JÉSSICA BEVENUTO MATTAR

DIETARY PATTERNS, GLOBAL SYNDEMIC COMPONENTS AND AN EXPOSOME APPROACH: A COMPREHENSIVE DATA ANALYSIS OF THE CUME STUDY

Dissertation submitted to the Nutrition Science Graduate Program of the Universidade Federal de Viçosa in partial fulfillment of the requirements for the degree of Doctor Scientiae.

Adviser: Josefina Bressan

Co-advisers: Ana Luiza Gomes Domingos
Helen Hermana Miranda Hermsdorff
Marcos Heil Costa

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Josefina Bressan
Adviser

Dedico este trabalho às futuras gerações. Que este pequeno grão de areia seja peça fundamental para a construção de um mundo melhor, com menos ideologias e mais práticas baseadas em evidências; com menos ganância e mais interesses coletivos; com menos poluição e mais vida ao ar livre; com menos doenças e mais realizações de sonhos.

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“If we cannot sustain the environment, we cannot sustain ourselves.”

Wangari Maathai

ABSTRACT

MATTAR, Jéssica Bevenuto, D.Sc., Universidade Federal de Viçosa, April, 2024. **Dietary patterns, global syndemic components and an exposome approach: a comprehensive data analysis of the cume study**. Adviser: Josefina Bressan. Co-advisers: Ana Luiza Gomes Domingos, Helen Hermana Miranda Hermsdorff, and Marcos Heil Costa.

The pandemics of obesity, malnutrition and climate change make up the Global Syndemic, which has food systems as one of the main determinants in common. Current food systems have changed eating patterns based on natural and fresh foods to patterns rich in foods from animal source and ultra-processed foods. Researchers have debated the impact of different dietary patterns on human and environmental health, but no study has focused on the relationship between Brazilian dietary patterns and the three components of the global syndemic. Furthermore, the multiple and complex etiology of obesity, in addition to new evidence that points to relationships between climate change and obesity, reveals the need to study obesity using the exposome approach, which is the cumulative measure of environmental influences and associated biological responses throughout the lifespan. Therefore, the objective of this thesis was to evaluate the association between the dietary patterns of participants of the Cohort of Universities of Minas Gerais (CUME Study) and the components of the global syndemic, focusing on the relationship between obesity and climate change. To this end, cross-sectional and longitudinal analyzes were conducted using data from the CUME Study. Graduates from Minas Gerais universities participating in the CUME Study answered baseline (Q_0), two (Q_2), four (Q_4) and six (Q_6) year follow-up questionnaires in a virtual environment. Q_0 consists of 83 questions about lifestyle, sociodemographic, anthropometric, and clinical data, individual and family morbidity, in addition to a semi-quantitative Food Frequency Questionnaire (FFQ). The follow-up questionnaires aimed to identify changes in the data provided in Q_0. Dietary patterns were determined from FFQ data, through principal component analysis, and were associated, using the linear regression technique, with (1)undernutrition, assessed as insufficient intake of vitamins and minerals; (2)climate change, assessed by the carbon, water and ecological footprints of the food consumed; and (3)obesity, assessed by Body Mass index (BMI). Air pollution is closely related to climate change. Therefore, an assessment of the effect of long-term exposure to fine particulate matter ($PM_{2.5}$) on longitudinal changes in BMI was conducted using multilevel linear mixed-effects models to assess the association between obesity and climate change. Furthermore, obesity was assessed using the exposome approach, using supervised classification models. Thus, five decision tree-based algorithms were conducted in RStudio® (4.3.3) to predict obesity using the Caret package. The algorithms performed were Random-Forest, Rpart/Cart, c5.0, Bagging and Boosting. Different partitions of the database were tested and accuracy was used as a criterion for determining the best model fit. Four dietary patterns were identified: (1)Unhealthy dietary pattern, which increased the odds of obesity and micronutrient inadequacy and presented the greatest environmental impact for the three parameters evaluated; (2)Brazilian dietary pattern, which increased the chance of obesity and micronutrient inadequacy and had the lowest environmental impact; (3)Healthy dietary pattern, which was protective against micronutrient inadequacy; and (4)Dairy dietary pattern, which had the greatest protective effect against Calcium inadequacy. No direct effect between $PM_{2.5}$ and BMI was found. However, an interaction effect between $PM_{2.5}$ and physical activity on BMI was observed. In adjusted analyses, BMI was significantly higher among those physically inactive and exposed to 15-30 $\mu g/m^3$ $PM_{2.5}$, compared to those who are insufficiently active. When compared with those who are physically active, those who are inactive had a significantly higher BMI when exposed to $PM_{2.5} \geq 15$ $\mu g/m^3$. The Boosting model presented the best performance for predicting obesity. Then, a plot of the importance of variables was extracted from this model. The plot revealed that unhealthy dietary pattern is the most significant predictor of obesity, followed by age, maternal obesity, TV usage, per capita income of the census tract where the participants live, siblings' obesity, exposure to $PM_{2.5}$, Brazilian dietary pattern, father's obesity and individual income. This study highlights the importance of public policy actions to incorporate the costs of effects on human and planetary health, to align the Brazilian diet with the Brazilian Dietary Guideline, to control air pollution while encouraging increasing the practice of physical activity and improving the housing conditions of those living in regions of lower socioeconomic status.

Keywords: Sustainable diet; Air pollution; Body Mass Index; Long-term effects; Machine learning.

RESUMO

MATTAR, Jéssica Bevenuto, D.Sc., Universidade Federal de Viçosa, abril de 2024. **Padrão alimentar, componentes da sindemia global e uma abordagem expossoma: uma abrangente análise de dados do Estudo CUME**. Orientadora: Josefina Bressan. Coorientadores: Ana Luiza Gomes Domingos, Helen Hermana Miranda Hermsdorff e Marcos Heil Costa.

As pandemias de obesidade, desnutrição e mudanças climáticas compõem a Sindemia Global, que tem os sistemas alimentares como um dos principais determinantes em comum. Os atuais sistemas alimentares têm alterado os padrões alimentares baseados em alimentos *in natura* e frescos para padrões ricos em alimentos de origem animal e ultraprocessados. Pesquisadores têm debatido sobre o impacto de diferentes padrões alimentares na saúde humana e ambiental, mas nenhum estudo focou na relação entre padrões alimentares brasileiros e os três componentes da sindemia global. Além disso, a múltipla e complexa etiologia da obesidade, em adição às novas evidências que apontam relações entre as mudanças climáticas e obesidade, revela a necessidade de estudar a obesidade sob a abordagem expossoma, que é a medida cumulativa de influências ambientais e respostas biológicas associadas ao longo da vida. Portanto, o objetivo desta tese foi avaliar a associação entre os padrões alimentares dos participantes da Coorte de Universidades Mineiras (Estudo CUME) e os componentes da sindemia global, com foco na relação entre obesidade e mudanças climáticas. Para isso, análises transversais e longitudinais foram conduzidas. Egressos de universidades mineiras participantes do Estudo CUME responderam questionários de linha de base (Q_0), de dois (Q_2), de quatro (Q_4) e de seis (Q_6) anos de seguimento em ambiente virtual. O Q_0 é composto por 83 questões sobre estilo de vida, dados sociodemográficos, antropométricos e clínicos, morbidade individual e familiar, além de um questionário de frequência de consumo alimentar (QFCA) semiquantitativo. Os questionários de seguimento objetivaram identificar alterações nos dados fornecidos no Q_0. Os padrões alimentares foram determinados a partir dos dados do QFCA, por meio de análise de componentes principais, e foram associados, com a técnica de regressão linear, à (1)desnutrição, avaliada como ingestão insuficiente de vitaminas e minerais; (2)às mudanças climáticas, avaliada pelas pegadas de carbono, de água e ecológica dos alimentos consumidos; e (3)à obesidade, avaliada pelo cálculo e classificação do Índice de Massa Corporal (IMC). A poluição do ar está intimamente relacionada às mudanças climáticas. Assim, a avaliação do efeito da exposição de longo prazo ao Material Particulado Fino ($PM_{2.5}$) nas mudanças longitudinais no IMC foi conduzida por meio de modelos lineares de efeitos mistos multinível, para avaliar a associação entre obesidade e mudanças climáticas. Ainda, a obesidade foi avaliada por meio da abordagem expossoma, a partir de modelos de classificação supervisionada. Assim, cinco algoritmos baseados em árvore de decisão foram conduzidos no RStudio® (4.3.3) para predizer a obesidade, usando o pacote Caret. Os algoritmos performados foram o Random forest, Rpart/Cart, c5.0, Bagging e Boosting. Diferentes partições do banco de dados foram testadas e a acurácia foi usada como critério para determinação do melhor ajuste de modelo. Quatro padrões alimentares foram identificados: (1)Padrão alimentar não saudável, que aumentou a chance de obesidade e de inadequação de micronutrientes e apresentou o maior impacto ambiental para os três parâmetros avaliados; (2)Padrão alimentar brasileiro, que aumentou a chance de obesidade e de inadequação de micronutrientes e apresentou o menor impacto ambiental; (3)padrão alimentar saudável, que foi protetivo contra a inadequação de micronutrientes; e (4)Padrão alimentar lácteo, que teve o maior efeito protetor contra a inadequação de Cálcio. Nenhum efeito direto entre $PM_{2.5}$ e IMC foi encontrado. No entanto, foi observado um efeito de interação entre $PM_{2.5}$ e atividade física no IMC. Nas análises ajustadas, o IMC foi significativamente maior entre aqueles fisicamente inativos e expostos a 15-30 $\mu g/m^3$ $PM_{2.5}$, em comparação com aqueles insuficientemente ativos. Quando comparados com os fisicamente ativos, aqueles inativos apresentaram IMC significativamente maior quando expostos a $PM_{2.5} \geq 15$ $\mu g/m^3$. O modelo Boosting apresentou a melhor performance para a predição de obesidade. Então, um gráfico de importância das variáveis foi extraído deste modelo. O gráfico revelou que o padrão alimentar não saudável é o preditor mais significativo para a obesidade, seguido por idade, obesidade materna, tempo gasto na televisão, renda per capta do setor censitário onde os participantes vivem, obesidade de irmãos, exposição à $PM_{2.5}$, padrão alimentar brasileiro, obesidade paterna e renda individual. Este estudo destaca a importância de ações de políticas públicas para a incorporação dos custos dos efeitos à saúde humana e planetária, para o alinhamento da dieta brasileira ao Guia Alimentar Para a População Brasileira, para controlar a poluição do ar ao mesmo tempo em que se incentiva o aumento da prática de atividade física e para melhorar as condições de moradia daqueles que vivem em regiões de menor nível socioeconômico.

Palavras-chave: Dieta sustentável; Poluição do ar; Índice de Massa Corporal; Efeito de longo prazo; Aprendizagem de máquina.

