlighting "The Twelve Steps to a Healthy Diet."¹²⁷

THE TWELVE STEPS TO A HEALTHY DIET

1. Breastfeed for at least two years, offering only breast milk until six months.
2. From six months, offer natural or minimally processed foods in addition to breast milk.
3. Give the child drinking water instead of juices, sodas, and other sugary drinks.
4. Introduce thick-consistency foods when starting solid foods.
5. Avoid giving sugar or any products containing sugar to the child until two years of age.
6. Do not offer ultra-processed foods to the child.
7. Cook the same food for the child and the family.
8. Ensure that mealtime is a positive experience for the child.
9. Pay attention to the child's hunger and satiety cues.
10. Maintain hygiene at all stages of food preparation for the child and the family.
11. Provide healthy and adequate food for the child even when outside the home.
12. Protect the child from food advertising.

Source: BRAZIL, 2019.



Photo: Tim Bish
Unsplash.com

INFANT ORAL HYGIENE

Chronic oral diseases such as caries and gingivitis may only occur with the presence of teeth.^{37,129} Therefore, associations of Pediatrics and Pediatric Dentistry around the world recommend the oral hygiene of the infant just after the eruption of the first teeth.^{130–132} Additionally, the microbiota of the gastrointestinal tract (including the mouth) adapt through exclusive breastfeeding,⁶³ and removing the bacterial flora that is consolidating in the mouth has no benefit for the baby.¹³³

After the appearance of the first tooth, caregivers should brush the baby's teeth twice a day using a soft-bristled toothbrush and fluoride toothpaste containing 1000-1500 ppm of fluoride to protect against dental caries. Initially, the amount of toothpaste used should be equivalent to a "grain of rice," as the number of erupted baby teeth increases, the quantity can gradually increase to the size of a "pea." These amounts are safe and help avoid fluorosis.^{134,135}



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ENVIRONMENTAL STRESSORS DURING THE FIRST TWO YEARS

ENVIRONMENTAL STRESSORS DURING THE FIRST TWO YEARS

In the first two years of a child's life, environmental factors such as cesarean delivery, artificial feeding, and early exposure to added sugars can lead to unfavorable systemic and oral outcomes during childhood and persist throughout life.

CESAREAN DELIVERY

The WHO recommends that cesarean sections should be performed only when the health or life of the mother and/or newborn is at risk. However, the frequency of this type of delivery has increased worldwide^{136,137} and is far above the levels recommended by the WHO, which are 10 to 15%.^{138,139}



Image created with FlatIcon.com

Being born by cesarean, whether elective or emergency, has been associated with the development of immunological and metabolic alterations during childhood, such as asthma, food allergies, type I diabetes, and obesity.¹⁴⁰

Therefore, prenatal consultations must encourage vaginal delivery and mention the long-term risks of cesarean section for the offspring. Here are some factors related to the decision to have a cesarean section:

FACTORS ASSOCIATED WITH THE DECISION FOR CESAREAN SECTION

- Maternal insecurity;
- Fear of childbirth;
- Fear of pain during childbirth;
- Healthcare team's predisposition toward cesarean section.

Source: MAGNE et al., 2017.



BOTTLES AND PACIFIERS

The way a baby sucks on the mother's breast is different from how they suck on a bottle, regardless of the type of nipple used. Sucking from a bottle can confuse the baby, causing "nipple confusion." The flow from a bottle is more abundant than the flow from the breast, which can frustrate the baby as they have to exert more

effort during breastfeeding.¹⁴¹

Additionally, the content of bottles is usually high in sugars, which can impair the child's ability to regulate their appetite and predispose them to obesity and NCDs (later in this chapter, we'll look at the effects of added sugars on baby's health). The movement and position of the tongue caused by bottle nipples can also affect the development of swallowing, chewing, and speaking. In contrast, complementary feeding with cups enhances breastfeeding duration and extent compared to bottle use, even in preterm infants.¹⁴²

Using pacifiers is associated with shorter breastfeeding times and early weaning.¹⁴³ Breastfeeding is an important protective factor against malocclusions such as anterior crossbite, posterior crossbite, skeletal Class II, distocclusion, and crowding in deciduous and mixed dentition.¹⁴⁴

Pacifiers are also linked to an increased risk of oral infections, especially thrush.¹⁴⁵ Removing the pacifier after 12 months improved the inter-canine distance (both upper and lower), as well as aspects related to the pressure of the teeth during chewing, and indicators of speech and breathing development.¹⁴⁶

ADDED SUGARS

Early exposure to added sugars, especially through beverages rich in these sugars, has been linked to adverse outcomes in childhood, such as obesity, asthma, allergies, dental caries, and gingivitis, as well as an increased risk of future NCDs like cardiovascular diseases (CVDs).^{14,18,147,148}



Evidence of the harmful effects of sugar consumption has led the American Heart Association to issue guidelines aiming to reduce sugar intake to 25 grams per day for children and adolescents, recommending that **children under two years of age should not consume added sugars**.¹⁴⁹

The WHO has published guidelines aimed at reducing sugar intake to prevent obesity and dental caries, suggesting that free sugars should not exceed 10% of total daily caloric intake, with an additional recommendation to further reduce sugar consumption to less than 5% of total daily calories.⁷



The intake of sugars **should not exceed 25 g/day** for adolescents and children older than two years, equivalent to six teaspoons of sugar



CHILDREN UNDER TWO YEARS OF AGE SHOULD NOT CONSUME ADDED SUGARS

Source: VOS *et al.*, 2017. Image created with Flaticon.com

Next, we will explore some adverse outcomes associated with early exposure to added sugars, i.e., the consumption of these sugar-rich foods before a child is two years old.

CHILD DEVELOPMENT

Recent studies suggest that early exposure to sugar-sweetened beverages may be linked to an increased risk of developing attention deficit hyperactivity disorder (ADHD), indicating that the amount of consumption is an important factor in this association. Conversely, a healthy diet rich in fruits and vegetables appears to protect against these developmental issues.^{150–152}



ASTHMA

Asthma is a condition affecting the lower respiratory airways, impacting individuals of all ages, though it typically begins in childhood, with symptoms such as wheezing, coughing, or chest tightness.¹⁵³

The WHO describes asthma as an NCD associated with inflammation, causing airway narrowing, and it poses a risk for other future NCDs, including diabetes and cardiovascular diseases.¹⁵⁴

Studies indicate that consumption of beverages high in added sugars is associated with an increased risk of asthma in childhood.^{14,155} On the other hand, exclusive breastfeeding has been shown to protect against respiratory infections in childhood,¹¹ and extended breastfeeding duration is also associated with protection against childhood asthma.^{14,156}



OVERWEIGHT

Maternal sugar consumption and pre-gestational obesity may explain childhood obesity, as well as high sugar exposure and early childhood caries in their offspring.¹²¹ The consumption of added sugars is associated with childhood overweight and obesity, and obese children are more likely to develop NCDs throughout their lives.¹⁵⁶

CHRONIC ORAL DISEASES

It is estimated that approximately 600 million babies worldwide still suffer from early childhood dental caries, leading to pain and difficulty in chewing, which affects the quality of life for children and their families and is challenging to treat.^{66,157}



Source: Authors

Sugars play an unquestionable role in the etiology of dental caries.^{7,38} Emerging epidemiological evidence also points to a consistent association between sugar consumption and an increased burden of chronic oral diseases in early childhood.^{17,42–44} Children who consume sweetened beverages, such as industrialized juices, chocolate milk, and sodas, exhibit increased gingival inflammation, higher levels of pro-inflammatory cytokines, and more carious lesions.^{122,123,158}



THE FIRST THOUSAND DAYS IN THE AGENDA FOR TACKLING NCDs

THE FIRST THOUSAND DAYS IN THE AGENDA FOR TACKLING NCDs

Sustainable Development Goals (SDGs) of the United Nations aim to address inequalities, protect the environment, promote economic and social development, and restore peace, health, and prosperity among peoples. The SDGs include 17 objectives to be achieved by 2030.¹⁵⁹



Source: United Nations, 2015.

As part of the SDG agenda (specifically SDG 3 on Health and Well-being), the WHO and several countries have individually presented strategic action plans to combat non-communicable diseases.¹⁶⁰ This plan outlines goals and proposed actions to tackle NCDs. A central theme in the development of this document is "Healthy Development across the Life Cycle," which emphasizes the importance of child health, particularly during the first 1000 days of life, to promote health and prevent future diseases.

Key targets established in the document for addressing NCD risk factors by 2030 include:

1. Reducing Childhood Obesity

Achieve a 2% reduction in obesity rates among children and adolescents.

2. Increasing Fruit and Vegetable Consumption

Achieve a 30% increase in the consumption of fruits and vegetables.

3. Reducing Ultra-processed Food Consumption

Decrease the consumption of ultra-processed foods.

4. Reducing Sugar-sweetened Beverages Consumption

Reduce regular consumption of sugar-sweetened beverages by 30%.

To support the development of actions aimed at reducing the consumption of sugary beverages and ultra-processed foods, three levels of strategic actions have been grouped:

STRATEGIES FOR REDUCING CONSUMPTION OF ULTRA-PROCESSED FOODS AND FOODS RICH IN ADDED SUGARS	
INDIVIDUAL	• Counseling on individual diet based on the Twelve Steps for Healthy Diet. • Health education, promoting autonomy by sharing information and knowledge about the effects of unhealthy diets. • Involvement of the family core in healthy eating practices.
COMMUNITY	• Guidance campaigns in schools and daycare centers. • Proposal for the introduction of healthier foods in school cafeterias. • Health education in community associations. • Training of Community Health Workers for the dissemination of information on the risks of unhealthy diets.
GOVERNMENTAL	• Front-of-package labeling of foods high in added sugars and saturated fats with information on their health risks. • Prohibition of advertising of ultraprocessed foods targeted at children. • Additional taxation of ultraprocessed foods. • Prohibition of the sale of ultraprocessed foods in schools and their surroundings. • Tax relief for fresh or minimally processed foods.

Source: PEREIRA *et al.*, 2021.



FINAL CONSIDERATIONS

FINAL CONSIDERATIONS

In this digital book, we have aligned our work with the strategic actions of the Sustainable Development Goals (SDGs), specifically focusing on health promotion. We propose this instructional resource to support the action "Train and qualify health professionals and civil society for the design and implementation of smart, healthy, and sustainable cities/territories." Additionally, on the axis of comprehensive health care, we present evidence supporting the action "Expand access to prenatal dental care to reduce the occurrence of caries and periodontal disease."

Based on the DOHaD theory, we present the first 1000 days of life as a "golden interval" for the integrated prevention of NCDs, including both systemic and oral diseases that contribute to higher mortality rates in the future. We highlight strategies for the primordial prevention of NCDs — keeping individuals free from risk factors during this critical life stage. This includes the importance of exclusive breastfeeding for the first six months. Evidence supports breastfeeding continuation until two years of age or beyond, complemented by an adequate and healthy diet based on natural or minimally processed foods. We propose an integrated approach to preventing caries and periodontal disease, focusing on common risk factors. Early intervention, starting within the first 1000 days of life, is essential for effectively reducing the burden of chronic oral diseases. Oral NCDs often precede and predict more severe NCDs that appear later in life, highlighting the importance of early prevention.

Within the multidisciplinary healthcare framework, dentists play a crucial role in the comprehensive prevention of women's health during pregnancy and the baby's health during the first 1000 days. Dentists are tasked with identifying risk exposures and early signs of NCDs and educating families about common risk factors. They should also support and propose policies for the labeling, taxation, and regulation of ultra-processed foods and sugary products while endorsing policies that encourage the consumption of healthier foods. These actions can have a broad impact on both the oral and general health of pregnant women and children, significantly contributing to reducing the future burden of NCDs in the offspring.