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LIST OF ABBREVIATIONS AND ACRONYMS

ACAG – Atmospheric Composition Analysis Group
AI – Adequate Intake
AOD – Aerosol Optical Depth
BAT – Brown Adipose Tissue
BMI – Body Mass Index
BTS – Bartlett's Sphericity Test
Ca – Calcium
CF – Carbon Footprint
CH4 – Methane
CI – Confidence Interval
CNAE – National Classification of Economic Activities (Classificação Nacional das Atividades Econômicas *from Portuguese*)
CO – Carbon Monoxide
CO2 – Carbon Dioxide
CO_2e – Carbon Dioxide equivalent
CTM – Chemical Transport Model
Cu – Copper
CUME – Cohort of Universities of Minas Gerais
DAG – Directed Acyclic Graphs
DP – Dietary Patterns
DRIs – Dietary Reference Intake
EAR – Estimated Average Requirement
EF - Ecologic Footprint
Fe – Iron
FFQ – Food Frequency Questionnaire
GBD – Global Burden Disease
GDP – Gross Domestic Product
GGE – Greenhouse Gas Emissions
GHG – Greenhouse gas
GWP – Global Warming Potential factor
GWR – Geographically-weighed regression
IBGE – Brazilian Institute of Geography and Statistics
IMC – Índice de Massa Corporal
IPCC – Intergovernmental Panel on Climate Change
K – Potassium
Kcal – kilocalories
KMO – Kaiser-Meyer-Olkin test
LMICs – Low-Middle Income Countries
Mg – Manganese
MODIS – Moderate Resolution Imaging Spectroradiometer
N2O - Nitrous oxide
NASA – National Aeronautics and Space Administration
NCD – Non-Communicable Diseases
NDVI – Normalized Difference Vegetation Index
NO2 – Nitrogen Dioxide
O3 – Ozone
PCA – Principal Components Analysis

PM – Particulate Matter
$PM_{0.1}$ – Particulate Matter < 0.1 µm
PM_{10} – Particulate Matter < 10 µm
$PM_{2.5}$ – Particulate Matter < 2.5 µm
POF – Household Budget Survey (Pesquisa de Orçamentos Familiares *from Portuguese*)
Q_0 – Baseline questionnaire
Q_2 – 2 years follow-up questionnaire
Q_4 – 4 years follow-up questionnaire
Q_6 – 6 years follow-up questionnaire
ROS – Reactive Oxygen Species
ROSE – Random Over-Sampling Examples
Se – Selenium
SMOTE – Synthetic Minority Over-sampling Technique
SO2 – Sulfur Dioxide
UFJF – Universidade Federal de Juiz de Fora
UFLA – Universidade Federal de Lavras
UFMG – Universidade Federal de Minas Gerais
UFOP – Universidade Federal de Ouro Preto
UFV – Universidade Federal de Viçosa
UFVJM – Universidade Federal dos Vales de Jequitinhonha e Mucuri
UNIFAL – Universidade Federal de Alfenas
UPF – Ultra-processed food
WAT – White Adipose Tissue
WF – Water Footprint
WHO – World Health Organization
Zn – Zinc

SUMMARY

1. INTRODUCTION

The world faces an increase in urbanization and the emergence of new technologies that are shifting the manners of transportation, leisure, and employment. It results in a modern society characterized by a busy life, with an accumulation of activities and lack of time, altering food demand (FAO, 2013, 2023; FIESP, 2010; MACKAY et al., 2017). The current model of living is also related to increasing per capita Gross Domestic Product (GDP) that changes per capita demand for crop calories or protein (TILMAN et al., 2011). Thus, food systems are responding and shaping these demands (FAO, 2013; FIESP, 2010), generating a nutritional transition that has changed dietary patterns worldwide (FAO, 2013; KAC; SICHIERY; GIGANTE, 2007).

Current food patterns are characterized by higher consumption of animal-source foods and ultra-processed food (UPF) (FAO, 2013; KAC; SICHIERY; GIGANTE, 2007; MAGKOS et al., 2020; PAHO, 2015), making them one of the underlying factors to contribute to three components of The Global Syndemic (SWINBURN et al., 2019): undernutrition (CROVETTO et al., 2014; FAO, 2013; LOUZADA et al., 2015a, 2015b; MONTEIRO et al., 2010a; RAUBER et al., 2018), climate change (FAO, 2006, 2015; FOLEY et al., 2011; FRESÁN et al., 2021; IPCC, 2019; TILMAN et al., 2011; VERMEULEN; CAMPBELL; INGRAM, 2012), and obesity (JUUL et al., 2018; MONTEIRO et al., 2017; SILVA et al., 2018).

Among the three components of the Global Syndemic, obesity stands out in this research. Despite the recommendations from international authority organizations to reverse the obesity pandemic scenario, obesity continues to increase inexorably worldwide (WHO, 2000, 2018, 2024; WORLD OBESITY FEDERATION, 2023).

Obesity is widely studied. However, given its complexity and multiple associated factors, its understanding is arranged across different and specific areas of study. Research on the determinants of obesity indicates to genetic factors and their complex gene-gene and gene-environment interactions (HERMSDORFF; BRESSAN, 2019a, 2019b; WEI; TANG; LI, 2014; WHO, 2000), environmental factors that mold an obesogenic environment (SWINBURN; EGGER; RAZA, 1999), which is associated with the physical inactivity and overconsumption of unhealthy foods (BURGOINE et al., 2014; DREWNOWSKI et al., 2020; WILKINS et al., 2019, 2017), and even air pollution has been identified as another possible factor associated with obesity (AN et al., 2018; DI GREGORIO et al., 2019; HERSOUG; SJODIN; ASTRUP, 2012; HUANG; LEUNG; SCHOOLING, 2019).

The links between climate change and undernutrition, and undernutrition and obesity are already very well established. It is known that there are also links between climate change and obesity. However, it deserves new investigations (SWINBURN et al., 2019). In this context, $PM_{2.5}$, a common proxy indicator of air pollution, is closely associated with climate change, making it a useful tool for studying the connection between climate change and obesity (WHO, 2022). Also, so that this relationship can be investigated, analysis tools that go beyond of reductionist approach on disease´s basis that isolate the effects of individual factors need to be explored. Emergent approaches are making the simultaneous evaluation of multiple stressors more feasible (MCHALE et al., 2018). Among them, the exposome stands out, which can be understood as "life-course environmental exposures, from the prenatal period onwards" (WILD, 2005).

The multiple and complex etiology of obesity added to this new evidence of its relationship with climate change and the lack of studies that assess the determinants of obesity in an integrated, simultaneous manner and with more robust statistical techniques and computational analysis, capable of aggregating such heterogeneous data in the same analysis, reveal the importance of studying obesity under an exposome approach. In addition, data about what type of dietary patterns are both healthy and sustainable are still uncertain, mainly in the Brazilian context.

2. LITERATURE REVIEW

2.1. The Global Syndemic of Obesity, Undernutrition, and Climate Change

A syndemic is defined as two or more diseases that (1)co-occur in time and place; (2)interact with each other at biological, psychological, or social levels; and (3)share common underlying determinants (SINGER, 1996).

The syndemic concept was originally used to describe the interaction of two or more diseases at the individual level (SINGER, 1996; SWINBURN et al., 2019). However, it has received a rearrangement to describe health problems within a population that synergistically contributes to, and results from, persistent social and economic inequalities (MENDENHALL et al., 2017; SWINBURN et al., 2019).

Therefore, the syndemic concept also can provide a useful construct to consider the interaction of two or more pandemics (SWINBURN et al., 2019). The syndemic framework goes beyond disease-specific models to evaluate how social and economic conditions favor disease clustering in populations and what interventions might be most effective for mitigating it (MENDENHALL et al., 2017).

Thereby, considering that (1)the syndemic theory provides a basis to advance health systems by bringing several fields together to recognize, and correctly intervene in the complex multiple diseases that affect susceptible populations; and, (2)despite the recommendations from international health authority organizations to reverse the obesity pandemic scenario, obesity continues to increase worldwide (WHO, 2000, 2018) (MENDENHALL et al., 2017), The Lancet Commission on Obesity developed a wider approach to obesity, based on the notion that the obesity pandemic is one component of The Global Syndemic, which also includes undernutrition and climate change (SWINBURN et al., 2019).

The Commission calls these three pandemics The Global Syndemic because (1)their interactions occur at both the individual and population levels; (2) emphasize the major global importance of this cluster of pandemics, which are the dominant causes of human and planetary illness; and (3)because its acknowledgment as such provides a more comprehensive view of their interactions, allowing common systemic actions to simultaneously mitigate them (SWINBURN et al., 2019).

The background for The Global Syndemic is the wider representation of the four major global outcomes of concern for people and the planet, which are economic prosperity, social equity, and human and ecological health and well-being. To achieve economic prosperity, the human systems have been designed in a way that causes negative externalities for the other three outcomes (SWINBURN et al., 2019).

2.1.1. Obesity, undernutrition, and climate change co-occur in time and place

Globally, the prevalence of obesity has more than doubled since 1990. In 2022, 2.5 billion adults were with overweight (about 43% of the world population). Of these, 890 million were with obesity, which represents about 16% of the world population (WHO, 2024). Projections estimate that by 2035, almost two billion people will be affected by obesity, which will rise to 24% of the population (WORLD OBESITY FEDERATION, 2023).

Once considered a problem in high-income countries, obesity rates are now increasing in all regions of the world, regardless of the economic level of the countries. Although it is still more prevalent in high- and upper-middle-income countries (where it nearly tripled between 1975 and 2016, from 8.8% to 25.9%), the obesity prevalence increased more than 7-fold in low-income countries in the same period, increasing from 0.8% to 5.8% (WORLD HEALTH ORGANIZATION, 2018, 2020).

In Brazil, the frequency of obesity increased, on average, by 0.63 percentage points per year from 2006 to 2019 (BRASIL. MINISTÉRIO DA SAÚDE, 2020). In 2023, the frequency of Brazilians with obesity was 24.3% (BRASIL. MINISTÉRIO DA SAÚDE, 2023).

The prevalence of obesity among children is also relentless. In 2016, 40 million children under 5 years old, and 340 million children and adolescents 5–19 years old were considered with overweight or obesity. Children with obesity are more likely to present Non-Communicable Diseases (NCD), and premature death in adult life (WORLD HEALTH ORGANIZATION, 2018, 2020). Based on these data, almost half of the world's adult population will be with overweight or obesity by 2030 (MCKINSEY GLOBAL INSTITUTE, 2014).

Global Burden Disease (GBD) study data show that in 2017, high Body Mass Index (BMI) was the fourth biggest cause of premature mortality globally, accounting for 4.72 million deaths and 148 million years of healthy life lost to disability (STANAWAY et al., 2018), which generates high costs, reaching about 2.8% of the global GDP (MCKINSEY GLOBAL INSTITUTE, 2014).

On the other hand, although the prevalence of undernutrition has been declining, it is still unacceptably high. Even though undernutrition is more prevalent in Low-Middle Income Countries (LMICs), every country in the world is affected by a burden of at least one malnutrition problem (childhood stunting, anemia in women of reproductive age, overweight in adult women) (DEVELOPMENT INITIATIVES, 2018).

In 2018, the Global Nutrition Report pointed out that of 141 countries, 88% face a high level of at least two types of malnutrition, and 29% face high levels of all three types. The Coexisting of malnutrition burdens exists not just within countries, but also within people. To exemplify, 8.23 million children are affected by stunting and overweight. Estimates of the global costs of malnutrition in all its forms are up to US$3.5 trillion per year (DEVELOPMENT INITIATIVES, 2018).

Malnutrition in all its forms is the main health problem worldwide, and it will be intensified by the effects of climate change (SWINBURN et al., 2019). Anthropogenic climate change is now unquestionable and represents the biggest global health threat (IPCC, 2023a; WATTS; ADGER; AGNOLUCCI, 2015). Data from the Sixth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) point out that widespread and fast changes in the atmosphere, ocean, cryosphere, and biosphere have occurred, and that increases in greenhouse gas (GHG) concentrations observed since 1750 are clearly anthropogenic (IPCC, 2021, 2023a).

Global surface temperature has increased at a faster rate since 1970 than in any other 50-year period in the last 2000 years. In 2011-2022, the temperature was 1.09°C higher than it was in 1850-1900. From 1850 to 2019, the total net CO_2 emissions were 2400 ± 240 $GtCO_2$, with more than half (58%) occurring between 1850 and 1989, and the remaining 42% between 1990 and 2019. As of 2019, the concentration of atmospheric CO_2 was higher than any other point in at least 2 million years, and CH_4 and N_2O concentrations were higher than at any time within the last 800,000 years (IPCC, 2023a). Likewise, the global mean sea level has risen faster since 1900 than over any previous century in the last 3000 years, increasing 0.20m between 1901 and 2018 (IPCC, 2021, 2023b, 2023a). Since 1950, human activities have increased the likelihood of extreme weather events such as heatwaves, heavy precipitation, droughts, and tropical cyclones. (IPCC, 2023a).

Estimates reveal that global surface temperature will continue to increase, and there is high confidence in saying that it is likely that global warming will exceed 1.5°C during the 21st century and make it harder to limit warming below 2°C (IPCC, 2023b).

Although LMICs are those that produce the fewest Greenhouse Gas Emissions (GGE), they are more damaged by climate change than the countries that produce the highest GGE (IPCC, 2023a; WATTS; ADGER; AGNOLUCCI, 2015). Therefore, it is estimated that climate change will cost 5 – 10% of the global GDP, with costs in LMICs surpassing 10% of their GDP (STERN, 2007).

The three components of The Global Syndemic not only coexist but also interact with each other, and share common underlying factors. There are several possible interactions among the components of The Global Syndemic, most of them display the food systems as a background.

2.1.2. Obesity, undernutrition, and climate change interact with each other

Figure 1 shows possible interactions among the components of The Global Syndemic. Climate change can affect the quantity and quality of food production through extreme weather events, such as drought or storms and floods, coastal erosion, warming oceans, rising sea levels, and air pollution (IPCC, 2023b; POTER et al., 2014; UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, 2017).