Thank you for reading, and see you next time!

REFERENCES

- 1 World Health Organization. Noncommunicable Diseases Progress Monitor 2022. Geneva, 2022 <https://www.who.int/publications/i/item/9789240047761> (accessed June 27, 2022).
- 2 World Health Organization. Noncommunicable diseases. World Health Organization. 2021. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases> (accessed July 12, 2024).
- 3 World Health Organization. The impact of the COVID-19 pandemic on noncommunicable disease resources and services: results of a rapid assessment. Geneva, 2020 <https://www.who.int/publications/i/item/9789240010291> (accessed June 29, 2022).
- 4 Alavaikko S, Jaakkola MS, Tjaderhane L, Jaakkola JJK. Asthma and Caries: A Systematic Review and Meta-Analysis. *Am J Epidemiol* 2011; 174: 631–41.
- 5 van Dyke TE, Kholy K el, Ishai A, et al. Inflammation of the periodontium associates with risk of future cardiovascular events. *J Periodontol* 2021; 92: 348–58.
- 6 Majbauddin A, Tanimura C, Aoto H, et al. Association between dental caries indicators and serum glycated hemoglobin-levels among patients with type 2 diabetes mellitus. *J Oral Sci* 2019; 61: 335–42.
- 7 World Health Organization. Guideline: sugars intake for adults and children. Geneva, 2015.
- 8 Subcomisión DOHaD. Concepto de Developmental Origins of Health and Disease: El ambiente en los primeros mil días de vida y su asociación con las enfermedades no transmisibles. *Arch Argent Pediatr* 2020; 118: 118–29.
- 9 Suzuki K. The developing world of DOHaD. *J Dev Orig Health Dis* 2018; 9: 266–9.
- 10 Pietrobelli A, Agosti M. Nutrition in the First 1000 Days: Ten Practices to Minimize Obesity Emerging from Published Science. *Int J Environ Res Public Health* 2017; 14: 1491.
- 11 Abraham M, Alramadhan S, Iniguez C, et al. A systematic review of maternal smoking during pregnancy and fetal measurements with meta-analysis. *PLoS One* 2017; 12: e0170946.
- 12 May PA, Hasken JM, Blankenship J, et al. Breastfeeding and maternal alcohol use: Prevalence and effects on child outcomes and fetal alcohol spectrum disorders. *Reproductive Toxicology* 2016; 63: 13–21.
- 13 Gustavson K, Ystrom E, Stoltenberg C, et al. Smoking in Pregnancy and Child ADHD. *Pediatrics* 2017; 139: e20162509.
- 14 Nascimento JXPT, Ribeiro CCC, Batista RFL, et al. The First 1000 Days of Life Factors Associated with “Childhood Asthma Symptoms”: Brisa Cohort, Brazil. *Sci Rep* 2017; 7: 16028.

- 15 Victora CG, Adair L, Fall C, et al. Maternal and child undernutrition: consequences for adult health and human capital. *The Lancet* 2008; 371: 340–57.
- 16 Bhutta ZA, Ahmed T, Black RE, et al. What works? Interventions for maternal and child undernutrition and survival. *The Lancet* 2008; 371: 417–40.
- 17 Lula EC, Ribeiro CC, Hugo FN, Alves CM, Silva AA. Added sugars and periodontal disease in young adults: an analysis of NHANES III data. *Am J Clin Nutr* 2014; 100: 1182–7.
- 18 Carmo CDS, Ribeiro MRC, Teixeira JXP, et al. Added Sugar Consumption and Chronic Oral Disease Burden among Adolescents in Brazil. *J Dent Res* 2018; 97: 508–14.
- 19 Bianco-Miotto T, Craig JM, Gasser YP, van Dijk SJ, Ozanne SE. Epigenetics and DOHaD: from basics to birth and beyond. *J Dev Orig Health Dis* 2017; 8: 513–9.
- 20 Barker D. Infant Mortality, Childhood Nutrition, and Ischaemic Heart Disease in England and Wales. *The Lancet* 1986; 327: 1077–81.
- 21 Gluckman PD, Hanson MA, Buklijas T. A conceptual framework for the developmental origins of health and disease. *J Dev Orig Health Dis* 2010; 1: 6–18.
- 22 Barker DJP. Developmental origins of chronic disease. *Public Health* 2012; 126: 185–9.
- 23 Barker DJP. The Developmental Origins of Adult Disease. *J Am Coll Nutr* 2004; 23: 588S–595S.
- 24 Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2019. Periodontal diseases — Level 4 cause. 2019
https://www.healthdata.org/results/gbd_summaries/2019/periodontal-diseases-level-4-cause (accessed Jan 3, 2022).
- 25 Marcenes W, Kassebaum NJ, Bernabé E, et al. Global burden of oral conditions in 1990–2010: a systematic analysis. *J Dent Res* 2013; 92: 592–7.
- 26 Eke PI, Page RC, Wei L, Thornton-Evans G, Genco RJ. Update of the Case Definitions for Population-Based Surveillance of Periodontitis. *J Periodontol* 2012; 83: 1449–54.
- 27 Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJL, Marcenes W. Global burden of severe periodontitis in 1990–2010: a systematic review and meta-regression. *J Dent Res* 2014; 93: 1045–53.
- 28 Salamonowicz M, Zalewska A, Maciejczyk M. Oral consequences of obesity and metabolic syndrome in children and adolescents. *Dent Med Probl* 2019; 56: 97–104.
- 29 Ferreira MKM, Ferreira R de O, Castro MML, et al. Is there an association between asthma and periodontal disease among adults? Systematic review and meta-analysis. *Life Sci*. 2019; 223: 74–87.
- 30 Hwang SH, Park SG. The relationship between depression and periodontal diseases. *Community Dent Health* 2018; 35: 23–9.

- 31 Hugo FN, Hilgert JB, de Sousa M d. LR, Cury JA. Depressive Symptoms and Untreated Dental Caries in Older Independently Living South Brazilians. *Caries Res* 2012; 46: 376–84.
- 32 Cademartori MG, Gastal MT, Nascimento GG, Demarco FF, Corrêa MB. Is depression associated with oral health outcomes in adults and elders? A systematic review and meta-analysis. *Clin Oral Investig* 2018; 22: 2685–702.
- 33 Genco RJ, Borgnakke WS. Diabetes as a potential risk for periodontitis: association studies. *Periodontol 2000* 2020; 83: 40–5.
- 34 Dietrich T, Webb I, Stenhouse L, et al. Evidence summary: the relationship between oral and cardiovascular disease. *Br Dent J* 2017; 222: 381–5.
- 35 Liccardo D, Cannavo A, Spagnuolo G, et al. Periodontal Disease: A Risk Factor for Diabetes and Cardiovascular Disease. *Int J Mol Sci* 2019; 20: 1414.
- 36 Glodny B, Nasser P, Crismani A, et al. The occurrence of dental caries is associated with atherosclerosis. *Clinics* 2013; 68: 946–53.
- 37 European Federation of Periodontology. What is periodontitis? European Federation of Periodontology. 2021. <https://www.efp.org/what-is-periodontitis/> (accessed Jan 13, 2022).
- 38 Sheiham A, James WPT. Diet and Dental Caries. *J Dent Res* 2015; 94: 1341–7.
- 39 Nyvad B, Takahashi N. Integrated hypothesis of dental caries and periodontal diseases. *J Oral Microbiol* 2020; 12: 1710953.
- 40 Reis RA, Stolf CS, de Carvalho Sampaio HA, et al. Impact of dietary inflammatory index on gingival health. *J Periodontol* 2024; 95: 550–62.
- 41 Chapple ILC, Bouchard P, Cagetti MG, et al. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. *J Clin Periodontol* 2017; 44: S39–51.
- 42 Menezes CC, Ribeiro CCC, Alves CMC, et al. Soft drink consumption and periodontal status in pregnant women. *J Periodontol* 2019; 90: 159–66.
- 43 Moreira ARO, Batista RFL, Ladeira LLC, et al. Higher sugar intake is associated with periodontal disease in adolescents. *Clin Oral Investig* 2021; 25: 983–91.
- 44 Araújo SMP, da Silva GQTL, Costa EL, Nunes AMM, Ribeiro CCC. Pathways in the association between added sugar consumption, obesity in mother-child dyads, and chronic oral disease burden in early childhood. *Eur J Oral Sci* 2022; 130. DOI:10.1111/eos.12847.
- 45 Alves-Costa S, Nascimento GG, Peres MA, et al. Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study. *J Clin Periodontol* 2024; 51: 712–21.

- 46 Araújo SMP, Nascimento GG, Ladeira LLC, et al. Chronic oral disease burden at the first 1000 days: Intergenerational risk factors, BRISA cohort. *Oral Dis* 2024; published online June 9. DOI:10.1111/odi.15010.
- 47 Ladeira LLC, Nascimento GG, Leite FRM, et al. Obesity, Insulin Resistance, Caries, and Periodontitis: Syndemic Framework. *Nutrients* 2023; 15. DOI:10.3390/NU15163512.
- 48 Costa SA, Ribeiro CCC, Leite FRM, Peres MA, Souza S de FC, Nascimento GG. Chronic oral diseases burden: The confluence of caries and periodontitis throughout life. *J Clin Periodontol* 2023; 50: 452–62.
- 49 Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: What they are and how to identify them. *Public Health Nutr* 2019; 22: 936–41.
- 50 U.S. Department of Agriculture, U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 2020; published online Dec. [dietaryguidelines.gov](https://www.dietaryguidelines.gov) (accessed Nov 15, 2023).
- 51 DiNicolantonio JJ, O’Keefe JH, Wilson WL. Sugar addiction: is it real? A narrative review. *Br J Sports Med* 2018; 52: 910–3.
- 52 Barbosa JMA, Silva AAM da, Kac G, et al. Is soft drink consumption associated with gestational hypertension? Results from the BRISA cohort. *Brazilian Journal of Medical and Biological Research* 2021; 54: 1–9.
- 53 Muniz AKOA, Vianna EO, Padilha LL, et al. Sugar-Sweetened Beverages and Allergy Traits at Second Year of Life: BRISA Cohort Study. *Nutrients* 2023; 15: 3218.
- 54 Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr* 2013; 98: 1084–102.
- 55 Kim Y, Je Y. Prospective association of sugar-sweetened and artificially sweetened beverage intake with risk of hypertension. *Arch Cardiovasc Dis* 2016; 109: 242–53.
- 56 Dekker MJ, Su Q, Baker C, Rutledge AC, Adeli K. Fructose: a highly lipogenic nutrient implicated in insulin resistance, hepatic steatosis, and the metabolic syndrome. *American Journal of Physiology-Endocrinology and Metabolism* 2010; 299: E685–94.
- 57 Pase MP, Himali JJ, Beiser AS, et al. Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia. *Stroke* 2017; 48: 1139–46.
- 58 Huang C, Huang J, Tian Y, Yang X, Gu D. Sugar sweetened beverages consumption and risk of coronary heart disease: A meta-analysis of prospective studies. *Atherosclerosis* 2014; 234: 11–6.
- 59 Bray GA, Popkin BM. Calorie-sweetened beverages and fructose: what have we learned 10 years later. *Pediatr Obes* 2013; 8: 242–8.
- 60 Ley RE, Peterson DA, Gordon JL. Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell*. 2006; 124: 837–48.
- 61 Qin J, Li R, Raes J, et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 2010; 464: 59–65.

- 62 Laursen MF, Bahl MI, Licht TR. Settlers of our inner surface – factors shaping the gut microbiota from birth to toddlerhood. *FEMS Microbiol Rev* 2021; 45. DOI:10.1093/femsre/fuab001.
- 63 Laursen MF. Gut Microbiota Development: Influence of Diet from Infancy to Toddlerhood. *Ann Nutr Metab* 2021; 77: 1–14.
- 64 Cheng Y-J, Yeung C-Y. Recent advance in infant nutrition: Human milk oligosaccharides. *Pediatr Neonatol* 2021; 62: 347–53.
- 65 Bode L. Human milk oligosaccharides: Every baby needs a sugar mama. *Glycobiology* 2012; 22: 1147–62.
- 66 World Health Organization. Ending childhood dental caries: WHO implementation manual. Geneva, 2019 <https://apps.who.int/iris/handle/10665/330643> (accessed Nov 29, 2021).
- 67 Victora CG, Bahl R, Barros AJD, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet* 2016; 387: 475–90.
- 68 Thomaz EBAF, Alves CMC, Gomes e Silva LF, et al. Breastfeeding Versus Bottle Feeding on Malocclusion in Children: A Meta-Analysis Study. *Journal of Human Lactation* 2018; 34: 089033441875568.
- 69 Fonseca ALM, Albernaz EP, Kaufmann CC, Neves IH, de Figueiredo VLM. Impact of breastfeeding on the intelligence quotient of eight-year-old children. *J Pediatr (Rio J)* 2013; 89: 346–53.
- 70 Feldens CA, Rodrigues PH, de Anastácio G, Vítolo MR, Chaffee BW. Feeding frequency in infancy and dental caries in childhood: a prospective cohort study. *Int Dent J* 2018; 68: 113–21.
- 71 Moynihan P, Tanner LM, Holmes RD, et al. Systematic Review of Evidence Pertaining to Factors That Modify Risk of Early Childhood Caries. *JDR Clin Trans Res* 2019; 4: 202–16.
- 72 Neves PAM, Ribeiro CCC, Tenuta LMA, et al. Breastfeeding, Dental Biofilm Acidogenicity, and Early Childhood Caries. *Caries Res* 2016; 50: 319–24.
- 73 Campos Vieira J, Cury JA, Ricomini Filho AP. Combination Effect of Diurnal Exposure to Sucrose and Nocturnal Exposure to Lactose on Enamel Demineralization. *Caries Res* 2022; 56: 47–54.
- 74 World Health Organization. Key components of a well functioning health system. Geneva: World Health Organization, 2010 <https://www.aapd.org/research/oral-health-policies--recommendations/overview/> (accessed July 28, 2024).
- 75 Butler AS, Clayton EW. A Review of the HHS Family Planning Program: Mission, Management, and Measurement of Results. Washington, DC: The National Academies Press, 2009.
- 76 Brazil. Ministry of Health. Low-risk prenatal care [portuguese: Atenção ao pré-natal de baixo risco]. *Cadernos de Atenção Básica*, nº 32, 2013 www.saude.gov.br/dab.

- 77 Silva CC da, Savian CM, Prevedello BP, Zamberlan C, Dalpian DM, Santos BZ dos. Access and use of dental services by pregnant women: an integrative literature review. *Cien Saude Colet* 2020; 25: 827–35.
- 78 Bernardi C, Masieiro AV, Oliveira JB. Dental care for pregnant women: knowledge and practice of public dentists and their role in the network [portuguese: Assistência odontológica à gestante: conhecimento e prática de dentistas da rede pública e seu papel na rede cegonha]. *Arquivos Em Odontologia* 2019; 55. DOI:10.7308/aodontol/2019.55.e18.
- 79 Reis DM, Pitta DR, Ferreira HMB, Jesus MCP de, Moraes MEL de, Soares MG. Health education as a strategy for the promotion of oral health in the pregnancy period. *Cien Saude Colet* 2010; 15: 269–76.
- 80 Sundermann AC, Zhao S, Young CL, et al. Alcohol Use in Pregnancy and Miscarriage: A Systematic Review and Meta-Analysis. *Alcohol Clin Exp Res* 2019; 43: 1606–16.
- 81 Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *BJOG* 2007; 114: 243–52.
- 82 Pineles BL, Hsu S, Park E, Samet JM. Systematic Review and Meta-Analyses of Perinatal Death and Maternal Exposure to Tobacco Smoke During Pregnancy. *Am J Epidemiol* 2016; 184: 87–97.
- 83 Kuperman AA, Koren O. Antibiotic use during pregnancy: how bad is it? *BMC Med* 2016; 14: 91.
- 84 Smilack JD. The Tetracyclines. *Mayo Clin Proc* 1999; 74: 727–9.
- 85 Ciarrocchi I, Masci C, Spadaro A, Caramia G, Monaco A. Dental enamel, fluorosis and amoxicillin. *La Pediatria Medica e Chirurgica* 2012; 34: 148–54.
- 86 Souza JF, Jeremias F, Alaluusua S, et al. The effect of amoxicillin on dental enamel development in vivo. *Braz Oral Res* 2020; 34: 1–9.
- 87 Gottberg B, Berne J, Quinonez B, Solorzano E. Prenatal effects by exposing to amoxicillin on dental enamel in Wistar rats. *Med Oral Patol Oral Cir Bucal* 2014; 19: e38–43.
- 88 Bookstaver PB, Bland CM, Griffin B, Stover KR, Eiland LS, McLaughlin M. A Review of Antibiotic Use in Pregnancy. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 2015; 35: 1052–62.
- 89 Genco RJ, Grossi SG, Ho A, Nishimura F, Murayama Y. A Proposed Model Linking Inflammation to Obesity, Diabetes, and Periodontal Infections. *J Periodontol* 2005; 76: 2075–84.
- 90 Saltiel AR, Olefsky JM. Inflammatory mechanisms linking obesity and metabolic disease. *Journal of Clinical Investigation* 2017; 127: 1–4.
- 91 Eckel RH, Kahn SE, Ferrannini E, et al. Obesity and Type 2 Diabetes: What Can Be Unified and What Needs to Be Individualized? *Diabetes Care* 2011; 34: 1424–30.

- 92 Dai R, He X-J, Hu C-L. Maternal pre-pregnancy obesity and the risk of macrosomia: a meta-analysis. *Arch Gynecol Obstet* 2018; 297: 139–45.
- 93 Howell KR, Powell TL. Effects of maternal obesity on placental function and fetal development. *Reproduction* 2017; 153: R97–108.
- 94 Rasmussen L, Poulsen CW, Kampmann U, Smedegaard SB, Ovesen PG, Fuglsang J. Diet and healthy lifestyle in the management of gestational diabetes mellitus. *Nutrients*. 2020; 12: 1–24.
- 95 Institute of Medicine. National Research Council. *Weight Gain During Pregnancy*. Washington, D.C.: National Academies Press, 2009 DOI:10.17226/12584.
- 96 Amaral LM, Wallace K, Owens M, LaMarca B. Pathophysiology and Current Clinical Management of Preeclampsia. *Curr Hypertens Rep* 2017; 19: 61.
- 97 Wu P, Green M, Myers JE. Hypertensive disorders of pregnancy. *BMJ* 2023; : e071653.
- 98 Ford ND, Cox S, Ko JY, et al. Hypertensive Disorders in Pregnancy and Mortality at Delivery Hospitalization — United States, 2017–2019. *MMWR Morb Mortal Wkly Rep* 2022; 71: 585–91.
- 99 Rehder PM, Borovac-Pinheiro A, de Araujo ROMB, et al. Gestational Diabetes Mellitus and Obesity are Related to Persistent Hyperglycemia in the Postpartum Period. *Revista Brasileira de Ginecologia e Obstetrícia / RBGO Gynecology and Obstetrics* 2021; 43: 107–12.
- 100 Berger H, Gagnon R, Sermer M. Diabetes in Pregnancy. *Journal of Obstetrics and Gynaecology Canada* 2016; 38: 667-679.e1.
- 101 Mustad VA, Huynh DTT, López-Pedrosa JM, Campoy C, Rueda R. The role of dietary carbohydrates in gestational diabetes. *Nutrients*. 2020; 12: 385.
- 102 Figueiredo CS de A, Rosalem CGC, Cantanhede ALC, Thomaz ÉBAF, Cruz MCFN. Systemic alterations and their oral manifestations in pregnant women. *Journal of Obstetrics and Gynaecology Research* 2017; 43: 16–22.
- 103 Gonçalves KF, Giordani JM do A, Bidinotto AB, Ferla AA, Martins AB, Hilgert JB. Oral healthcare utilization during prenatal care in primary healthcare: data from PMAQ-AB. *Cien Saude Colet* 2020; 25: 519–32.
- 104 Saluja P. Comparative Evaluation of the Effect of Menstruation, Pregnancy and Menopause on Salivary Flow Rate, pH and Gustatory Function. *Journal of Clinical and Diagnostic Research* 2014. DOI:10.7860/JCDR/2014/9935.5071.
- 105 Brown JE, Toma RB. Taste changes during pregnancy. *Am J Clin Nutr* 1986; 43: 414–8.
- 106 Wu M, Chen S-W, Jiang S-Y. Relationship between Gingival Inflammation and Pregnancy. *Mediators Inflamm* 2015; 2015: 1–11.
- 107 Ortiz-Sánchez BJ, Legorreta-Herrera M, Rodriguez-Sosa M. Influence of Gestational Hormones on the Bacteria-Induced Cytokine Response in Periodontitis. *Mediators Inflamm* 2021; 2021: 1–12.

- 108 Sanz M, Kornman K. Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Clin Periodontol* 2013; 40: S164–9.
- 109 Figuero E, Han YW, Furuichi Y. Periodontal diseases and adverse pregnancy outcomes: Mechanisms. *Periodontol* 2000. 2020; 83: 175–88.
- 110 Jakovljevic A, Sljivancanin Jakovljevic T, Duncan HF, et al. The association between apical periodontitis and adverse pregnancy outcomes: a systematic review. *Int Endod J* 2021; 54: 1527–37.
- 111 Cho GJ, Kim S, Lee HC, et al. Association between dental caries and adverse pregnancy outcomes. *Sci Rep* 2020; 10: 5309.
- 112 Casas R, Castro Barquero S, Estruch R. Impact of Sugary Food Consumption on Pregnancy: A Review. *Nutrients* 2020; 12: 3574.
- 113 Englund-Ögge L, Brantsæter AL, Haugen M, et al. Association between intake of artificially sweetened and sugar-sweetened beverages and preterm delivery: a large prospective cohort study. *Am J Clin Nutr* 2012; 96: 552–9.
- 114 Petherick ES, Goran MI, Wright J. Relationship between artificially sweetened and sugar-sweetened cola beverage consumption during pregnancy and preterm delivery in a multi-ethnic cohort: analysis of the Born in Bradford cohort study. *Eur J Clin Nutr* 2014; 68: 404–7.
- 115 Grundt JH, Nakling J, Eide GE, Markestad T. Possible relation between maternal consumption of added sugar and sugar-sweetened beverages and birth weight – time trends in a population. *BMC Public Health* 2012; 12: 901.
- 116 Whincup PH, Kaye SJ, Owen CG, et al. Birth weight and risk of type 2 diabetes: a systematic review. *JAMA* 2008; 300: 2886–97.
- 117 Yu ZB, Han SP, Zhu GZ, et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. *Obesity Reviews* 2011; 12: 525–42.
- 118 Sipola-Leppänen M, Vääräsmäki M, Tikanmäki M, et al. Cardiovascular Risk Factors in Adolescents Born Preterm. *Pediatrics* 2014; 134: e1072–81.
- 119 Sonnenschein-van der Voort AMM, Arends LR, de Jongste JC, et al. Preterm birth, infant weight gain, and childhood asthma risk: A meta-analysis of 147,000 European children. *Journal of Allergy and Clinical Immunology* 2014; 133: 1317–29.
- 120 Kuciene R, Dulskiene V, Medzioniene J. Associations between high birth weight, being large for gestational age, and high blood pressure among adolescents: a cross-sectional study. *Eur J Nutr* 2018; 57: 373–81.
- 121 Pinto DAS, Nascimento JXPT, Padilha LL, et al. High sugar content and body mass index: modelling pathways around the first 1000 d of life, BRISA cohort. *Public Health Nutr* 2021; 24: 4997–5005.