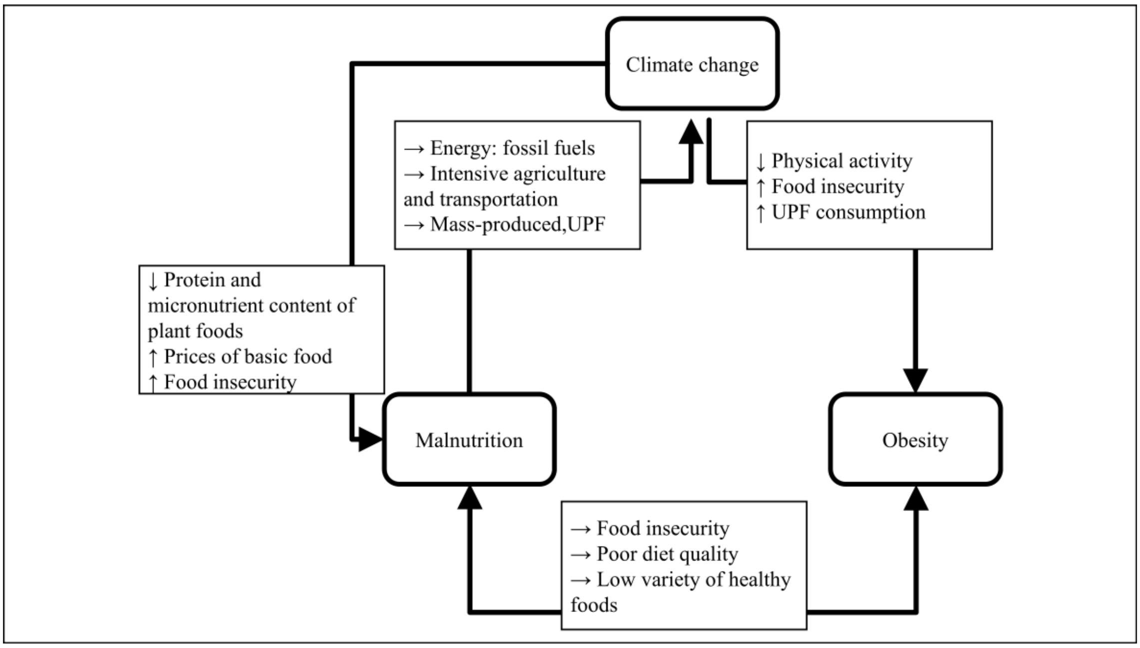

Figure 1. *Theoretical model of the interaction between components of The Global Syndemic.* ***Legend:*** *UPF: Ultra-Processed Food. Bold boxes represent the three components of the global syndemic. Lean boxes represent the interaction factors between the components of the global syndemic. Arrows indicate the directions of these interactions.* ***Source:*** *Own elaboration based on literature review.*

Several factors associated with climate change can decrease yields. Estimates suggest that climate change trends since 1980 have reduced global maize and wheat production by nearly 5%. Furthermore, climate change also can shift the nutritional composition of crops by reducing the protein and micronutrient content of plant foods. Grains and roots such as rice, wheat, barley, and potatoes experience 7–15% reductions in protein content. Cereal grains and legumes can present 3–11% decreases in zinc and iron concentrations. Also, under more severe conditions, a wide range of crops can experience 5–10% reductions in the concentration of phosphorus, potassium, calcium, sulfur, magnesium, iron, zinc, copper, and manganese (MYERS et al., 2017).

These changes in the nutrient value of foods contribute to undernutrition. When these nutrient changes are modeled across current diets, it is expected that more than 200 million new people will not reach their protein intake recommendations, 150–200 million new people will be placed at risk for zinc deficiency. Moreover, almost 60% of children ages 1–5 age and women of childbearing age live in countries where anemia rates exceed 20% of the population and where these nutrient changes will reduce even more dietary iron intake by 3.8% (MYERS et al., 2017).

All of these changes in quantity and quality of food production will also increase the prices of basic food, increasing chronic undernutrition among the most food-insecure population groups (POTER et al., 2014; UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, 2017).

Food systems are one of the largest ecosystem stressors. Globally, it is one of the biggest sources of biodiversity damage, water polluter and GGE, contributing 19–29% of total global anthropogenic GGE (VERMEULEN; CAMPBELL; INGRAM, 2012). In 2020, agricultural emissions (related to crops and livestock) accounted for the release of 10.5 billion tonnes of Carbon Dioxide equivalent (CO_2e) to the atmosphere. Agriculture emissions within the farm gate correspond to 70% of the total emission from the food systems, and it increased by 13% between 2000 and 2020. Livestock alone represents around 57% of this value (FAO, 2022). In 2021, food systems in Brazil emitted 1.8 billion tons of CO2e, accounting for 73.7% of the total emissions (OBSERVATÓRIO DO CLIMA, 2023).

The globalization of food systems depends on cheap energy from fossil fuels for intensive large-scale, agricultural production and long-haul transportation. It has exposed people to unhealthy food environments, dominated by UPF, which changes diet patterns worldwide (LOUZADA et al., 2019; SWINBURN et al., 2019).

Despite less understood, there are numerous interactions between climate change and obesity as well (SWINBURN et al., 2019). Changes in food production mentioned to be related to undernutrition are also related to obesity. The effect of climate change on fresh and natural food supply will make these products more expensive, changing eating patterns globally to UPF (high in fats, sugars, and sodium, and poor in bioactive compounds) (AN; JI; ZHANG, 2018), that are related to malnutrition, especially obesity (LOUZADA et al., 2019). Additionally, a mild level of food insecurity is associated with increased risks of obesity in high-income countries (MORADI et al., 2018). Therefore, the increase in food insecurity from changes in food production could elevate the prevalence of obesity (SWINBURN et al., 2019). Furthermore, increasing ambient temperatures could reduce physical activity, contributing to obesity as well (AN; JI; ZHANG, 2018).

Likewise, obesity and undernutrition interact with each other. Early-life malnutrition effects on adult life can be attributed to interconnected biological pathways, such as inflammation, metabolic dysregulation, and impaired insulin signaling (WELLS et al., 2020).

Exposure to early undernutrition is a predictor of future obesity. The mechanisms that explain this relationship include the fact that (1)there is a compensatory weight gain that prioritizes liponeogenesis over accretion of lean body mass, as an energy-saving mechanism;

and (2) through a reduction in metabolic capacity for homeostasis, mainly due to impaired insulin signaling (WELLS et al., 2020).

On the other hand, obesity is characterized by excess of metabolic fuel and elevated adiposity, creating a chronic inflammation status that challenges homeostasis, impairing micronutrients bioavailability. Also, the poor micronutrient status existent in obesity is a reflex of a poor diet quality characterized by a low variety of healthy foods (KIM et al., 2019; WELLS et al., 2020).

2.1.3. Obesity, undernutrition, and climate change have common underlying determinants

According to The Lancet Commission's report about The Global Syndemic, it is necessary to understand and address the underlying drivers of The Global Syndemic in a context that allows reaching the four major global outcomes of concern for people and the planet, that are economic prosperity, social equity, and human and ecological health and wellbeing. The report points out that five critical feedback loops (to know: the business, supply and demand, governance, ecological, and health feedback) need to be assessed within the major systems driving The Global Syndemic, that are food and agriculture, transportation, urban design, and land use (SWINBURN et al., 2019).

2.1.3.1. Food systems as syndemic drivers

Figure 2 presents the theoretical model of food systems acting as a syndemic driver. Current food systems are market-based, which combine businesses' profit motives with the demands of their customers. It results in a food value chain, which means, as food travels one way from one private operator to another, profits flow back the other way. This idea of adding value along the chain is responsible for making food systems more industrialized, globalized, and dominated by large actors capable of economies of scale and maintaining long supply chains, and creating a food environment dominated by ultra-processed foods (SWINBURN et al., 2019).

An inadequate diet is a shared denominator for all types of malnutrition (whether undernutrition, micronutrient deficiencies or overweight and obesity). It is important to notice that food systems regulate the diversity, quantity, quality, and nutritional content of the foods available (FAO, 2013).

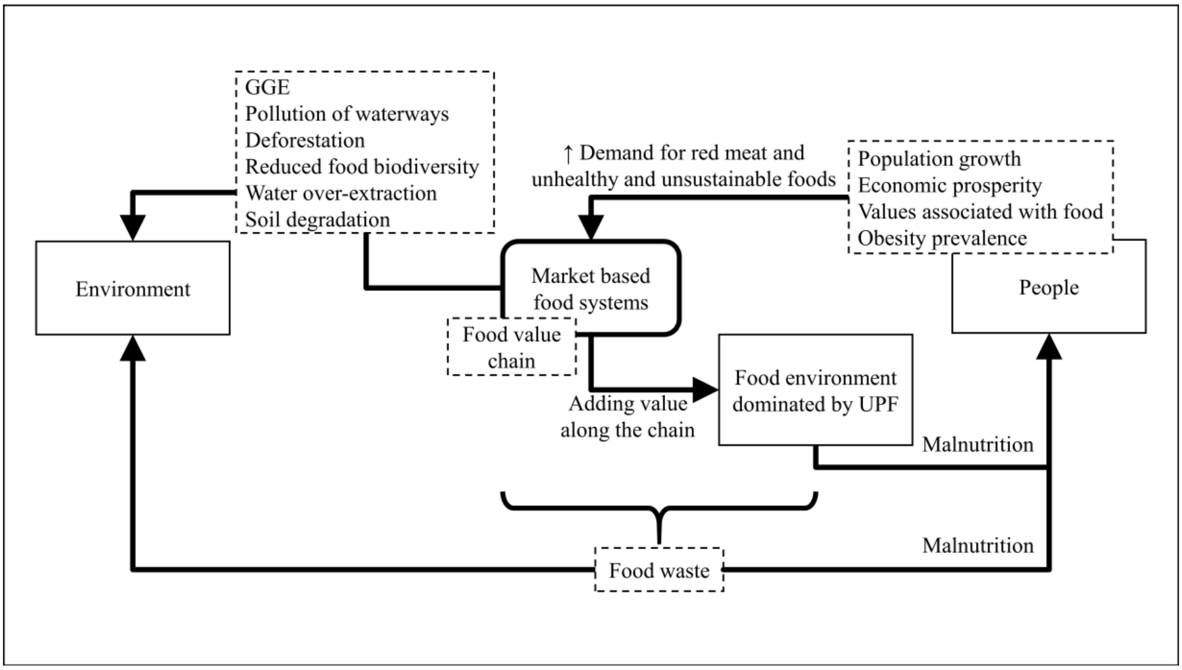

Figure 2. *Theorical model of food systems as a syndemic driver.* ***Legend:*** *GGE: Greenhouse Gas Emissions; UPF: Ultra-Processed Food. The bold box represents the food systems. Lean boxes represent the components that have been affected. Dashed boxes represent the characteristics of those components. Arrows indicate the directions of the interactions.* ***Source:*** *Own elaboration based on literature review.*

Current global food systems tend to favor energy-rich and nutrient-poor food production (SWINBURN et al., 2019). Thus, they are dominated by UPF, which accounts for a large proportion of diets around the world, becoming a big issue for nutrition, health, and well-being. The dominance of UPF in food systems makes food environments insalubrious and reproduces the negative effects of these foods on health (LOUZADA et al., 2019; MONTEIRO et al., 2012).

Ultra-processed foods induce unhealthy eating patterns (MONTEIRO et al., 2012, 2010b). Research has shown an association between consumption of UPF, poorer diet quality and negative health outcomes worldwide. Diets based on such foods present a less healthy nutritional profile (ADAMS; WHITE, 2015), with higher energy density, higher content of carbohydrates, free sugars, total fat, saturated fat, trans fat, and sodium (ADAMS; WHITE, 2015; CROVETTO et al., 2014; LOUZADA et al., 2015a; MONTEIRO et al., 2010a; MOUBARAC et al., 2012), which induce overweight, obesity, and associated diseases (CANELLA et al., 2014; FARDET, 2016; FIOLET et al., 2018; HALL et al., 2019; JUUL et al., 2018; LOUZADA et al., 2015c; MONTEIRO et al., 2017; SCHNABEL et al., 2019; SILVA et al., 2018; TAVARES et al., 2011).