- 122 Costa EL, Costa JF, Santos MP, Ladeira LLC, Silva RA, Ribeiro CCC. Streptococcus mutans in Mother-Child Dyads and Early Childhood Caries: Examining Factors Underlying Bacterial Colonization. Caries Res 2017; 51: 582–9.
- 123 Ribeiro CCC, Pachêco C de JB, Costa EL, et al. Proinflammatory cytokines in early childhood caries: Salivary analysis in the mother/children pair. Cytokine 2018; 107: 113–7.
- 124 Martens L, de Smet S, Yusof MYPM, Rajasekharan S. Association between overweight/obesity and periodontal disease in children and adolescents: a systematic review and meta-analysis. European Archives of Paediatric Dentistry 2017; 18: 69–82.
- 125 Diez-Sampedro A, Flowers M, Olenick M, Maltseva T, Valdes G. Women’s Choice Regarding Breastfeeding and Its Effect on Well-Being. Nurs Womens Health 2019; 23: 383–9.
- 126 Calil VMLT, Falcão MC. Composição do leite humano: o alimento ideal. Rev Med (Rio J) 2003; 82: 1–10.
- 127 Brazil. Ministry of Health. Secretariat of Health Care. Primary Health Care Department. Dietary Guidelines for Brazilian children under 2 years of age. Brasília: Ministério da Saúde, 2021
https://bvsms.saude.gov.br/bvs/publicacoes/dietary_guidelines_brazilian_chhildren_under.pdf (accessed July 28, 2024).
- 128 Brazil. Ministry of Health. Secretariat of Health Care. Primary Health Care Department. Dietary Guidelines for the Brazilian population. 2015
https://bvsms.saude.gov.br/bvs/publicacoes/dietary_guidelines_brazilian_population.pdf (accessed July 28, 2024).
- 129 Machiulskiene V, Campus G, Carvalho JC, et al. Terminology of Dental Caries and Dental Caries Management: Consensus Report of a Workshop Organized by ORCA and Cariology Research Group of IADR. Caries Res 2020; 54: 7–14.
- 130 Ruiz DR. Guidelines for parents on oral health care for babies and children [portuguese: Orientações ao pais sobre cuidados com a saúde bucal do bebê e das crianças]. Brazilian Association of Pediatric Dentistry. 2021; published online Feb.
- 131 American Academy of Pediatric Dentistry. Periodicity of examination, preventive dental services, anticipatory guidance/ counseling, and oral treatment for infants, children, and adolescent. In: The Reference Manual of Pediatric Dentistry. Chicago, 2023: 288–300.
- 132 Global Child Dental Fund. Oral Health and Your Baby. Global Child Dental Fund. 2023. <https://www.gcdfund.org/publications> (accessed July 28, 2024).
- 133 Lopes A, Cardoso V, Moreira L, Ramos-Jorge J, Ramos-Jorge M, Fernandes I. Effect of oral hygiene in infants before dental eruption on Candida spp. colonization and the occurrence of oral candidiasis: A randomized clinical trial. J Clin Exp Dent 2023; : e920–8.

- 134 Ellwood RP, Cury JA. How much toothpaste should a child under the age of 6 years use? *European Archives of Paediatric Dentistry* 2009; 10: 168–74.
- 135 Toumba KJ, Twetman S, Splieth C, Parnell C, van Loveren C, Lygidakis NA. Guidelines on the use of fluoride for caries prevention in children: an updated EAPD policy document. *European Archives of Paediatric Dentistry* 2019; 20: 507–16.
- 136 Betran AP, Ye J, Moller A-B, Souza JP, Zhang J. Trends and projections of caesarean section rates: global and regional estimates. *BMJ Glob Health* 2021; 6: e005671.
- 137 Betran AP, Torloni MR, Zhang JJ, Gülmezoglu AM, WHO Working Group on Caesarean Section. WHO Statement on Caesarean Section Rates. *BJOG* 2016; 123: 667–70.
- 138 World Health Organization. Declaração da OMS sobre Taxas de Cesáreas. World Health Organization. 2015.
- 139 Betran AP, Torloni MR, Zhang J, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. *Reprod Health* 2015; 12: 57.
- 140 Magne F, Puchi Silva A, Carvajal B, Gotteland M. The Elevated Rate of Cesarean Section and Its Contribution to Non-Communicable Chronic Diseases in Latin America: The Growing Involvement of the Microbiota. *Front Pediatr* 2017; 5. DOI:10.3389/fped.2017.00192.
- 141 Zimmerman E, Thompson K. Clarifying nipple confusion. *J Perinatol* 2015; 35: 895–9.
- 142 Collins CT, Gillis J, McPhee AJ, Suganuma H, Makrides M. Avoidance of bottles during the establishment of breast feeds in preterm infants. *Cochrane Database of Systematic Reviews* 2016; 2016. DOI:10.1002/14651858.CD005252.pub4.
- 143 Turke KC, dos Santos LR, Matsumura LS, Sarni ROS. Risk factors for the lack of adherence to breastfeeding. *Rev Assoc Med Bras* 2021; 67: 107–14.
- 144 Silva Júnior AC, Alves CMC, Martins RFM, et al. Adverse pregnancy outcomes and occlusal traits in the primary dentition: A prospective cohort (BRISA). *Orthod Craniofac Res* 2022; published online Jan 20. DOI:10.1111/ocr.12563.
- 145 Mattos-Graner RO, de Moraes AB, Rontani RM, Birman EG. Relation of oral yeast infection in Brazilian infants and use of a pacifier. *ASDC J Dent Child* 2001; 68: 33–6, 10.
- 146 Scudine KG de O, Freitas CN de, Nascimento de Moraes KSG, et al. Multidisciplinary Evaluation of Pacifier Removal on Oro-Dentofacial Structures: A Controlled Clinical Trial. *Front Pediatr* 2021; 9. DOI:10.3389/fped.2021.703695.
- 147 Nunes AMM, da Silva AAM, Alves CMC, Hugo FN, Ribeiro CCC. Factors underlying the polarization of early childhood caries within a high-risk population. *BMC Public Health* 2014; 14: 988.
- 148 Stevens A, Hamel C, Singh K, et al. Do sugar-sweetened beverages cause adverse health outcomes in children? A systematic review protocol. *Syst Rev* 2014; 3: 96.

- 149 Vos MB, Kaar JL, Welsh JA, et al. Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. *Circulation* 2017; 135: e1017–34.
- 150 Del-Ponte B, Quinte GC, Cruz S, Grellert M, Santos IS. Dietary patterns and attention deficit/hyperactivity disorder (ADHD): A systematic review and meta-analysis. *J Affect Disord*. 2019; 252: 160–73.
- 151 Farsad-Naeimi A, Asjodi F, Omidian M, et al. Sugar consumption, sugar sweetened beverages and Attention Deficit Hyperactivity Disorder: A systematic review and meta-analysis. *Complement Ther Med*. 2020; 53. DOI:10.1016/j.ctim.2020.102512.
- 152 Yu CJ, Du JC, Chiou HC, et al. Sugar-sweetened beverage consumption is adversely associated with childhood attention deficit/hyperactivity disorder. *Int J Environ Res Public Health* 2016; 13. DOI:10.3390/ijerph13070678.
- 153 National Heart Lung and Blood Institute. Asthma. 2020; published online Dec. <https://www.nhlbi.nih.gov/health-topics/asthma> (accessed Dec 1, 2021).
- 154 World Health Organization. Asthma. 2021; published online May 3. <https://www.who.int/news-room/fact-sheets/detail/asthma> (accessed Dec 1, 2021).
- 155 Padilha LL, Vianna EO, Vale ATM, Nascimento JXPT, Silva AAM, Ribeiro CCC. Pathways in the association between sugar sweetened beverages and child asthma traits in the 2nd year of life: Findings from the BRISA cohort. *Pediatric Allergy and Immunology* 2020; 31: 480–8.
- 156 Noutsios G, Floros J. Childhood asthma: causes, risks, and protective factors; a role of innate immunity. *Swiss Med Wkly* 2014; 144. DOI:10.4414/smw.2014.14036.
- 157 Early Childhood Caries: IAPD Bangkok Declaration. *Int J Paediatr Dent* 2019; 29: 384–6.
- 158 Lima GQT, Brondani MA, Silva AAM da, Carmo CDS do, Silva RA da, Ribeiro CCC. Serum levels of proinflammatory cytokines are high in early childhood caries. *Cytokine* 2018; 111: 490–5.
- 159 United Nations. Department of Economic and Social Affairs. Sustainable Development. The 17 goals. 2015. <https://sdgs.un.org/goals/goal3>.
- 160 United Nations. Department of Economic and Social Affairs. Sustainable Development. SDG Actions Platform. United Nations. 2024. <https://sdgs.un.org/partnerships> (accessed July 28, 2024).

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TÍTULO	The first thousand days of life: a DOHaD perspective to dentistry
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PROJETO GRÁFICO E CAPA	Silas Alves-Costa PROJETO GRÁFICO Raul Angel FOTO DA CAPA
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6 CONSIDERAÇÕES FINAIS

Os achados desta tese refletem um percurso investigativo que se iniciou com a análise das inter-relações entre fatores comportamentais e metabólicos e a periodontite em adultos, avançando para a aplicação inovadora da análise de redes complexas com o objetivo de mapear as interações entre doenças crônicas não transmissíveis (DCNTs) ao longo do ciclo vital. Na sequência, a investigação ampliou seu escopo para incluir a avaliação e projeção do consumo global de açúcares de adição. Durante o doutorado tive a oportunidade de um doutorado sanduiche na *Duke-NUS Medical School* em Singapura, sob a supervisão do Prof. Dr. Fábio Leite; e um estágio de curta duração no Instituto de Ciências Matemáticas e da Computação (ICMC/USP) em São Carlos (SP) sob a supervisão do Prof. Dr. Francisco Rodrigues.

Os três capítulos que exploram redes complexas tiveram destaque na comunidade acadêmica capazes de mostrar através de modelos matemáticos avançados a complexidade da saúde identificando agrupamento de doenças crônicas bucais e sistêmicas e seus fatores de risco em diferentes fases da vida. Esses trabalhos foram reconhecidos com premiações relevantes no Brasil: 1º lugar no Fórum Científico – Prêmio Marco Antônio Barbieri, durante o Congresso DOHaD Brasil (Campinas-SP, 2024); 2º lugar no Fórum Científico da Sociedade Brasileira de Pesquisa Odontológica (Campinas-SP, 2024). No exterior, esses achados também receberam reconhecimento no *IADR GOHIRN Travel Award for New Investigator* (Barcelona, 2025), concedido pelo *IADR Global Oral Health Inequalities Research Network* e o *Travel Award for The DOHaD World Congress 2025* (Buenos Aires, 2025).