On the other hand, the same dietary pattern is also related to lower fiber content, protein, vitamins (B12, D, E, niacin, and pyridoxine), and minerals (potassium, copper, iron, phosphorus, magnesium, selenium, and zinc) (CROVETTO et al., 2014; LOUZADA et al., 2015a, 2015b; MONTEIRO et al., 2010a; RAUBER et al., 2018), which induce undernutrition and micronutrient deficiencies (FAO, 2013). Moreover, in several regions, fruits, vegetables, and animal-source foods are unavailable and/or inaccessible, resulting in monotonous diets low in nutritional quality (SWINBURN et al., 2019).

The population growth in a world with economic systems that value GDP growth to the detriment of social equity, human and ecological health, increases the demand for red meat and unhealthy and unsustainable food. Thus, it leverages the current food systems model, which is a major contributor to climate change (FAO, 2006; FOLEY et al., 2011; LOUZADA et al., 2019; SWINBURN et al., 2019; TILMAN et al., 2011).

About 25-30% of total GGE are attributable to food systems. During 2007-2016, the major source of emission was agricultural production, accounting for 142Tg of CH4, 8.3Tg of N2O, and 4.8Gt of CO2 annually. This implies that the total GGE from agriculture was 6.2 Gt CO2e per year, increasing to 11Gt CO2e per year. Without intervention, these are likely to grow by 30%–40% by 2050, due to increasing demand based on population and income growth and changes in eating patterns (IPCC, 2019).

Besides, long supply chains in a food system favor food loss, which is related to (1) undernutrition by making fresh and healthy food unavailable and/or inaccessible; (2) obesity, by making fresh and healthy food more expensive than UPF; and (3) climate change by forcing the food production systems to produce more, and consequently pollute more. The necessary natural resources for the production of lost foods emit more than 3.3 billion tons of carbon dioxide annually, making food lost the third top GHG emitter in the world (FAO, 2015; SWINBURN et al., 2019; VERMEULEN; CAMPBELL; INGRAM, 2012).

2.1.3.2. Transportation systems, urban design, and land use as syndemic drivers

Transportation systems, urban design, and land use are interrelated systems that are associated with climate change and obesity through their effects on GGE, physical activity, and diet (SWINBURN et al., 2019).

Urban design and land-use planning include shaping, building, or retrofitting the built environment, open spaces, buildings (residential and commercial), and transportation systems. And, for that, they rely on the use of tools, such as land-use zoning and planning layouts of streets, roads, transportation, public spaces, and residential and commercial areas. Currently, there is increasing acknowledgment of the many ways in which urban planning and design can affect human health, and the many overlaps that exist between health and sustainability at the urban level. Therefore restoring the link between urban planning, public health and sustainability is of high urgency (SWINBURN et al., 2019).

The fitting urban design, land use planning, and transportation systems can facilitate and promote safe outdoor physical activity and active transportation. This includes eight key built-form characteristics stated as the 8Ds: density; destination; distance; design; diversity; demand; distribution; and desirability (MÜNZEL et al., 2021).

Higher population and development density lead to shorter travel distances. Shorter distances are easier and more convenient to walk or cycle and reduce car use. Destination accessibility concerns how accessible places are. Distance to transit means the shortest distance to a bus stop or railway station, encouraging the use of public and active transportation. Design defines the overall infrastructure and connectivity, and a good design encourages public and active transportation and discourages the use of cars. Diversity of land use is characterized by a mix of homes, shopping centers, schools, parks, entertainment centers, and workplaces in an area; greater diversity encourages walking and cycling (CONGDON, 2019; MÜNZEL et al., 2021; NIEUWENHUIJSEN, 2020). Demand management refers to the cost and availability of parking. The equitable distribution of employment across a city affects the traveling time. Also desirability means to increase the attractiveness of active travel through personal and traffic safety, safe neighborhoods, safe, reasonable, and comfortable public transportation, and attractiveness of streetscapes (MÜNZEL et al., 2021; SWINBURN et al., 2019).

Roadways, bike lanes, and streetscapes with green cover have a double benefit of making occasions for physical activity more attractive while increasing the uptake of CO2 by plants (SWINBURN et al., 2019). Greening cities are related to better mood, better cognitive function, less mental health problems, and longer life expectancy. Additionally, green areas mitigate air pollution, through carbon sequestration and offsetting carbon emissions (NIEUWENHUIJSEN, 2020).

The 8Ds mentioned above are also related to dietary patterns. An unfitting urban design and land use planning have as a consequence sprawled cities, creating areas with diminished access to fresh fruits, vegetables, and other whole foods (CONGDON, 2019). However, if well-fitting, land-use zoning can create urban environments that promote food systems for healthy and sustainable diets through the promotion of urban agriculture and government regulation of the location, nature, and size of food establishments (SWINBURN et al., 2019).

2.2 Obesity

Obesity is a disease characterized by excessive and abnormal fat accumulation in adipose tissue, which produces harm to health. BMI is often used for obesity diagnosis (WHO, 2000). Simplistically, obesity is the consequence of a positive energy balance over a significant period. However, several factors can result in this positive energy balance, but it is a complex interaction between them that determines this balance (ABESO, 2016, 2022; HERMSDORFF; BRESSAN, 2019a; WHO, 2000).

Body weight is mainly regulated by a series of physiological processes but is also influenced by environmental and societal forces that affect food intake and physical activity patterns. Besides, other medical, physiological, and biological factors can determine an individual's susceptibility to obesity (WHO, 2000).

2.2.1. Genetic factors

It is postulated that there is substantial individual variation in BMI, that there are people who are more susceptible to obesity, and that around 40–70% of this variability has been attributed to genetic factors (LOCKE et al., 2015; VAN DER KLAAUW; FAROOQI, 2015; WHO, 2000).

Obesity may be described as Mendelian disease and/or a non-Mendelian monogenic disease, all of which cause early childhood obesity. However, common obesity is polygenic (ABESO, 2016). The genetic variance depends on the nature and amount of mutational variance, the frequency of risk alleles, the effect sizes of the variants, and the degree of genetic control of variance studied (VAN DER KLAAUW; FAROOQI, 2015).

Genome-wide association studies (GWAS) pursue to identify the common variants that contribute to the heritability of diseases, including obesity. Currently, more than 80 genetic loci associated with BMI and body fat distribution have been identified by GWAS approaches, and many of these have been replicated in different populations (VAN DER KLAAUW; FAROOQI, 2015).

Although GWAS may be the best way to study the influence of genetic factors on obesity, collecting biological samples may not be feasible in some cases. Thus, studying familiar obesity may be an option, since a study showed that traditional risk factors for obesity, such as socioeconomic factors and parental BMI, accurately predicted obesity in European children (MOSCHONIS et al., 2022).

A study aimed to identify risk factors for obesity in early-life children in the United Kingdom. Among all variables investigated, parental obesity was the second most significant determinant for obesity (OR: 10.44) in those children (MOSCHONIS et al., 2022). Another study conducted in England concluded that there is a strong and graded association between parental obesity and the risk of obesity in their children. This association was stronger for the maternal weight than for the paternal weight (WHITAKER et al., 2010). No study evaluating the influence of family obesity on adult obesity was found.

Despite the numerous studies that show the genetic influence on obesity, the fast growth in its rates has occurred in too short a time for there to have been important genetic changes. It suggests that behavioral and environmental factors support unbalanced energy. Obesity may be the result of complex genetic interactions, which increase the individual's probability of developing obesity when exposed to an adverse environment (HETHERINGTON; CECIL, 2010; WHO, 2000).

2.2.2. Lifestyle factors

The modern lifestyle is a major stimulus for obesity. Socio-behavioral changes, such as increased population’s purchasing power, greater access to information, increased education level, and change in families’ structure, with more participation of women in the labor market, have stimulated a fast-tracked pace of life. It reflects: in the need to have meals in a short time, damaging mechanisms of satiety; in the decrease in the number of meals eaten at home, and compensatory increased consumption in fast-food chains; in the increased size of portions, increasing caloric content of each meal; in addition to the interruption of physical exercise, with a consequent reduction in daily energy expenditure. Additionally, current leisure activities can result in behavioral changes related to eating habits in which the reward system overlaps the homeostatic system (ABESO, 2016; FIESP, 2010; INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA, 2019; MACHADO et al., 2017; MATTAR et al., 2022).

Alcohol consumption has been associated with increased body weight (ALBANI et al., 2018; CHAPMAN et al., 2012; SOUZA E SOUZA et al., 2020). Although this relationship is complex and inconclusive, a recent systematic review with meta-analysis suggests that adults do not compensate for alcohol energy by eating less. Unlike, a relatively modest alcohol dose may lead to increased food consumption, increasing thus total energy intake (KWOK et al., 2019).

Sleep deprivation is also a consequence of modern lifestyle and influences body weight. A meta-analysis and meta-regression conducted with data from prospective cohort studies show that short sleepers have a risk ratio 1.38 times higher to developing obesity compared with normal sleepers (ITANI et al., 2017).

Sleep deprivation increases ghrelin levels as well as decreases leptin levels. These hormonal changes result in increased hunger, especially for high fat and high carbohydrate foods, which leads to obesity. Additionally, this overconsumption increases the activity of neuronal reward pathways, reinforcing the augmented caloric intake. Bigger eating due to more time spent awake is also suggested as a possible link between sleep deprivation and obesity. Furthermore, a sleep debt results in fatigue, which may reduce physical activity and, as a consequence, energy expenditure, leading to obesity as well (BAYON et al., 2014; COOPER et al., 2018).

The modern lifestyle has also shaped current dietary patterns, which are characterized by higher consumption of animal-source foods and UPF (FAO, 2013; KAC; SICHIERY; GIGANTE, 2007; MAGKOS et al., 2020; MATTAR et al., 2022; PAHO, 2015), resulting in obesity, as well (JUUL et al., 2018; MONTEIRO et al., 2017; SILVA et al., 2018).

Brazilian studies have sought to investigate the association between dietary patterns and obesity. Overall, the results point out that Brazilian traditional dietary patterns (composed of rice, beans, butter/margarine, meats, whole milk, and sugar) are negatively associated with obesity (CASTRO et al., 2016; MACHADO ARRUDA et al., 2016). While others dietary patterns identified, such as pub dietary patterns (composed of alcoholic beverages, salty snacks, pork meat, sausages, eggs, bacon, seafood and mayo) (MACHADO ARRUDA et al., 2016) and Regional dietary patterns (from Serra Gaúcha, Rio Grande do Sul, Brazil) (composed of white bread, jam, white rice, pasta, pumpkin, common regional fruits – grapes and tangerines – and fried polenta) (FRANÇA et al., 2021) were positively associated with obesity.

Another approach to investigating the association between dietary patterns and obesity concerns vegetarian dietary patterns. A review study summarized available evidence from three prospective cohorts of Adventists in North America and found out that, when compared with non-vegetarians, vegetarians, lacto-ovo-vegetarians and vegans had respectively 2–4, 3, and 5 points lower BMI (LE; SABATÉ, 2014).

However, every dietary pattern exhibits a wide diversity of dietary practices. There are several types of vegetarian dietary patterns, and while some may be healthy, others may be unhealthy containing refined grains, potatoes/fries, sweets, and sweetened beverages.

Therefore, it is reasonable to say that, only some, but not all, vegetarian diet patterns have beneficial effects on body weight. Despite that, concerns regarding the nutritional inadequacy of vegetarian diet patterns should be taken into account, especially concerning protein, vitamin B-12, calcium, iron, and zinc (MAGKOS et al., 2020).

Since physical activity involves voluntary body movements, with energy expenditure above the level of rest, its absence is related to obesity as well (BRASIL. MINISTÉRIO DA SAÚDE, 2021).

Worldwide, in 2016, 28% of adults aged 18 years and older were insufficiently physically active (WHO, 2018). In Brazil, data are even more worrying. Most recent data from VIGITEL reveal that 37% of adults are insufficiently physically active, and 13.1% are physically inactive. Regarding sedentary activities, 49.1% of Brazilians spend three hours or more a day of their free time watching television or using a computer, tablet, or cell phone (BRASIL. MINISTÉRIO DA SAÚDE, 2023).

Current dietary and physical activity patterns are a reflex of behavioral changes due to the modern world that contribute to and result from obesogenic environments, which are defined as "the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations". Thus, an obesogenic environment is one that promotes unhealthy food choices and discourages physical activity (SWINBURN; EGGER; RAZA, 1999).

2.2.3. Environmental factors

People interact with the environment in several microenvironments (or settings), including schools, workplaces, homes, and neighborhoods. These microenvironmental are influenced by macro environments (or sectors), such as education and health systems, government, industry, and society's attitudes and beliefs (SWINBURN; EGGER; RAZA, 1999). Within these settings or sectors, there are different types of environments, as presented in Board 1.