Consolidando a proposta de tradução do conhecimento científico em ação prática, o percurso da tese culmina na elaboração do Capítulo 7, que apresenta um material educativo, um livro em formato digital voltado a cirurgiões-dentistas, com linguagem acessível e fundamentação técnico-científica, visando ampliar a compreensão e a atuação profissional frente aos desafios contemporâneos das DCNTs. Desde sua publicação, o material teve mais de sete mil acessos, demonstrando seu alcance e relevância para a qualificação da prática odontológica, inclusive de outros países. Esse alcance internacional nos instigou a publicar também uma versão em inglês deste livro que, no momento da defesa, contava com cerca de 300 downloads.

O fio condutor que perpassa cada capítulo é a convicção de que só será possível mitigar o ônus crescente das DCNTs por meio de uma abordagem de integralidade em saúde, capaz de articular prevenção, vigilância e promoção de práticas saudáveis desde

os primeiros mil dias de vida até a velhice. Nesse *continuum* de DCNTs, o consumo excessivo de açúcares, presente sobretudo em alimentos ultraprocessados e bebidas ricas em açúcares de adição, evidencia-se como um eixo comum, recorrente em todas as redes complexas analisadas: associado não apenas à cárie e à periodontite, mas igualmente à obesidade, à resistência à insulina, à hipertensão e a outras condições inflamatórias que se reforçam mutuamente.

Com base nesse conjunto de evidências, a tese destaca a urgência de políticas públicas articuladas, que vão além da regulamentação da rotulagem nutricional e da publicidade de produtos com alto teor de açúcares adicionados. Defende-se a adoção de medidas como a taxação de bebidas e alimentos ultraprocessados, a ampliação da oferta de ambientes alimentares saudáveis em escolas, locais de trabalho e unidades de saúde, apoio agricultura familiar, reforço das políticas de distribuição de renda, além de programas de educação continuada voltados a profissionais e populações vulneráveis. Essas estratégias não apenas reduzem o consumo de açúcares, mas também enfrentam os determinantes sociais das desigualdades em saúde, promovendo ações intersetoriais que envolvem a educação, o planejamento urbano, o desenvolvimento social e a agricultura sustentável.

O material educativo desenvolvido exemplifica como a ciência pode ultrapassar os limites da academia, transformando conhecimento em ação para a qualificação de profissionais e a conscientização das comunidades. Essa iniciativa reafirma o compromisso desta tese não apenas com a produção científica, mas com a transformação concreta de realidades. Com as redes complexas, identificando de fatores que levam às DCNTs, mostramos alvos de atuação para práticas clínicas e políticas públicas capazes de antecipar riscos, interromper trajetórias de adoecimento e promover, em cada fase da vida, o pleno direito à saúde.

No contexto da aplicação do conhecimento científico em ações concretas de saúde, destaco minha participação na elaboração de um dos projetos vencedores do edital *Grand Challenges Brazil*, financiado em 2024 pelo DECIT/CNPq em parceria com a *Gates Foundation*. O projeto recebeu R\$500.000 e tem como objetivo o desenvolvimento de um *Large Language Model* (LLM), ou Modelo de Linguagem de Ampla, voltado para apoiar Agentes Comunitários de Saúde na Atenção Primária na identificação de riscos para cárie, asma e obesidade nos primeiros 1000 dias de vida.

Durante o doutorado, participei ativamente do treinamento da equipe envolvida na pesquisa e também atuei diretamente na coleta de dados do seguimento aos 12 anos da

Coorte BRISA, contribuindo de forma significativa para a continuidade e o fortalecimento das investigações longitudinais conduzidas pelo grupo de pesquisa ao qual integro. Além disso, publiquei quatro trabalhos em coautoria com minha orientadora e outros quatro em colaboração com pesquisadores internacionais, ampliando o impacto e a visibilidade científica das investigações.

Por fim, os achados desta tese convergem com os Objetivos de Desenvolvimento Sustentável (ODS), em especial o ODS 2 (Fome Zero e Agricultura Sustentável), ODS 3 (Saúde e Bem-Estar), ODS 4 (Educação de Qualidade) e ODS 10 (Redução das Desigualdades), além de oferecer subsídios ao “Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas e Agravos Não Transmissíveis no Brasil, 2021–2030” (Plano DANT). Ao identificar padrões de consumo de bebidas ricas em açúcares de adição, além de outros fatores comportamentais, metabólicos e determinantes sociais em todas as fases do ciclo de vida, este trabalho fornece evidências para o fortalecimento de iniciativas intersetoriais e o monitoramento baseado em dados, com foco em ações de prevenção e redução da carga das DCNTs.

REFERÊNCIAS

- ABADIE, A. *et al.* When Should You Adjust Standard Errors for Clustering? **The Quarterly Journal of Economics**, v. 138, n. 1, p. 1–35, 15 dez. 2022.
- AHUJA, M.; SHARMA, K. Complex Networks: A Review. **International Journal of Computer Applications**, v. 101, n. 15, p. 31–35, 18 set. 2014.
- ALVES-COSTA, S.; NASCIMENTO, G. G.; *et al.* Sugar-sweetened beverage consumption and periodontitis among adults: A population-based cross-sectional study. **Journal of Clinical Periodontology**, v. 51, n. 6, p. 712–721, 7 jun. 2024.
- ALVES-COSTA, S.; SOUZA, B. F. DE; *et al.* High free sugars, insulin resistance, and low socioeconomic indicators: the hubs in the complex network of non-communicable diseases in adolescents. **Diabetology & Metabolic Syndrome**, v. 16, n. 1, p. 235, 28 set. 2024.
- ALVES-COSTA, S. *et al.* Caries Is the Hub of a Complex Network of Chronic Diseases across the Life Decades. **Journal of Dental Research**, 27 abr. 2025.
- ANTUNES, J. L. F.; CARDOSO, M. R. A. Using time series analysis in epidemiological studies. **Epidemiol. Serv. Saúde**, v. 24, n. 3, p. 565–576, set. 2015.
- ARAÚJO, S. M. P. *et al.* Chronic oral disease burden at the first 1000 days: Intergenerational risk factors, BRISA cohort. **Oral Diseases**, 9 jun. 2024.
- ASSOCIATION OF RESEARCH COMPANIES. **Brazilian Economic Classification Criteria ABEP**, 2008. Disponível em: <<http://www.abep.org/criterio-brasil>>. Acesso em: 26 maio. 2024
- AZAAD MOONESAR, I.; AL-ALAWY, K.; GAAFAR, R. Taxing sugar-sweetened beverages: Knowledge, beliefs and where should the money go? **Heliyon**, v. 10, n. 8, p. e28226, abr. 2024.
- BARABÁSI, A.-L.; OLTVAI, Z. N. Network biology: understanding the cell's functional organization. **Nature Reviews Genetics**, v. 5, n. 2, p. 101–113, fev. 2004.
- BARBOSA, J. M. A. *et al.* Behavioral risk factors for noncommunicable diseases associated with depression and suicide risk in adolescence. **Cadernos de Saúde Pública**, v. 38, n. 2, 2022.
- BENZIGER, C. P.; ROTH, G. A.; MORAN, A. E. The Global Burden of Disease Study and the Preventable Burden of NCD. **Global Heart**, v. 11, n. 4, p. 393, 1 dez. 2016.
- BLONDEL, V. D. *et al.* Fast unfolding of communities in large networks. **Journal of Statistical Mechanics: Theory and Experiment**, v. 2008, n. 10, p. P10008, 1 out. 2008.
- BLOOM, D. E. *et al.* **The Global Economic Burden of Noncommunicable Diseases**. Geneva: [s.n.].
- BODANESE, L. C. *et al.* Association between Periodontitis and Myocardial Infarction: Systematic Review and Meta-Analysis. **International Journal of Cardiovascular Sciences**, 26 maio 2021.
- BOUSQUET, J. *et al.* Systems Medicine Approaches for the Definition of Complex Phenotypes in Chronic Diseases and Ageing. From Concept to Implementation and Policies. **Current Pharmaceutical Design**, v. 20, n. 38, p. 5928–5944, 14 mar. 2014.
- BRAUER, M. *et al.* Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. **The Lancet**, v. 403, n. 10440, p. 2162–2203, 18 maio 2024.

- BRIDGE, G.; GROISMAN, S.; BEDI, R. Sugar-sweetened beverage taxes in Brazil: past, present, and future. **Journal of public health policy**, v. 43, n. 2, p. 281–291, 1 jun. 2022.
- BUDREVICIUTE, A. *et al.* Management and Prevention Strategies for Non-communicable Diseases (NCDs) and Their Risk Factors. **Frontiers in Public Health**, v. 8, 26 nov. 2020.
- BUUREN, S. VAN; GROOTHUIS-OUDSHOORN, K. mice: Multivariate Imputation by Chained Equations in R. **Journal of Statistical Software**, v. 45, n. 3, 2011.
- CARRAMOLINO-CUELLAR, E.; TOMAS, I.; JIMENEZ-SORIANO, Y. Relationship between the oral cavity and cardiovascular diseases and metabolic syndrome. **Medicina Oral Patología Oral y Cirugía Bucal**, p. e289–e294, 2014.
- CENTERS FOR DISEASE CONTROL AND PREVENTION. **Third National Health and Nutrition Examination Survey (NHANES III), 1988-94**. Disponível em: <<https://wwwn.cdc.gov/nchs/data/nhanes3/1a/ADULT-acc.pdf>>. Acesso em: 27 mar. 2023.
- CHEN, G.; LOU, Y. Preliminaries. *Em: Naming Game. Emergence, Complexity and Computation*. [s.l.] Springer, 2019. v. 34p. 11–22.
- CHESNAYE, N. C. *et al.* An introduction to inverse probability of treatment weighting in observational research. **Clinical Kidney Journal**, v. 15, n. 1, p. 14–20, 12 jan. 2022.
- COMIN, C. H. *et al.* Complex systems: Features, similarity and connectivity. **Physics Reports**, v. 861, p. 1–41, maio 2020.
- CONFORTIN, S. C. *et al.* RPS Brazilian Birth Cohorts Consortium (Ribeirão Preto, Pelotas and São Luís): history, objectives and methods. **Cadernos de Saúde Pública**, v. 37, n. 4, 2021.
- CORTE, K. DELLA *et al.* World trends in sugar-sweetened beverage and dietary sugar intakes in children and adolescents: a systematic review. **Nutrition Reviews**, v. 79, n. 3, p. 274–288, 11 fev. 2021.
- COSTA JUNIOR, S. DA *et al.* Brazilian Oral Health Policy: metasynthesis of studies on the Oral Health Network. **Rev. Saúde Pública**, v. 55, p. 105, 17 dez. 2021.
- COSTA, L. DA F. *et al.* Characterization of complex networks: A survey of measurements. **Advances in Physics**, v. 56, n. 1, p. 167–242, jan. 2007.
- COSTA, L. DA F.; RODRIGUES, F. A.; CRISTINO, A. S. Complex networks: the key to systems biology. **Genetics and Molecular Biology**, v. 31, n. 3, p. 591–601, 2008.
- CRIELAARD, L. *et al.* Understanding the impact of exposure to adverse socioeconomic conditions on chronic stress from a complexity science perspective. **BMC Medicine**, v. 19, n. 1, p. 242, 12 dez. 2021.
- DINICOLANTONIO, J. J.; MANGAN, D.; O'KEEFE, J. H. The fructose–copper connection: Added sugars induce fatty liver and insulin resistance via copper deficiency. **Journal of Metabolic Health**, v. 3, n. 1, 26 set. 2018.
- EAGLE, N.; MACY, M.; CLAXTON, R. Network Diversity and Economic Development. **Science**, v. 328, n. 5981, p. 1029–1031, 21 maio 2010.
- EKE, P. I. *et al.* Update of the Case Definitions for Population-Based Surveillance of Periodontitis. **Journal of Periodontology**, v. 83, n. 12, p. 1449–1454, dez. 2012.
- _____. Periodontitis in US Adults: National Health and Nutrition Examination Survey 2009–2014. **Journal of the American Dental Association (1939)**, v. 149, n. 7, p. 576, 1 jul. 2018.