2.2.3.1. Air pollution

Another environmental risk is air pollution. Air pollution can be defined as the change of the natural characteristics of the atmosphere, due to any chemical, physical or biological agent. The main source of air pollution is the incomplete combustion of fuels or chemical reactions between gases. It can include motor vehicles, industrial facilities and forest fires that alter the air quality. Since many drivers of air pollution are also sources of GGE, air quality is closely linked to the earth's climate (WHO, 2023a, 2023b).

Board 1. Classification of environmental types that influence on obesity occurrence

Physical environment	It refers to "what is available" and includes the availability of training opportunities, nutrition and exercise expertise, technological innovations, and information. Concerning food, it refers to what is available in a variety of food establishments and point-of-purchase information such as nutrition labels. For physical activity, it includes the opportunities for participation in leisure activity and environmental factors which influence the use of active transport over motorized transport.
Economic environment	It refers to the costs related to food and physical activity. Concerning food, it involves costs of food production and retailing, apart from economic incentives and disincentives. Factors that influence opportunities for physical activity include budget allocations for building recreation centers or cycle paths and improved public transport.
Political environment	It refers to the rules related to food and physical activity and consists of laws, regulations, policies, and institutional rules, which have effects on the behavior of individuals and organizations. Concerning food, it refers to government food and nutrition policies, and food industry policies and standards. Regulations, laws, and urban planning are concerning the political environment for physical activity.
Sociocultural environment	It refers to a society's attitudes, beliefs, and values related to food and physical activity. These cultural and social norms are influenced by gender, age, ethnicity, religion, and traditions, and influence the behavior of people.

Source: SWINBURN; EGGER; RAZA, 1999.

Almost the entire world population (99%) lives in areas where the air pollution is above World Health Organization (WHO) air quality guidelines limits (WHO, 2023a), and currently, it is one of the greatest environmental risk to health, being associated to the burden of Non-Communicable Diseases (NCDs) and millions of premature deaths worldwide (WHO, 2018). Health problems can occur as a result of short- and long-term exposure. The air pollutants with the strongest evidence for public health concern include Carbon Monoxide (CO), Ozone (O3), Nitrogen Dioxide (NO2), Sulfur Dioxide (SO2), and Particulate Matter (PM), which is the object of study of this thesis (WHO, 2023b).

PM is a common proxy indicator for air pollution (WHO, 2022). It can be defined as a complex mixture of inhalable components having diverse chemical and physical characteristics, including sulphate, nitrates, ammonia, sodium chloride, black carbon, mineral dust, or water. Its nature is dynamic, as it can be derived from primary sources, such as combustion of fuels, or secondary sources, such as chemical reactions between gases, and then it continues to undergo chemical and physical transformation in the atmosphere. Nonetheless, PM is commonly classified according to its aerodynamic diameter (WHO, 2021, 2023b), as shown in Board 2.

Board 2. Classification of Particulate matter

PM classification	**PM_{10}**	**$PM_{2.5}$**	**$PM_{0.1}$**
Scale	Aerodynamic diameter < 10 µm	Aerodynamic diameter < 2.5 µm	Aerodynamic diameter < 0.1 µm
PM definition	Coarse particulate matter	Fine particulate matter	Ultrafine particulate matter
Main components	Cristal materials, sea salt, and biological components	Predominantly produced by combustion processes and consist primarily of metals, hydrocarbons, and secondary particles generated by chemical reactions with gaseous compounds in the atmosphere	Predominantly produced by combustion processes and consist primarily of metals, hydrocarbons, and secondary particles generated by chemical reactions with gaseous compounds in the atmosphere

Source: MÜHLFELD et al., 2008.

Due to its heterogeneity, research on the effect of PM on health is difficult. However, it is well established that the size of particles is directly linked to their harmful potential. PM can penetrate deep into the lung and the lower the particle, the greater its ability to enter the bloodstream and cause health problems (US EPA, 2023).

It is well documented that both short and long-term exposure to $PM_{2.5}$ is associated with morbidity and mortality by cardiovascular (ischemic heart disease), cerebrovascular (stroke) and respiratory effects. Long-term exposure also has been further related to adverse perinatal outcomes and lung cancer (WHO, 2023b). Nevertheless, literature about the effect of $PM_{2.5}$ on obesity is recent and controversial.

Literature shows positive association between $PM_{2.5}$ exposure and BMI and obesity among adolescents (LIANG et al., 2022; TAMAYO-ORTIZ et al., 2021), but in adults this association is mixed. A systematic review analyzed 16 papers on the effects of air pollution on obesity, of which four were related to $PM_{2.5}$, and found null or mixed results for this association (AN et al., 2018).

Although the results are conflicting, there are some mechanisms proposed to explain the effect of $PM_{2.5}$ on obesity. An experimental study explored the molecular mechanisms underlying $PM_{2.5}$-impaired functions in adipose tissue in the diabetic mice model (*db/db*). The authors found out that in both White (WAT) and Brown Adipose Tissue (BAT), the exposure to $PM_{2.5}$ leads to an increase of Reactive Oxygen Species (ROS), leading to chronic low-grade inflammation (a common condition that leads to and results from obesity). Also, the weight percentage of WAT content was significantly higher in the $PM_{2.5}$-exposed group, which also presented an increased lipogenesis and decreased lipolysis. Thus, $PM_{2.5}$ exposure can lead to obesity through fat accumulation in WAT. Specifically for the BAT, the thermogenesis was inhibited, reducing then the energy expenditure, leading to obesity as well.

2.2.4. Exposome approach

As presented, obesity is widely studied. However, given its complexity and multiple associated factors, its understanding is arranged across different and specific areas of study. Therefore, assessing the determinants of obesity in an integrated, simultaneous manner and with more robust analysis techniques is still necessary. Emergent approaches are making the simultaneous evaluation of multiple stressors more feasible, including the exposome approach (MCHALE et al., 2018; WILD, 2005).

The exposome concept was developed to draw attention to the need for a more complete environmental exposure assessment in epidemiological studies and to provide a comprehensive description of lifelong exposure history, beyond genetics (WILD, 2012).

The exposome includes every exposure that an individual is subject to from conception to death, and three categories of non-genetic exposures may be considered: internal (metabolism, endogenous circulating hormones, body morphology, physical activity, gut microbiota, inflammation, lipid peroxidation, oxidative stress, and aging); specific external (radiation, infectious agents, chemical contaminants and environmental pollutants, diet, lifestyle factors, occupation, and medical interventions); and general external (social capital, education, financial status, psychological and mental stress, urban-rural environment and climate) (WILD, 2012).

Considering that the exposome approach encompasses a wide range of combined variables, estimating the association between them and their impact on health is a major challenge for exposome research since the current statistical methods are not sufficient to do so precisely. To address this issue, Machine Learning algorithms can be applied to identify complex patterns in exposome data and predict the health effects of environmental exposures (VINEIS et al., 2017; WILD, 2012).

Machine Learning is a subset of Artificial Intelligence that aims to identify patterns in large datasets. It has been widely used in scientific research due to its ability to find relevant relations in multidimensional data (KODATI; VIVEKANANDAM; RAVI, 2019; SIQUEIRA-BATISTA; SILVA, 2019). It involves several methods that can be used for supervised or unsupervised learning, such as neural networks, nearest neighbor classifiers, and decision tree models (FULLER; BUOTE; STANLEY, 2017).

2.3. Undernutrition – Inadequacy of micronutrients

Undernutrition is a complex phenotype that may be displayed across the life course in diverse ways, but its classification remains unsophisticated. When assessed as a simple anthropometric measure, malnutrition is understood as low birth weight, stunting or wasting in childhood, and as short stature or low BMI in adulthood, being most prevalent among younger age groups (WELLS et al., 2020). However, malnutrition can be defined as "*a state of nutritional imbalance resulting from insufficient nutrient intake to meet normal physiological needs*" (HEALTH SCIENCES DESCRIPTORS: DECS, 2022). Thus, undernutrition can also be assessed as depleted stores or circulating concentrations of nutrients, reflecting dietary inadequacy (WELLS et al., 2020).

Adequate micronutrient status is critical for optimal metabolic function, and insufficiency or deficiency should be expected whenever food intake is unbalanced (KIM et al., 2019). Contrary to what many believe, micronutrient deficiencies remain prevalent in adults (WELLS et al., 2020).

A Dutch cohort measured a micronutrient panel in 384 adults and identified that there was a deficiency or low levels for all the nutrients investigated (Folate, Vitamin B6, Vitamin B12, Vitamin D, and iron). In addition, at least one nutritional imbalance was observed in 86.5% of participants (VISIOLI et al., 2022).

An analysis of micronutrient usual intake based on nationally representative data from the 2005–2016 National Health and Nutrition Examination Surveys (NHANES) reveals that 45% of the U.S. population had a prevalence of inadequacy for vitamin A, 46% for vitamin C, 95% for vitamin D, 84% for vitamin E, and 15% for zinc (REIDER et al., 2020).

Data from Canadian Community Health Survey (CCHS) disclose that 47% of the Canadian population had a prevalence of inadequacy for vitamin A, 94% for vitamin D, 45%

for magnesium, and 44% for calcium. A high prevalence of inadequate intake was also seen for vitamin C (29% for nonsmokers and 59% for smokers) (AHMED; PRANEET NG; L'ABBE, 2021).

Insufficient intake of micronutrients may be related to a suboptimal consumption of healthy food groups, such as vegetables, leafy greens, whole grains, legumes, fresh fruit, nuts and seeds, eggs, and meats (VISIOLI et al., 2022). A low socioeconomic status may also be a risk factor for insufficient intake of micronutrients, through the poorest diet quality (BAILEY et al., 2017; ZHU et al., 2020).

Moreover, micronutrient requirements are not linear with physical activity-related energy expenditure. Thus, people with low physical activity levels may have a lower micronutrient intake because of low energy intake. This hypothesis was confirmed in an analysis based on NHANES 2003–2006 on 4,015 adults, revealing that inactive participants had a lower intake of all micronutrients except for copper, vitamins A, B12, C, and K. In addition, participants with higher physical activity levels had a lower risk of insufficient micronutrient intake. (HEYDENREICH et al., 2017).

Economic, social, and behavioral changes mentioned above are related to obesity are also related to malnutrition, mainly due to great changes observed in food systems (POPKIN; CORVALAN; GRUMMER-STRAWN, 2019; SWINBURN et al., 2019). Current global food systems are dominated by UPF which induce unhealthy eating patterns, reflecting an unbalanced diet (ADAMS; WHITE, 2015; LOUZADA et al., 2019; MONTEIRO et al., 2012, 2010b), characterized, as well, by lower fiber content, protein, vitamins (B12, D, E, niacin, and pyridoxine), and minerals (potassium, copper, iron, phosphorus, magnesium, selenium, and zinc) (CROVETTO et al., 2014; LOUZADA et al., 2015a, 2015b; MONTEIRO et al., 2010a; RAUBER et al., 2018), which induce micronutrient deficiencies (FAO, 2013), and such dietary patterns result in individuals with obesity and micronutrient deficiencies (KIM et al., 2019).

A Brazilian study aimed to investigate the association between insufficient intake of micronutrients and obesity indicators and found a high prevalence of inadequate consumption of calcium, iron, zinc, and vitamins A, C, D, and E among 1,222 participants of the EpiFloripa Study. Moreover, an inverse association was observed between lower calcium and iron consumption and higher BMI and waist circumference, as well as, between lower vitamins A and D consumption and higher waist circumference. (CEMBRANEL et al., 2017).

In this vein, CUME Study is a Brazilian cohort that aims to assess the impact of the Brazilian dietary pattern and nutritional transition on NCD. Since its baseline data show a population predominantly young, employed, highly educated, and with a high prevalence of overweight and obesity (DOMINGOS et al., 2018), it may be a great source to research this topic.

2.4. Climate change and dietary patterns

Climate change is now a reality, and according to IPCC, it is unequivocal that human influence has warmed the atmosphere, ocean, and land at an unprecedented rate (IPCC, 2021, 2023a). Through several activities, humans are introducing upward amounts of pollutants into the air, water, and soil, and using the natural resources at rates that exceed their capabilities to renew themselves. One of the main anthropogenic stressors of ecosystems are the agricultural and livestock sectors (FAO, 2006).

According to the National Classification of Economic Activities (CNAE), agriculture and livestock comprise the exploitation of natural vegetal and animal resources. Agriculture involves the cultivation of crops, whether temporary or permanent, horticulture and floriculture or the production of certified seeds and seedlings. This includes traditional, organic, or genetically modified plant cultivation processes. Livestock is concerned with animal production, which also provides for the creation of genetically modified animals (IBGE, 2007).