FEKADU, H. *et al.* Barriers to equitable healthcare services for under-five children in Ethiopia: a qualitative exploratory study. **BMC Health Services Research**, v. 24, n. 1, p. 613, 10 maio 2024.

FLETCHER, S.; ISLAM, M. Z. Comparing sets of patterns with the Jaccard index. **Australasian Journal of Information Systems**, v. 22, 7 mar. 2018.

GASPAR, R. S. *et al.* Income inequality and non-communicable disease mortality and morbidity in Brazil States: a longitudinal analysis 2002-2017. **The Lancet Regional Health - Americas**, v. 2, p. 100042, out. 2021.

GAUR, V. *et al.* **A Review of Metrics, Algorithms and Methodologies for Network Reliability** 2019 IEEE International Conference on Industrial Engineering and Engineering Management (IEEM). **Anais...IEEE**, dez. 2019

GBD 2021 DIABETES COLLABORATORS. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. **Lancet**, v. 402, n. 10397, p. 203–234, 15 jul. 2023.

GEIFMAN, N.; COHEN, R.; RUBIN, E. Redefining meaningful age groups in the context of disease. **Age**, v. 35, n. 6, p. 2357–2366, 27 dez. 2013.

GLOBAL BURDEN OF DISEASE COLLABORATIVE NETWORK. **Global Burden of Disease Study 2019 (GBD 2019) Results**. Disponível em: <<https://vizhub.healthdata.org/gbd-results/>>. Acesso em: 22 out. 2023a.

_____. **Periodontal diseases — Level 4 cause**. Disponível em: <https://www.healthdata.org/results/gbd_summaries/2019/periodontal-diseases-level-4-cause>. Acesso em: 22 out. 2023b.

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE. **Gold Spirometry Guide**. Disponível em: <<https://goldcopd.org/gold-spirometry-guide/>>. Acesso em: 16 maio. 2024.

GOLLUST, S. E.; BARRY, C. L.; NIEDERDEPPE, J. Americans' opinions about policies to reduce consumption of sugar-sweetened beverages. **Preventive Medicine**, v. 63, p. 52–57, jun. 2014.

GOMAA, N. *et al.* Social-Biological Interactions in Oral Disease: A ‘Cells to Society’ View. **PLOS ONE**, v. 11, n. 1, p. e0146218, 11 jan. 2016.

GUARNER, V.; RUBIO-RUIZ, M. E. Low-Grade Systemic Inflammation Connects Aging, Metabolic Syndrome and Cardiovascular Disease. *Em: Interdisciplinary Topics in Gerontology*. [s.l.] S. Karger AG, 2015. v. 40p. 99–106.

GUPTA, V. *et al.* Sugar-sweetened beverages and periodontal disease: A systematic review. **Oral Diseases**, 16 set. 2022.

HAREGU, T. N. *et al.* Co-occurrence of behavioral risk factors of common non-communicable diseases among urban slum dwellers in Nairobi, Kenya. **Global Health Action**, v. 8, n. 1, p. 28697, 16 dez. 2015.

ITRIA, A. *et al.* Taxing sugar-sweetened beverages as a policy to reduce overweight and obesity in countries of different income classifications: a systematic review. **Public Health Nutrition**, v. 24, n. 16, p. 5550–5560, 5 nov. 2021.

- KNOL, M. J.; VANDERWEELE, T. J. Recommendations for presenting analyses of effect modification and interaction. **International journal of epidemiology**, v. 41, n. 2, p. 514–520, abr. 2012.
- KOSYREVA, A. *et al.* Alzheimer's Disease and Inflammaging. **Brain Sciences**, v. 12, n. 9, p. 1237, 13 set. 2022.
- KRIEGER, J. *et al.* Sugar-Sweetened Beverage Reduction Policies: Progress and Promise. **Annual Review of Public Health**, v. 42, n. 1, p. 439–461, 1 abr. 2021.
- KURING, J. K.; MATHIAS, J. L.; WARD, L. Risk of Dementia in persons who have previously experienced clinically-significant Depression, Anxiety, or PTSD: A Systematic Review and Meta-Analysis. **Journal of Affective Disorders**, v. 274, p. 247–261, 1 set. 2020.
- KUSAMA, T. *et al.* Free Sugar Intake and Periodontal Diseases: A Systematic Review. 2022.
- LADEIRA, L. L. C. *et al.* Precursors of insulin resistance underlying periodontitis in adolescents aged 17–18 years. **Oral Diseases**, v. 00, p. 1–10, 12 jul. 2022.
- LADEIRA, L. L. C. *et al.* Obesity, Insulin Resistance, Caries, and Periodontitis: Syndemic Framework. **Nutrients**, v. 15, n. 16, 1 ago. 2023.
- LIMA, G. Q. T. *et al.* Serum levels of proinflammatory cytokines are high in early childhood caries. **Cytokine**, v. 111, p. 490–495, nov. 2018.
- LULA, E. C. O. *et al.* Added sugars and periodontal disease in young adults: an analysis of NHANES III data. **The American Journal of Clinical Nutrition**, v. 100, n. 4, p. 1182–1187, 1 out. 2014.
- LUSTIG, R. H. Fructose: Metabolic, Hedonic, and Societal Parallels with Ethanol. **Journal of the American Dietetic Association**, v. 110, n. 9, p. 1307–1321, set. 2010.
- LYMAN, M. *et al.* Neuroinflammation: The role and consequences. **Neuroscience Research**, v. 79, p. 1–12, fev. 2014.
- MACDONALD, I. A. A review of recent evidence relating to sugars, insulin resistance and diabetes. **European Journal of Nutrition**, v. 55, n. S2, p. 17–23, 23 nov. 2016.
- MALIK, V. S.; HU, F. B. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. **Nature Reviews Endocrinology**, v. 18, n. 4, p. 205–218, 21 abr. 2022.
- MARK, A. M. Preventing tooth loss. **The Journal of the American Dental Association**, v. 151, n. 9, p. 712, set. 2020.
- MEGHANATHAN, N. Correlation Coefficient Analysis of Centrality Metrics for Complex Network Graphs. *Em: [s.l: s.n.]*. p. 11–20.
- MINERBA, L. *et al.* A complex network analysis of a health organization. **Igiene e sanità pubblica**, v. 64, n. 1, p. 9–25, jan. 2008.
- MOUTSOPOULOS, N. M.; MADIANOS, P. N. Low-Grade Inflammation in Chronic Infectious Diseases: Paradigm of Periodontal Infections. **Annals of the New York Academy of Sciences**, v. 1088, n. 1, p. 251–264, 1 nov. 2006.
- MURRAY, C. J. L. *et al.* Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. **The Lancet**, v. 396, n. 10258, p. 1223–1249, out. 2020.

- MUTH, M. K. *et al.* How Much Can Product Reformulation Improve Diet Quality in Households with Children and Adolescents? **Nutrients**, v. 11, n. 3, p. 618, 14 mar. 2019.
- NASCIMENTO, G. G. *et al.* Does diabetes increase the risk of periodontitis? A systematic review and meta-regression analysis of longitudinal prospective studies. **Acta diabetologica**, v. 55, n. 7, p. 653–667, 1 jul. 2018.
- NASCIMENTO, J. X. P. T. *et al.* The First 1000 Days of Life Factors Associated with “Childhood Asthma Symptoms”: Brisa Cohort, Brazil. **Scientific Reports**, v. 7, n. 1, p. 16028, 22 dez. 2017.
- NORDHAUSEN, K.; TASKINEN, S. Locally Weighted Scatterplot Smoother. *Em: [s.l: s.n.].* p. 1–4.
- NYVAD, B.; TAKAHASHI, N. Integrated hypothesis of dental caries and periodontal diseases. **Journal of Oral Microbiology**, v. 12, n. 1, p. 1710953, 1 jan. 2020.
- PETERS, R. *et al.* Common risk factors for major noncommunicable disease, a systematic overview of reviews and commentary: the implied potential for targeted risk reduction. **Therapeutic Advances in Chronic Disease**, v. 10, 2019.
- QAISER, S.; HJ IBRAHIM, M. Y.; HUSAIN, S. S. The Global Burden and Impacts of Non-Communicable Diseases (NCDs): A Review of Literature. **Borneo Journal of Medical Sciences (BJMS)**, v. 12, p. 3–4, 21 set. 2018.
- RECKZIEGEL, M. B. *et al.* The triglyceride-glucose index as an indicator of insulin resistance and cardiometabolic risk in Brazilian adolescents. **Archives of Endocrinology and Metabolism**, 18 jan. 2023.
- REYES-ANGEL, J. *et al.* Obesity-related asthma in children and adolescents. **The Lancet Child & Adolescent Health**, v. 6, n. 10, p. 713–724, out. 2022.
- RIBEIRO, C. C. C. *et al.* Proinflammatory cytokines in early childhood caries: Salivary analysis in the mother/children pair. **Cytokine**, v. 107, p. 113–117, 1 jul. 2018.
- RIBEIRO, C. C. C. *et al.* Systemic circulating inflammatory burden and periodontitis in adolescents. **Clinical Oral Investigations**, v. 25, n. 10, p. 5855–5865, 24 out. 2021.
- RICARDO, C. Z. *et al.* Co-occurrence and clustering of the four major non-communicable disease risk factors in Brazilian adolescents: Analysis of a national school-based survey. **PLOS ONE**, v. 14, n. 7, p. e0219370, 3 jul. 2019.
- ROBINSON, H. M.; HORT, K. Non-communicable diseases and health systems reform in low-and-middle-income countries. **Pacific health dialog**, v. 18, n. 1, p. 179–90, abr. 2012.
- ROMDHANE, H. BEN *et al.* Health system challenges of NCDs in Tunisia. **International Journal of Public Health**, v. 60, n. S1, p. 39–46, 16 jan. 2015.
- ROSINGER, A.; BETHANCOURT, H.; FRANCIS, L. A. Association of Caloric Intake From Sugar-Sweetened Beverages With Water Intake Among US Children and Young Adults in the 2011-2016 National Health and Nutrition Examination Survey. **JAMA Pediatrics**, v. 173, n. 6, p. 602, 1 jun. 2019.
- RUANPENG, D. *et al.* Sugar and artificially sweetened beverages linked to obesity: a systematic review and meta-analysis. **QJM: An International Journal of Medicine**, v. 110, n. 8, p. 513–520, 1 ago. 2017.