The agricultural and livestock sectors are significant for health, food and nutrition, and economic and social security. The technological advances that these sectors have experienced in the last decades have promoted a revolution in how food is produced and distributed. With greater production capacity, food price was reduced, facilitating access to food with a significant nutritional contribution, reducing hunger and malnutrition in Brazil and the world (CONFEDERAÇÃO DA AGRICULTURA E PECUÁRIA DO BRASIL, 2020; FAO, 2006, 2020).

The global demand for food is growing and agricultural and livestock sectors have central relevance to this problem (FOLEY et al., 2011; TILMAN et al., 2011). The current global food system feeds the world population and supports the livelihoods of around 200 million people (IPCC, 2019).

However, depending on the characteristics of a food system, it can promote social justice and protect the environment, or generate social inequalities and threats to natural resources and biodiversity (MINISTÉRIO DA SAÚDE, 2014). Greenhouse gas emissions from the agricultural sector are related to the size of the herd, the quantity, and quality of agricultural production, in addition to the types of fertilizers used in soil management (MCTIC, 2020).

Since 1961, the food supply per capita has increased by more than 30%, rising 800% the use of nitrogen fertilizers, and 100% the water resources used for irrigation. Around 25-30% of GGE are attributable to food systems (involving production, transport, processing, packaging, storage, retail, consumption, loss, and waste) (IPCC, 2019).

Between 2007 and 2016, crop and livestock activities generated 142 ± 43 Tg CH_4 yr-1 and 8.3 ± 2.3 Tg N_2O yr-1, respectively. Yet within the food system, land-use change dynamics, involving deforestation and peatland degradation, generated 4.8 ± 2.4 Gt CO_2 yr-1 in the same period (IPCC, 2019).

Personal food choice may offer major opportunities for reducing GGE from food systems. Sustainable diets are known to be rich in minimally processed plant-based foods and low in animal-sourced products (CHAPA et al., 2020; FRESÁN et al., 2021; MAGKOS et al., 2020). However, animal-sourced products are not homogeneous in terms of the resources needed per consumed calories.

A study that aimed to enable a direct comparison of animal-based food categories (dairy, beef, poultry, pork, and eggs) by their resource use reveals that beef is reliably the least resource-efficient in all considered metrics (land use, water use, GGE, and reactive N). Each 1,000 kcal of beef needs about 28, 11, 5, and 6 times the average land, irrigation water, EEG, and reactive N of the other animal categories, that are similar among them (ESHEL et al., 2014).

Nonetheless, the total mitigation potential of consumption of sustainable diets (rich in whole grains, pulses, fruits, vegetables, nuts, and seeds) is estimated as a reduction 1.8-3.4 $GtCO_2eq$ yr-1 (IPCC, 2019).

3. OBJECTIVES

3.1. General objective

To estimate the association between CUME Project participant's dietary patterns and components of the global syndemic, focusing on the relationship between obesity and climate change, under an exposome approach.

3.2. Specific objectives

- To determine the prevalence of obesity and undernutrition among CUME Project participants;

- To identify CUME Project participant's dietary patterns and their association with components of the global syndemic;
- To estimate the association between long-term exposure to $PM_{2.5}$ and longitudinal changes on body mass index among CUME Project participants;

To develop prediction models for obesity, based on the exposome approach.

4. METHODS

4.1. The CUME Study

The "Cohort of Universities of Minas Gerais (CUME Study): impact of the Brazilian dietary pattern and nutritional transition on non-communicable diseases" is a concurrent open cohort that aims to assess the impact of the Brazilian dietary pattern and nutritional transition on NCD in adults who hold bachelor and postgraduate degrees from federal higher education institutions located in the state of Minas Gerais, Brazil. The evaluation waves happen biannually via an online questionnaire (DOMINGOS et al., 2018).

The cohort baseline (Q_0) was established in 2016. Its participants were alumni from Universidade Federal de Viçosa (UFV) and Universidade Federal de Minas Gerais (UFMG) who graduated between 1994 and 2014.

In 2018 besides the first follow-up questionnaire (Q_2), the cohort was extended to Universidade Federal de Ouro Preto (UFOP), Universidade Federal de Juiz de Fora (UFJF), and Universidade Federal de Lavras (UFLA). In 2020 the second follow-up questionnaire (Q_4) was applied, and Universidade Federal de Alfenas (UNIFAL) and Universidade Federal dos Vales de Jequitinhanha e Mucuri (UFVJM) were included. In 2022, the third follow-up questionnaire (Q_6) was applied (Figure 3).

4.2. Ethical aspects

The CUME Study is under the ethical principles of non-maleficence, beneficence, justice, and autonomy contained in resolution No. 466/12 of the National Health Council and was approved by the Human Research Ethics Committee of the participating institutions (protocol no. UFV 596741-0/2013; UFMG 2491366/18; UFOP 2565240/2018; UFJF 2615738/2018; and UFLA 2676682) (attachment 01).

All participants read and signed an Informed Consent Form (with an online command). Also, the preservation of the anonymous character of the participants, the protection of their identities, and the freedom to withdraw their consent were ensured throughout the study.

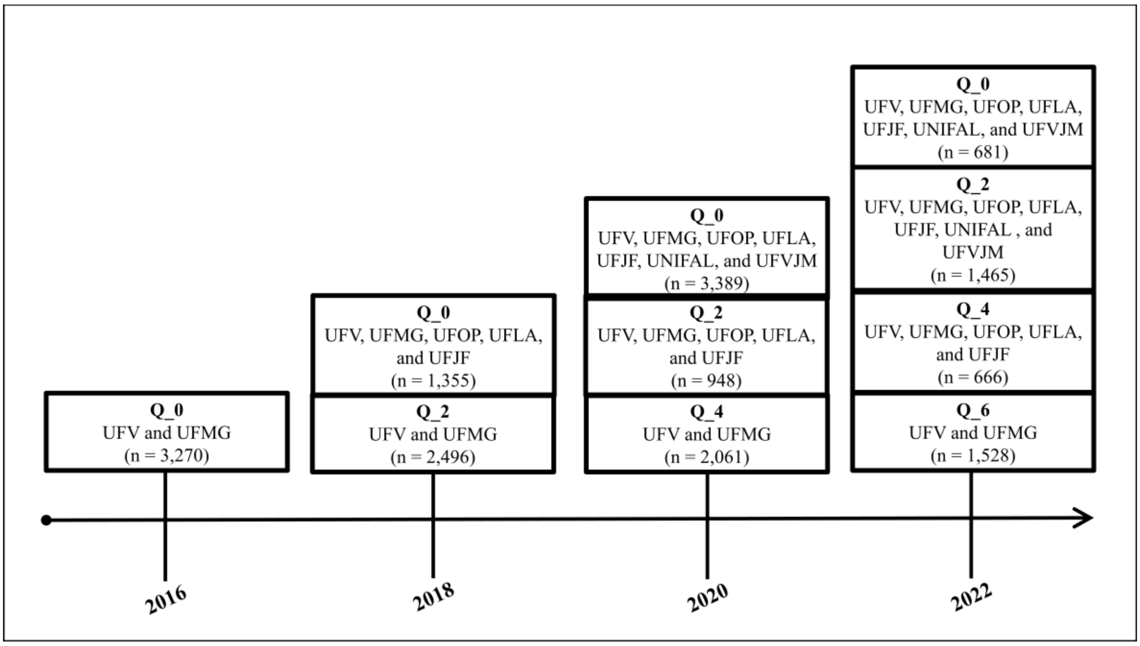

Figure 3. *Flowchart of CUME Project data collection waves.* ***Source:*** *Own elaboration. UFV: Universidade Federal de Viçosa; UFMG: Universidade Federal de Minas Gerais; UFOP: Universidade Federal de Ouro Preto; UFLA: Universidade Federal de Lavras; UFJF: Universidade Federal de Juiz de Fora; UNIFAL: Universidade Federal de Alfenas; UFVJM: Universidade Federal dos vales de Jequitinhonha e Mucuri ; Q_0: baseline questionnaire; Q_2: first follow-up questinnaire; Q_4: second follow-up questionnaire; Q_6: third follow-up questionnaire.*

4.3. Subjects and study design

This study was conducted with graduates from Minas Gerais universities who participate in the CUME Study and completed the baseline questionnaire (for the cross-sectional analysis) and those who followed up on the study, by completing at least one follow-up questionnaire (for the longitudinal analysis).

The general non-inclusion criteria were: have not completed the baseline questionnaire (because of missing data), have resided abroad during the year before completing the questionnaire (due to changes in dietary patterns), or non-Brazilians (as they do not represent Brazilian dietary patterns), be ≥ 60 years of age, women who reported being pregnant in the year before completing the questionnaire (the last two were nor included because of changes on body composition), and extreme values of energy intake (< 500 kcal/day or ≥ 6000 kcal/day) (SCHMIDT et al., 2015; TEIXEIRA et al., 2016).

Additionally, for analyzes involving air pollution data, participants with incomplete address or missing georeferencing data were not included.

The specific non-inclusion criteria and total sample size for each specific objective are presented in Figure 4 and detailed on their respective papers.

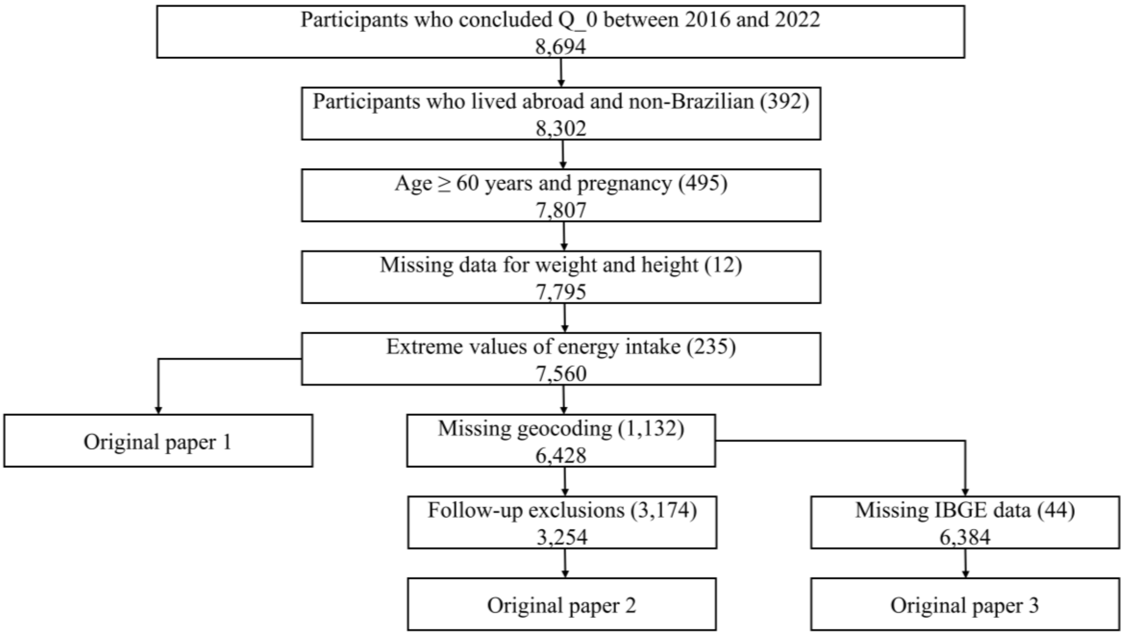

Figure 4. *Flowchart of non-inclusion criteria for each paper.* ***Source:*** *own elaboration.*

4.4. Data collection

4.4.1. Participants' personal data collection

Potential participants were invited to voluntarily participate in the study by email. Once registered, participants had access to the first phase of the questionnaire which consisted of 83 questions related to lifestyle, sociodemographic, anthropometric, biochemical, and clinical data; the practice of physical activity, as well as average screen time and other sedentary activities; individual and family morbidity; and personal health check history.

The volunteers received the second phase of the questionnaire a week after completing the first phase. The second phase was composed of a semi-quantitative Food Frequency Questionnaire (FFQ) and 15 questions on dietary habits.

The follow-up questionnaires were applied in a single step, according to volunteers' respective monitoring time (Q_2, Q_4, and Q_6) and aimed to identify changes in food consumption and lifestyle of the participants, as well as the incidence of diseases investigated by the cohort.

4.4.2. Environmental data collection

To characterize the environment, a georeferenced database was built. It contains the geographic coordinates from home addresses of the participants, air pollution data (measured as $PM_{2.5}$), Normalized Difference Vegetation Index (NDVI) data, and the characterization of the municipality, at census tract level, where each participant lives.

4.4.2.1. Participants' geographic coordinates

On the online questionnaire, participants were asked to voluntary inform their home address and further georeferencing was performed manually on *google maps* and automatically on QGIS® (3.22.14), through *Open street map* plug in. Then, the results were compared and data were complemented to reach the maximum number of participants with georeferencing data.

Additionally, participants had their geographic coordinates updated for each follow-up questionnaire they reported a different address information.

4.4.2.2. Air pollution data – $PM_{2.5}$

Satellite remote sensors are limited in detecting microscopic particles. This is due to the spatial resolution and technical limitations of the instruments used to measure air pollution from space. Consequently, satellite data often count on on $PM_{2.5}$ as a reliable measure of air pollution, once it can be detected and measured more accurately by remote satellite sensors. Thus, secondary data on $PM_{2.5}$ were obtained for 2011-2021 from Atmospheric Composition Analysis Group (ACAG). These are open-source global estimates of ground-level ambient $PM_{2.5}$, gridded at 0.01° x 0.01° (~ 1 km x 1 km), and available in raster format (V5.GL.03) (ACAG, 2023).

Annual ground-level $PM_{2.5}$ data for 1998-2021 was estimated using Aerosol Optical Depth (AOD) retrievals from National Aeronautics and Space Administration (NASA) satellites, and then combined with chemical transport model (CTM). Afterward, Geographically-weighed regression (GWR) was used to calibrate estimates with ground-based $PM_{2.5}$ observations collected by the WHO (ACAG, 2023; DONKELAAR et al., 2021).

Data interpolation was performed on QGIS® (3.22.14), using *Point Sampling Tool* plugin, in the configuration of the WGS 84 Geographic Coordinate System (EPSG 4326). Then, the $PM_{2.5}$ exposure was defined as the five-years average prior to participants' respective monitoring time for Q_0, as shown in Table 1.

The additional adjustment by post-enrollment $PM_{2.5}$ exposure was conducted by the respective follow-up time of the participants (Table 1).

Table 1. Definition of PM2.5 exposure, according to participants' respective monitoring time for baseline

Follow-up time	Mean of annual ground-level $PM_{2.5}$ data for pre-enrollment $PM_{2.5}$ exposure	Mean of annual ground-level $PM_{2.5}$ data for post-enrollment $PM_{2.5}$ exposure
2016 - 2018	2011 - 2015	2017 - 2018
2016 - 2020	2011 - 2015	2017 - 2020
2016 - 2022	2011 - 2015	2017 - 2021
2018 - 2020	2013 - 2017	2019 - 2020
2018 - 2022	2013 - 2017	2019 - 2021
2020 - 2022	2015 - 2019	2021

4.4.2.3. Normalized Difference Vegetation Index data – NDVI

Secondary data on NDVI were obtained for 2000-2023 from NASA website. Data are open-source and available as monthly average, in GeoTIFF raster format, gridded at 0.1° x 0.1° (~ 10 km x 10 km) (NASA, 2023).

Data collected by the Moderate Resolution Imaging Spectroradiometer (MODIS) aboard NASA's Terra Satellite were used to measure the greenness of Earth's landscapes and produce the NDVI maps. These maps are designed by measuring wavelengths of red and near-infrared light that is absorbed and reflected by plants. Thus, the values on these maps can range from -0.1 to 0.9 in which higher values represent more greenness and lower values represent lands with little or no vegetation (NASA, 2023).

Data interpolation was performed on QGIS® (3.22.14), using *Point Sampling Tool* plugin, in the configuration of the WGS 84 Geographic Coordinate System (EPSG 4326). Likewise for $PM_{2.5}$ data, NDVI data were treaded as the five-years average prior to participants' respective monitoring time for Q_0.

4.4.2.4. Data of municipality, at census tract level

Secondary data from the Brazilian Census were obtained on Brazilian Institute of Geography and Statistics (IBGE – from Portuguese: Instituto Brasileiro de Geografia e Estatística) website (IBGE, 2010).

Data on per capita income and situation of the census tract (if urban, peri urban or rural) were collect. To future compute the urbanization rate of each census tract, data on total number of houses, existence of street identification, street lighting, paved street, paved sidewalk, curb, and manhole were collected.

To future calculate the demographic density, data on total number of residents for each census tract were collected. Additionally, spatial data sets at census tract level were obtained through *geobr* package (version 1.7.0) (PEREIRA et al., 2019) on RStudio® (1.3.959). Then the area (km^2) of each census tract was calculated on QGIS® (3.22.14), in the configuration of WGS 84 World Mercator (EPSG 3395).

4.5. Determination of variables

The exposure and outcome variables were determined according to the theoretical model proposed to base this study (Figure 5). The dietary patterns identified were directly associated with undernutrition (evaluated by the insufficient intake of vitamins and minerals), climate change (assessed by carbon, water, and ecological footprints) and obesity. The association between climate change, as air pollution, and obesity was assessed directly and through the exposome approach. The exposome approach also included the dietary patterns and other variables.

4.5.1. Dietary Pattern

The food consumption was evaluated by a FFQ adapted and validated for the studied population. The FFQ applied in CUME Study was previously validated, obtaining excellent agreement correlation coefficients (AZARIAS et al., 2021). It consisted of 144 food items grouped into dairy, meat and fish, cereals and leguminous, fats and oils, fruits vegetables and greens, beverages, and other foods. Each participant reported the frequency, the number of times, and the portion size of each food ingested, having as reference the 12 months preceding the moment to answer the questionnaire. To adapt the instrument to the virtual environment, a photo album of the food portions was provided aiming to assist in the visualization of the portions of the foods and to improve the reliability of the answers.

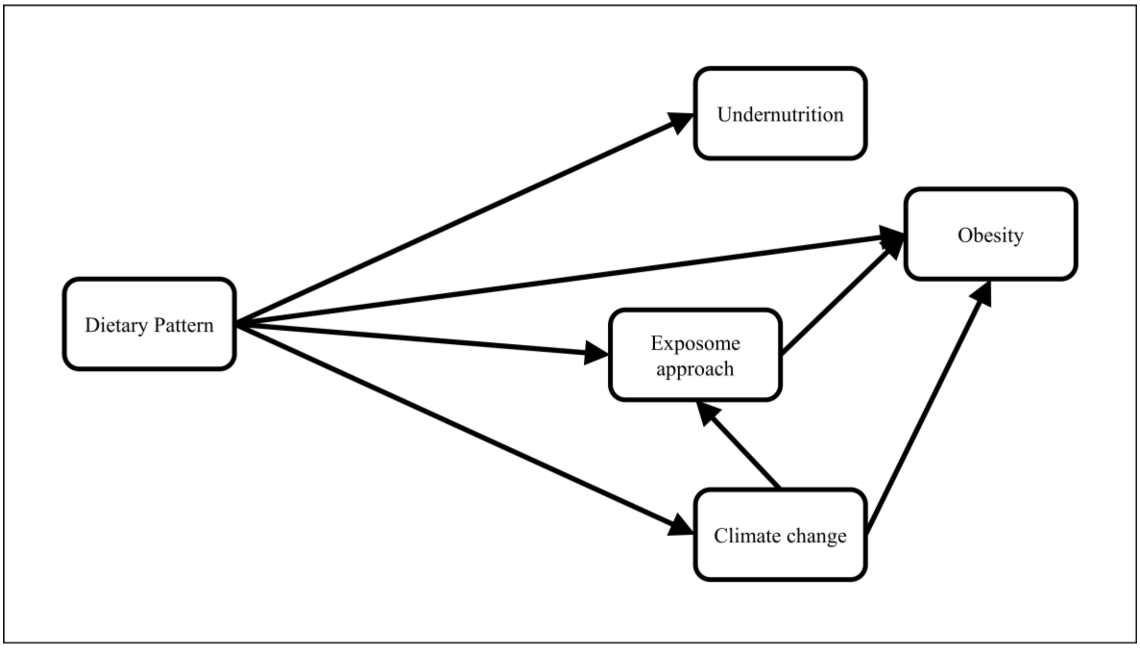

Figure 5. *Theorical model proposed to base this study.* ***Source:*** *Own Elaboration.*

The FFQ data were computed and the consumption of each food was transformed into grams or milliliters per day. Then nutrient intake was calculated, using Brazilian tables of the nutritional composition of foods as reference (IBGE, 2011; UNIVERSIDADE DE CAMPINAS, 2011).

To identify the major dietary patterns and to reduce the complexity of the data, the FFQ food items were first grouped into 27 groups, considering their nutritional composition, the level and intend of processing, according to NOVA classification (MONTEIRO et al., 2016) and the coefficients of environmental footprints (GARZILLO et al., 2019).

4.5.2. Undernutrition assessment

In this study, insufficient intake of micronutrients was considered as undernutrition. To this, the mean daily intake of vitamins A, B1 (Thiamin), B2 (Riboflavin), B3 (Niacin), B6 (Pyridoxine), B9 (Folate), B12 (Cobalamin), C, D and E, as well as Iron (Fe), Manganese (Mg), Zinc (Zn), Selenium (Se), Copper (Cu), Calcium (Ca) and Potassium (K), obtained on FFQ data, was compared and classified as “adequate intake” or “inadequate intake”, according to the Dietary Reference Intake (DRIs) of the Institute of Medicine. Estimated Average Requirement (EAR) was used for all nutrients investigated here, except for K, which was evaluated as Adequate Intake (AI) (INSTITUTE OF MEDICINE, 1997, 1998, 2000, 2001, 2019; MEDICINE, 2011).

4.5.3. Environmental impact from food patterns

To calculate the carbon, water, and ecological footprints, the table "Footprints of foods and culinary preparations consumed in Brazil" (GARZILLO et al., 2019) was used as reference.

The table (GARZILLO et al., 2019) presents carbon (CF), water (WF), and ecologic footprints (EF) relative to 100g of the edible part of food and culinary preparations consumed in Brazil, according to the nutritional composition of foods table of Household Budget Survey (POF from Portuguese – *Pesquisa de Orçamentos Familiares*) of Brazilian Institute of Geography and Statistics (IBGE, 2011).

To generate the values of CF, WF, and EF, the life cycle of products methodology was used, according to NBR-ISO 14040:2009. Thus, the CF measures the total amount of GGE (CO2, CH4, N2O, HFC, PFC, SF6, and others) in the course of a product's life cycle. The measurement is expressed in mass unit (g, kg, t), and the calculated mass for each of the different gases emitted is converted to carbon equivalent (CO2e) using the Global Warming Potential factor (GWP) of each gas, as established by the IPCC (GARZILLO et al., 2019).

The WF measures the total amount of used water in the course of a product's life cycle. Its account involves the sum of three main components: surface or groundwater (blue water); rainwater (green water) and the water needed to assimilate the pollution load from the production and consumption system (greywater). The WF is expressed in water volume (liters or cubic meters) (GARZILLO et al., 2019).

The EF is an aggregated index since it assesses in a combined way anthropogenic impacts that are normally assessed separately (carbon emissions, land-use change, biodiversity consumption, etc.). It reveals how much human activities appropriate the earth's regenerative capacity. Many of the ecological resources and ecosystem services are on the surface, where photosynthesis takes place. Therefore, it is expressed in bio productive area (hectare or m^2). The accounting of all environmental load used in the process is converted using conversion factors published by the Global Footprint Network (GARZILLO et al., 2019).

4.5.4. Obesity

To determinate the obesity, participants were asked to report their weight and height information on Q_0, as well as on all others follow-up questionnaires (Q_2, Q_4, and Q_6) to BMI calculation. The self-reported data on weight, height, and BMI were previously validated, obtaining excellent agreement correlation coefficients (ELIZABETH et al., 2017). The BMI was calculated as the weight in kilograms divided by the square of height in meters (kg/m^2). It was used as continuous variable and also classified into a binary variable for the presence of obesity (0/1), according to World Health Organization (WHO, 2000) classification, as shown in Table 2.

Table 2. Classification of the nutritional status of adults according to the Body Mass Index (kg / m²)

Classification	Body Mass Index (kg/m^2)
Underweight	< 18.5 kg/m^2
Normal weight	18.5 to 24.9 kg/m^2
Overweight	25 to 29.9 kg/m^2
Obesity	≥ 30 kg/m^2

Source: World Health Organization, 2000.