- SALAM, R. Expanding the definition of noncommunicable disease. **Journal of Social Health and Diabetes**, v. 04, n. 02, p. 067–070, 23 dez. 2016.
- SCHUMACHER, A. E. *et al.* Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950–2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. **The Lancet**, v. 403, n. 10440, p. 1989–2056, maio 2024.
- SHAYO, F. K. Co-occurrence of risk factors for non-communicable diseases among in-school adolescents in Tanzania: an example of a low-income setting of sub-Saharan Africa for adolescence health policy actions. **BMC Public Health**, v. 19, n. 1, p. 972, 22 dez. 2019.
- SIGALA, D. M.; STANHOPE, K. L. An Exploration of the Role of Sugar-Sweetened Beverage in Promoting Obesity and Health Disparities. **Current Obesity Reports**, v. 10, n. 1, p. 39–52, 7 jan. 2021.
- SILVA, A. A. M. DA *et al.* A protocol to identify non-classical risk factors for preterm births: the Brazilian Ribeirão Preto and São Luís prenatal cohort (BRISA). **Reproductive Health**, v. 11, n. 1, p. 79, 19 dez. 2014.
- SILVA, A. E. R. *et al.* A Saúde bucal está associada à presença de sintomas depressivos em idosos? **Ciência & Saúde Coletiva**, v. 24, n. 1, p. 181–188, jan. 2019.
- SOFTIC, S. *et al.* Divergent effects of glucose and fructose on hepatic lipogenesis and insulin signaling. **Journal of Clinical Investigation**, v. 127, n. 11, p. 4059–4074, 3 out. 2017.
- STANHOPE, K. L. Role of Fructose-Containing Sugars in the Epidemics of Obesity and Metabolic Syndrome. **Annual Review of Medicine**, v. 63, n. 1, p. 329–343, 18 fev. 2012.
- STEPOVIĆ, M. *et al.* Barriers affecting the oral health of people diagnosed with depression: A systematic review. **Slovenian Journal of Public Health**, v. 59, n. 4, p. 273–280, 18 out. 2020.
- STEVENS, G. A. *et al.* Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. **The Lancet**, v. 388, n. 10062, p. e19–e23, 10 dez. 2016.
- STEVENS, J. *et al.* Multilevel Interventions Targeting Obesity: Research Recommendations for Vulnerable Populations. **American Journal of Preventive Medicine**, v. 52, n. 1, p. 115–124, jan. 2017.
- THAKUR, J. *et al.* Social and Economic Implications of Noncommunicable diseases in India. **Indian Journal of Community Medicine**, v. 36, n. 5, p. 13, 2011.
- THE LANCET DIABETES & ENDOCRINOLOGY. The price of health. **The Lancet Diabetes & Endocrinology**, v. 12, n. 2, p. 83, fev. 2024.
- TONETTI, M. S.; GREENWELL, H.; KORNMAN, K. S. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. **Journal of Periodontology**, v. 89, n. S1, p. S159–S172, 21 jun. 2018.
- UNITED NATIONS. DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS. SUSTAINABLE DEVELOPMENT. **SDG Actions Platform**. Disponível em: <<https://sdgs.un.org/partnerships>>. Acesso em: 28 jul. 2024.
- VANDERWEELE, T. J. On the distinction between interaction and effect modification. **Epidemiology**, v. 20, n. 6, p. 863–871, nov. 2009.
- VANDERWEELE, T. J.; DING, P. Sensitivity Analysis in Observational Research: Introducing the E-Value. **Annals of Internal Medicine**, v. 167, n. 4, p. 268, 15 ago. 2017.

VERBURG, B. O. *et al.* New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. **Ultrasound in Obstetrics & Gynecology**, v. 31, n. 4, p. 388–396, 17 abr. 2008.

VISHWAKARMA, D.; GAIDHANE, A.; BHOI, S. R. Depression and Its Associated Factors Among the Elderly Population in India: A Review. **Cureus**, 27 jun. 2023.

VOS, M. B. *et al.* Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. **Circulation**, v. 135, n. 19, p. e1017–e1034, 9 maio 2017.

VOS, T. *et al.* Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. **The Lancet**, v. 396, n. 10258, p. 1204–1222, out. 2020.

VULLIARD, L.; MENCHE, J. Complex Networks in Health and Disease. *Em: Systems Medicine*. [s.l.] Elsevier, 2021. v. 1–3p. 26–33.

WANG, F. *et al.* **Application of network analysis on healthcare** 2014 IEEE/ACM International Conference on Advances in Social Networks Analysis and Mining (ASONAM 2014). **Anais...IEEE**, ago. 2014

WANG, J. *et al.* Consumption of Added Sugars from Liquid but Not Solid Sources Predicts Impaired Glucose Homeostasis and Insulin Resistance among Youth at Risk of Obesity. **The Journal of Nutrition**, v. 144, n. 1, p. 81–86, jan. 2014.

WIESNER, K.; LADYMAN, J. Measuring complexity. 2019.

WOLF, T. G. *et al.* Non-communicable Diseases and Oral Health: An Overview. **Frontiers in Oral Health**, v. 2, p. 57, 3 set. 2021.

WORLD HEALTH ORGANIZATION. **WHO Expert Committee on Physical Status: the Use and Interpretation of Anthropometry**. Geneva: [s.n.]. Disponível em: <<https://apps.who.int/iris/handle/10665/37003>>. Acesso em: 7 ago. 2022.

_____. **Oral health surveys: basic methods**. 5. ed. Geneva: [s.n.].

_____. **Noncommunicable diseases**. Disponível em: <<https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>>. Acesso em: 12 jul. 2024.

_____. **Noncommunicable diseases: Risk factors**.

_____. **Global Health Estimates: Life expectancy and leading causes of death and disability**. Disponível em: <<https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates>>. Acesso em: 6 jan. 2025.

XIAO FAN WANG; GUANRONG CHEN. Complex networks: Small-world, scale-free and beyond. **IEEE Circuits and Systems Magazine**, v. 3, n. 1, p. 6–20, 2003.

YE, L.; JIANG, Y.; ZHANG, M. Crosstalk between glucose metabolism, lactate production and immune response modulation. **Cytokine & Growth Factor Reviews**, v. 68, p. 81–92, dez. 2022.

ZHAO, M. *et al.* Static cut-points of hypertension and increased arterial stiffness in children and adolescents: The International Childhood Vascular Function Evaluation Consortium. **Journal of Clinical Hypertension**, v. 21, n. 9, p. 1335–1342, set. 2019.

ZHOU, M.; SHEN, H. Forecasting the global burden of disease to 2050. **The Lancet**, v. 403, n. 10440, p. 1961–1963, 18 maio 2024.

APÊNDICE – Outras produções ao longo do doutorado



OPEN ACCESS

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Socioeconomic determinants of low birth weight and its association with peripubertal obesity in Brazil

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Silas Alves-Costa⁴, Cecilia C. Costa Ribeiro⁴ and
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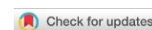
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Introduction: Low birth weight (LBW) is an early life adversity associated with various risk factors and metabolic dysfunction throughout life. However, the role of socioeconomic factors in the association between LBW and peripubertal health in low- and middle-income countries (LMICs) remains unclear. This ecological study investigated the factors contributing to LBW and its impacts in Brazil.

Methods: Data were collected from the Global Health Data Exchange as summary exposure values (SEVs), which serve as a proxy for population prevalence weighted by the relative risk. Additionally, information was sourced from official Brazilian government resources covering the years 1995 to 2017, resulting in a total of 338 state-year observations applied for temporal lagged analyses. First, we tested the SEV of 1-year lagged reproductive-age population (15–49 years) risk factors as exposures and the SEV of LBW as an outcome. In the second temporal lagged analysis, we tested the association between the SEV of LBW as the primary exposure and the SEV of high body mass index (HBMI) in peripubertal population 10 years later as the outcome. Fixed-effects multivariable linear regression models with lags were constructed, adjusting for socioeconomic covariates.

Results: The exposure of the reproductive-age population to smoking, alcohol, high systolic blood pressure, and HBMI was positively associated with the SEV of LBW. A diet high in sugar-sweetened beverages (SSB diet) was also positively associated, but the association disappeared when GDP per capita and access to primary care were added to the model. Regarding the repercussions of LBW, a 1-point increase in the SEV of LBW was associated with a 1.6-point increase in HBMI in the peripubertal population (95% CI: 0.66 to 2.55). However, this association disappeared after adjusting for GDP per capita and access to primary care, indicating their confounding roles.

Discussion: Our study highlights several risk factors in the adult population associated with LBW and its relationship with peripubertal HBMI. Interestingly, GDP per capita and access to primary care were found to be the socioeconomic determinants for birth outcomes as a result of exposure to the risk factors tested and the mid-term effects of LBW. These findings enhance our understanding of the role of socioeconomic factors contributing to LBW in LMICs and the need



ORIGINAL ARTICLE OPEN ACCESS

Oral and Systemic Health

Temporomandibular Disorders in Brain Injury Patients and Diagnostic Accuracy of the Assessment Tools

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Keywords: acquired brain injury | diagnostic validity | neurorehabilitation | stroke | temporomandibular disorders

ABSTRACT

Objectives: To evaluate the presence, severity and progression of temporomandibular disorders (TMD) in acquired brain injury (ABI) population and determine the diagnostic accuracy of 3Q/TMD and Fonseca Anamnestic Index (FAI) against the gold standard, Diagnostic Criteria for TMD (DC/TMD).

Methods: ABI individuals were assessed using 3Q/TMD and FAI at admission ($n = 73$) and Week 4 ($n = 52$), while DC/TMD was conducted only at Week 4. Diagnostic accuracy, sensitivity and specificity of 3Q/TMD and FAI were calculated against DC/TMD.

Results: TMD was detected in 66.0% (3Q/TMD) and 27.8% (FAI) at admission, with mild (75%) to moderate (25%) severity which was mostly pain-related. TMD frequency decreased to 11.3% (3Q/TMD) and 17.3% (FAI) by Week 4. Accuracy rates were 0.82 for 3Q/TMD and 0.83 for FAI. Sensitivity was 0.33 (3Q/TMD) and 0.50 (FAI), while specificity was high at 0.93 (3Q/TMD) and 0.90 (FAI).

Conclusions: TMD presence was higher in an ABI population compared to the general population however the frequency decreased over time. The high specificity and accuracy of 3Q/TMD and FAI indicate their potentials as screening tools but their low sensitivity limits their effectiveness in identifying all TMD cases. Patients with ABI should be assessed for TMD as part of their comprehensive care.

1 | Introduction

Acquired brain injury (ABI), which includes stroke and traumatic brain injury (TBI), is a major health concern and the main cause of disability and death in the high-income countries (Marshall et al. 2015; Sarti et al. 2000; Sussman et al. 2018; Wolfe 2000). In Denmark, over 230,000 people live with ABI

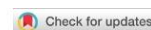
(Tibæk et al. 2018) with a prevalence of 4.4% of TBI and 2.1% of stroke in Danish population (Vestergaard et al. 2020). Depending on the severity of the central nervous system damage, sensorimotor deficits, speech and swallowing impairments, and psychological symptoms accompany stroke and TBI (Mayer and Esquenazi 2003; Sinanović 2010). Post-ABI sensorimotor deficits in the stomatognathic system that include the masticatory

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ORIGINAL ARTICLE



Oral conditions are associated with salt taste disability among American adults

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Abstract

Aim: To explore the association between oral conditions and their interaction with salt taste disability among American adults.

Methods: Data from the 2013–2014 NHANES cycle were used ($n=2373$). The exposures were periodontitis, defined by the 2017 EFP-AAP classification, dental caries, missing teeth, and edentulism, as per the DMF-T index, and xerostomia. The outcome was salt taste disability, objectively assessed. Covariates included sex, age, educational level, poverty index, obesity, diabetes, smoking, alcohol consumption, and medications related to mouth dryness. Weighted multivariable logistic regression modeling was used to evaluate the relationship between oral conditions and their interaction and salt taste disability.

Results: Participants who reported xerostomia were more likely to have salt taste disability (OR 2.42; 95%CI 1.44–4.07), especially those older than 60 years (OR 3.63; 95%CI 1.72–7.63). Among participants aged 40–59, xerostomia increased the chance of salt taste disability; however, the confidence interval included the null value. The interactions between xerostomia and edentulism increased the chance of salt taste disability.

Conclusion: Oral conditions seem to influence the ability to taste salt. Dental professionals may help identify individuals with taste alterations and raise their awareness of the risk of systemic diseases that require the reduction of salt intake.

KEYWORDS

chemosensory disorders, dental caries, edentulism, periodontal diseases, taste, xerostomia

1 | INTRODUCTION

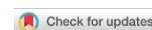
Taste perception refers to how individuals perceive and discriminate chemical stimuli like flavors (Dobrow et al., 2021). In the United States, distorted taste perception can be found in 17% of the adult population and is more common among older persons (Liu

et al., 2016). Taste impairment has been associated with an increased mortality risk, as it impacts one's ability to detect environmental hazards (Reed & Knaapila, 2010), such as rotten food.

Taste perception also influences diet and food intake (Boesveldt & de Graaf, 2017), which, in turn, has been associated with the development of non-communicable diseases (Catamo et al., 2021).

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SYSTEMATIC REVIEW

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Burden of severe periodontitis and edentulism in 2021, with projections up to 2050: The Global Burden of Disease 2021 study

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Abstract

Aim: To (i) assess the prevalence, incidence, and burden of severe periodontitis and edentulism in 2021, and (ii) forecast their rates in 2050.

Methods: Prevalence, incidence, and Years Lived with Disability (YLDs) for severe periodontitis and edentulism in 2021 were gathered globally, covering 204 countries, seven super regions, and 21 regions from the Global Burden of Disease (GBD) 2021 study. Prevalence, incidence, and YLDs due to periodontitis and edentulism to 2050 were projected using mixed-effects models with the socio-demographic index as the main covariate.

Results: In 2021, over 1 billion people were affected by severe periodontitis (1066.95 million; 95% UI: 896.55–1234.84), with a global age-standardized prevalence of 12.50% (10.53–14.49). South Asia had the highest prevalence rate, at 17.57% (14.73; 20.14). Edentulism affected 353 million people globally (300.60–416.20), resulting in an age-standardized prevalence of 4.11% (3.50; 4.83). The highest edentulism prevalence was found in Latin America and the Caribbean, at 7.39% (6.44; 8.39). By 2050, more than 1.5 billion people (+44.32%) are projected to have severe periodontitis, and over 660 million (+84.40%) to be edentulous. In the same year, 19.67% (130.23 million) of the edentulous people worldwide will be located in China. Severe periodontitis is expected to move up one position, and edentulism nine positions, among the most impactful Level 4 diseases/conditions affecting YLDs worldwide by 2050.

Conclusion: Severe periodontitis and edentulism remain major public health challenges in 2021, with the number of affected individuals projected to rise significantly in the coming decades.

KEYWORDS

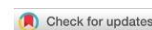
demography, edentulism, epidemiologic factors, epidemiology, forecasting, global disease burden, global health, morbidity, periodontal diseases

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NARRATIVE REVIEW

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Oral and systemic health in Singapore: Revisiting the past to define the future

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Abstract

Objectives: This study aimed to identify studies exploring oral and systemic conditions using Singapore data.

Methods: Studies were searched using the databases PubMed, Embase and Web of Science, with no publication date or language restrictions. Studies analysing Singaporean data were included in this review.

Results: Six domains were identified: pregnancy and gingivitis; tooth eruption, dental caries and early-life factors; Crohn's disease and oral microbiome; diabetes and periodontal diseases; number of teeth, chewing ability and cognitive status; and oral health and pneumonia. Using data from Singapore, oral-systemic studies have prompted reflections on the aetiopathogenesis of oral disorders, such as common causes connecting oral and systemic chronic conditions. Moreover, it is speculated whether oral conditions could be used as a marker to predict future systemic diseases or whether early-life factors could affect the development of oral and systemic immune responses.

Conclusions: While Singapore provides opportunities to explore challenges connected to healthy ageing, it also explores health development in many stages of life. Singapore has been prioritizing investigations on a healthier life, and new initiatives are paving the way for oral health research across the lifespan.

KEYWORDS

child development, dental caries, diabetes, intestinal diseases, mental health, microbiome, oral health, periodontal diseases, tooth loss

1 | INTRODUCTION

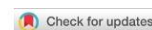
The pursuit of understanding the relationship between oral and systemic conditions represents a large portion of dentistry publications. Studies on the oral-systemic relationship have led to reflections on the aetiopathogenesis of oral conditions.¹ Rather than assuming causality, the field has started to explore common causes linking oral and systemic diseases and speculate whether oral conditions could

be used as markers to predict chronic diseases. Recent technological advancements have paved the way for integrating data generated from various omics techniques, such as genomics, proteomics, metabolomics and transcriptomics, to comprehend biological mechanisms that operate across the spectrum of oral health determinants (Figure 1). For instance, the association between higher levels of nitrate-reducing oral bacteria and lower levels of plasma glucose and blood pressure indicate a codependence between the oral

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ORIGINAL ARTICLE



Chronic oral disease burden at the first 1000 days: Intergenerational risk factors, BRISA cohort

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Abstract

Objective: To analyze multiple-causal models, including socioeconomic, obesity, sugar consumption, alcohol smoking, caries, and periodontitis variables in pregnant women with early sugar exposure, obesity, and the *Chronic Oral Disease Burden* in their offspring around the first 1000 days of life.

Methods: The BRISA cohort study, Brazil, had two assessments: at the 22nd–25th gestational weeks and during the child's second year ($n = 1141$). We proposed a theoretical model exploring the association between socioeconomic and pregnancy factors (age, smoking, alcohol, sugars, obesity, periodontitis, and caries) and child's variables (sugars and overweight) with the outcome, *Chronic Oral Disease Burden* (latent variable deduced from visible plaque, gingivitis, and tooth decay), using structural equation modeling.

Results: Caries and periodontitis were correlated in pregnant women. Addictive behaviors in the gestational period were correlated. Obesity (Standardized coefficient - $SC = 0.081$; $p = 0.047$) and added sugar consumption ($SC = 0.142$; $p = 0.041$) were observed intergenerationally in the pregnant woman-child dyads. Sugar consumption by the children ($SC = 0.210$; $p = 0.041$) increased the *Chronic Oral Disease Burden*.

Conclusions: Poor caries and periodontal indicators were correlated in pregnant women and their offspring. Obesity and sugar consumption act intergenerationally. Oral health in early life may change life trajectory since the worst oral conditions predict main NCDs.

KEYWORDS

dental caries, noncommunicable diseases, obesity, periodontal disease, pregnancy, sugars

1 | INTRODUCTION

Noncommunicable diseases (NCDs) are the leading cause of all deaths globally, represented by four main groups: cardiovascular diseases,

cancers, chronic respiratory diseases, and diabetes (WHO, 2021). Meanwhile, caries and periodontitis are the most prevalent NCDs worldwide (Peres et al., 2019). In childhood, caries is associated with asthma (Agostini et al., 2019). Later in life, periodontitis may predict

Article

Obesity, Insulin Resistance, Caries, and Periodontitis: Syndemic Framework

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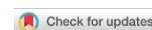
Abstract: (1) Background: To investigate the grouping of obesity and insulin resistance with caries and periodontitis from a syndemic perspective through pathways of socioeconomic inequalities, smoking, alcohol, and high sugar consumption in adolescence. (2) Methods: The population-based RPS Cohort study, São Luís, Brazil, in ages 18–19 years ($n = 2515$) was used. The outcomes were the grouping of obesity and Insulin Resistance Phenotype (latent variable formed by Triglycerides/HDL ratio, TyG index, and VLDL) and the Chronic Oral Disease Burden (latent variable comprising caries, bleeding on probing, probing depth ≥ 4 mm, clinical attachment level ≥ 3 mm, and visible plaque index $\geq 15\%$). Socioeconomic Inequalities influencing the Behavioral Risk Factors (latent variable formed by added sugar, smoking, and alcohol) were analyzed using structural equation modeling. (3) Results: Socioeconomic Inequalities were associated with the Chronic Oral Disease Burden [Standardized Coefficient (SC) = 0.222, $p < 0.001$]. Behavioral Risk Factors were associated with increased Chronic Oral Disease Burden (SC = 0.103; $p = 0.013$). Obesity was associated with the Insulin Resistance Phenotype (SC = 0.072; $p < 0.001$) and the Chronic Oral Disease Burden (SC = 0.066; $p = 0.005$). The Insulin Resistance Phenotype and the Chronic Oral Disease Burden were associated (SC = 0.053; $p = 0.032$). (4) Conclusion: The grouping of obesity and early events of diabetes with caries and periodontitis call for a syndemic approach in adolescence.

Keywords: syndemic; insulin resistance; obesity; caries; periodontitis; adolescents

1. Introduction

Syndemia is the interaction of two or more diseases, co-occurring or sequential, triggered by economic, social, and environmental contextual risks, multiplying the overall burden of diseases in a scenario of social injustice [1,2]. Social vulnerability favors aggregating behavioral risk factors to form a syndemic interplay, like non-communicable disease (NCD) grouping [1].

Syndemic models allow for the investigation of pathways through which inequality contributes to behavioral risk factors resulting in disease grouping. When sifting through the literature, no studies using the syndemic approach to analyze a set of NCDs in adolescence, including oral diseases, were found. Caries and periodontitis are among the



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ORIGINAL ARTICLE



Sugar intake above international recommendations and oral disease burden: A population-based study

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Abstract

Objective: To evaluate the association between added sugar intake above the daily limit for the risk of noncommunicable diseases (NCDs) and the *Chronic Oral Disease Burden* in adolescents.

Methods: This was a population-based study using cross-sectional data nested to RPS Cohorts Consortium, São Luís, Brazil, from the 18–19-year-old follow-up ($n = 2515$). High consumption of added sugars was estimated according to the limits of the World Health Organization guidelines (WHO) ($\geq 5\%$ of total energy/day) and the American Heart Association statement (AHA) (≥ 25 g/day). The *Chronic Oral Disease Burden* was a latent variable (number of decayed teeth, periodontal probing depth ≥ 4 mm, clinical attachment level ≥ 3 mm, and bleeding on probing). Models were adjusted for *Socioeconomic Status*, sex, obesity, and plaque index and analyzed through structural equation modeling.

Results: Adolescents had high sugar consumption according to the WHO (78.6%) and AHA (81.4%) recommendations. High sugar intake, according to WHO ($SC = 0.096$; $p = 0.007$) and AHA ($SC = 0.056$; $p = 0.027$), was associated with a heavier *Chronic Oral Disease Burden*. Even half of the recommended dose was sufficient to affect some oral disease indicators.

Conclusion: Sugar intake over international statements to prevent NCDs is associated with higher *Chronic Oral Disease Burden* among adolescents.

KEYWORDS

added sugars, caries, periodontal disease

1 | INTRODUCTION

Noncommunicable Diseases (NCDs) are the leading causes of death worldwide (WHO, 2021). Caries and periodontitis have been in the spotlight because they are the most prevalent NCDs (GBD, 2017) and predict other NCDs in the future, such as diabetes and cardiovascular diseases (Demmer et al., 2008; Morita et al., 2016).

An unhealthy diet is a behavioral risk factor for NCDs (WHO, 2021), represented by the inclusion of discretionary food and drinks with high energy density and low nutrients (AHA, 2017). Added sugars are the primary discretionary calories in the westernized diet (AHA, 2017; WHO, 2015). Systematic reviews showed an association between the consumption of added sugars, especially sugar-sweetened beverages, with obesity (Ruanpeng et al., 2017), diabetes (Qin et al., 2020) and