4.6. The exposome approach variables

The exposome approach involves the entire exposure that an individual suffers throughout life. Therefore, all variables of this study were considered as exposure variables and estimated in the construction of predictive models.

The exposome approach was used to predict obesity and involved genetic risk for obesity, internal, general external, and specific external factors, as described below.

4.6.1. Family history of obesity

The family history of obesity was assessed by familial obesity reported by participants on the Q_0. The analysis included binary variables (0/1) to indicate the presence of obesity in the participant's mother, father, siblings, and grandparents.

4.6.2. Internal factors

Sex (binary, 0 = female / 1 = male), age (continuous), skin color (dummy variables (0/1) for white, black, yellow, brown, and red color), physical activity (dummy variables (0/1) for physically active, insufficiently active, and inactive), and sedentary activities were considered as internal factors.

The practice of physical activity was investigated from a list of 23 leisure activities and the respective time dedicated to each one (MARTÍNEZ-GONZÁLEZ et al., 2005). The intensity of effort was obtained by converting the type of physical exercise reported into light, moderate or vigorous activity, following the recommendations of the physical activity compendium. Thus, individuals were classified as physically active, insufficiently active or inactive, according to the WHO (WHO, 2010).

The sedentary habit was estimated by screen time. On Q_ 0, participants were asked to report their daily TV and computer usage as well as their hours of sleep per night.

4.6.3. General external factors

Information about their income (continuous), marital status (dummy variables (0 / 1) for single, married, and divorced/widower), and professional status (dummy variables (0 / 1) for employed, unemployed, student, and retired) were self-reported by the participants in the first step of Q_0.

Municipality data, as detailed in 4.4.2.4. section "Data of municipality, at census tract level", were also considered as general external factors. Dummy variables (0/1) were created for the census tract (urban and non-urban). The urbanization rate and per capita income of participants' census tracts were modeled as continuous variables. Population density was modeled as a quintile.

Also, the perception of public open space for physical activity was modeled as a binary variable (0/1) assessed by the question "Is there a public open space (square, park, dead-end street) near your home for walking, exercise or sport?" presented in the first phase of Q_0.

4.6.4. Specific external factors

Food consumption (as detailed in 4.5.1. section "Dietary Pattern"), tobacco and alcohol use, air pollution (as detailed in 4.4.2.2. section "Air pollution data – $PM_{2.5}$") and NDVI (as detailed in 4.4.2.3. section "Normalized Difference Vegetation Index – NDVI") data were considered as specific external factors.

The coefficient of each dietary pattern identified was modeled as continuous variable. Additionally, in the second phase of Q_0, participants' eating habits were investigated. Participants were asked if they tend to skip breakfast, have their lunch outside of home, and eat visible fat from meat. These variables were used as binary (0/1). Participants were also asked to report the number of meals they consume daily. This information was converted into a binary (0/1) variable categorized as ≤ 3 and ≥ 4.

In the first phase of Q_0, the participants were asked to identify themselves as former smokers (0/1), active smokers (0/1), or non-smokers (0/1). For alcohol exposure, a binary variable (0/1) was created based on the frequency of alcohol abuse behavior. This was defined as consuming five or more alcoholic drinks for males or four or more drinks for females in a single episode, at least once in the past month (NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM, 2015).

$PM_{2.5}$ and NDVI exposures were treated as continuous variables.

4.7. Statical analysis

In general, the normality of the continuous variables was analyzed using the Shapiro Wilk test. Qualitative variables were presented in absolute and relative frequency tables.

The evaluation of the applicability of the Principal Components Analysis (PCA) was done through Bartlett's sphericity test (BTS) and Kaiser-Meyer-Olkin (KMO) statistical test. Then, PCA was performed to identify eating patterns, and the number of dietary patterns to retain was determined considering the eigenvalue more than one, scree test (i.e. identifying the breaking point in the scree plot of components' eigenvalues), and natural interpretability.

Varimax rotation was used to achieve a simple matrix and uncorrelated dietary patterns, and positive factor loading values ≥ 0.25 were used to determine the food groups in each dietary pattern. Lastly, a score for each dietary pattern for every individual based on their intakes of different food groups weighted by corresponding factor loadings was calculated. The labeling of dietary patterns identified was based on the literature and our interpretation of the data.

To answer the specific aim two, logistic and linear regression models were performed to evaluate the association between dietary patterns and the components of the global syndemic.

To answer the specific aim three, a Directed Acyclic Graphs (DAG) was elaborated in order to identify the minimal sufficient adjustment for estimating the total effect of air pollution (measured as $PM_{2.5}$) at baseline on long-term BMI. Then multilevel mixed-effects linear regression models were performed to estimate the direct effect of $PM_{2.5}$ on BMI as well as its interaction with physical activity level and the average total kilocalories (kcal) intake.

All analyses were performed on STATA/SE® (version 17) software, with an α value of 5%. Detailed information on each statistical analysis can be found on their respective article in the results chapter of this document.

4.8. Machine learning approach

To answer the specific aim four, the supervised learning classification approach was performed to develop prediction models for obesity.

To conduct learning classification analyses, the first step was to identify any missing data in the dataset. After applying the non-inclusion criteria, a total of 6,523 individuals were included in the dataset. However, 139 individuals were excluded as they had missing data for municipality variables such as census tract situation, urbanization rate, population density, and/or per capita income. Then imputation was performed for 676 missing data for NDVI.

Five tree-based algorithms were used on RStudio® (4.3.2) to predict obesity using the Caret package. The algorithms included Random Forest, Rpart/CART, c5.0, Bagging, and Boosting.

The Random Forest model constructs multiple decision trees during training and combines their outputs to enhance predictive performance and control overfitting.

The Rpart/CART model simplifies complex data structures, making decision trees for predictive models more interpretable.

The C5.0 model builds decision trees to predict the value of a target variable based on several input variables.

The Bagging model enhances the stability and accuracy of machine learning algorithms. It involves creating multiple versions of a predictor and using them to create an aggregated predictor.

The Boosting model combines the predictions of several base estimators to improve overall performance, converting a set of weak learners into a strong learner.

In order to identify the best partition training/test set, considering this is a small sample for machine learning, different data partitions were tested, including 50%-50%, 70%-30%, 80%-20%, and 90%-10%. Due to the unbalanced data, a test for probability-weighted split was also executed. Thus, models were performed using under-sampling, oversampling, Random Over-Sampling Examples (ROSE), and Synthetic Minority Over-sampling Technique (SMOTE) techniques.

Performance metrics were obtained for all models from both the test and training datasets. Accuracy was used as the primary criterion to determine the best fitting model. Additionally, Kappa index, sensitivity and specificity were also considered. To ensure robustness and consistency, each model underwent 10-fold cross-validation, repeated three times. Hence, the metrics obtained reflect the average of the three runs.

5. RESULTS

With the purpose to answer the specific aims one and two, the original paper titled "Relationship between Brazilian dietary patterns and the global syndemic: data from the CUME

Study" was elaborated. It was submitted and is under review at The American Journal of Clinical Nutrition.

In order to answer the specific aim three, the original paper titled "The interaction between chronic ambient $PM_{2.5}$ exposure and physical activity on BMI in a Brazilian prospective cohort (CUME Study)" was elaborated. It will be submitted to the journal Environmental Health Perspectives.

So as to answer the specific aim four, the original paper "Understanding the complexity of obesity through predictive models based on the exposome approach" was elaborated and will be submitted to The American Journal of Clinical Nutrition.

The three original papers cited above are presented below.

Relationship between Brazilian dietary patterns and the global syndemic: data from the CUME Study

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Abstract

Current global food systems are contributing to a shift towards an unhealthy diet, which is linked to the three components of the global syndemic: obesity, undernutrition, and climate change. This cross-sectional study evaluates how four dietary patterns in Brazil are associated with the components of the global syndemic. Anthropometric and food intake data were obtained from the CUME Study – a prospective cohort conducted with Brazilian university graduate sample. BMI was used to classify individuals with obesity. Insufficient intake of micronutrients was considered undernutrition. Carbon, water, and ecological footprint assessed the environmental impact of dietary patterns. Dietary patterns were identified through Principal Components Analysis. Logistic and linear regression models were performed to evaluate the association between dietary patterns and the components of the global syndemic investigated in this study. The Unhealthy Dietary Pattern increased the odds of obesity and micronutrient inadequacy and had the highest environmental impact. Brazilian Dietary Pattern increased the odds of obesity, and micronutrient inadequacy and had the lowest environmental impact. Healthy Dietary Pattern was protective against micronutrient inadequacy. Dairy Dietary Pattern exhibited the most protective effect against Calcium inadequacy. The diet has affected the environment and people's health in this sample. Dietary patterns identified here to contribute to poor health and environmental damage can help the government develop policies that incorporate the costs of these effects into the prices of the food.

Key-words

Obesity. Undernutrition. Carbon footprint. Water footprint. Ecological footprint. Sustainable diet.

Introduction

The Global Syndemic constitutes a framework developed to emphasize attention to the scale and urgency of mitigating the three greatest threats to human and planetary health: obesity, undernutrition, and climate change (Swinburn et al., 2019).

While food demand worldwide is increasing (Foley et al., 2011; Tilman et al., 2011), and global food systems can produce enough food to feed the global population (IPCC, 2019), hunger and food insecurity persist while obesity rates are rising. This is because current global food systems are shifting towards a less diverse and low-quality diet rich in animal-source and ultra-processed foods (FAO, 2013; FAO et al., 2020; Swinburn et al., 2019). In Brazil, a continental dimensions country and remarkable biodiversity, the dietary pattern has been undergoing a process of standardization, in which ten products account for more than 45% of food consumption: rice, beans, white bread, beef, chicken, banana, milk, soft drinks, beers and sugar (Belik, 2020).

Additionally, food systems contribute to about a third of global greenhouse gas emissions that cause climate change, because of land use/land-use change activities (71%), with the remaining were from supply chain activities: retail, transport, consumption, fuel production, waste management, industrial processes and packaging (Crippa et al., 2021). Consequently, food systems are one of the underlying factors contributing to the Global Syndemic's three components.

Changes in global dietary patterns adversely affect human and planetary health (der Pahlen, 2017). Studies on the individual impact of food, food groups, and dietary patterns on health (Bliznashka et al., 2021; França et al., 2021; Wang et al., 2021) and environment (J. T. da Silva et al., 2021; Marlow et al., 2015; Notarnicola et al., 2017) have been conducted, but none has focused on the assessment of dietary patterns on the three components of the global syndemic at once. Therefore, this study aimed to evaluate how dietary patterns in Brazil are associated with the components of the global syndemic.

Methods

CUME Study

This study used baseline data from the Cohort of Universities of Minas Gerais (CUME Study), carried out biennially since 2016 (Domingos et al., 2018). Alumni of seven Federal Universities from Minas Gerais State in Brazil were invited to participate in the study. Once registered, participants had access to the baseline questionnaire, divided into two phases. The first phase included questions related to lifestyle, socio-demographic, anthropometric, biomedical, and clinical data, individual and family morbidity, and personal examination history.

In the second phase, participants completed a semi-quantitative Food Frequency Questionnaire (FFQ), validated for the study population (Azarias et al., 2021). The FFQ included 144 food items grouped into dairy, meat and fish, cereals and leguminous, fats and oils, fruits and vegetables, beverages, and other foods. Participants reported each item's frequency, number of times consumed, and portion size over the previous 12 months.

Participants

Between 2016 and 2022, 8694 participants completed the baseline questionnaire. Individuals who resided abroad during the year before completing the questionnaire (n = 338), non-Brazilians (n = 54), individuals over 60 years (n = 187), women who reported being pregnant in the year before completing the questionnaire (n = 308), those who did not answer questions about their weight or height (n = 12), and individuals who consumed either < 500 or ≥ 6,000 kcal/day (n = 235) (Schmidt et al., 2015; Teixeira et al., 2016) were not included in the analysis. Thus, the final sample of this study is composed by 7560 individuals.

The study was conducted following the guidelines of the Declaration of Helsinki and approved by the ethics committees of the universities involved (protocol no. UFV 596741-0/2013; UFMG 2491366/18; UFOP 2565240/2018; UFJF 2615738/2018; and UFLA 2676682). All participants read and agreed to the online informed consent form before answering the questionnaire.

Malnutrition outcome variables

<u>Obesity</u>

Data on weight (kg) and height (m) were self-reported in the first phase of the questionnaire and used to calculate the Body Mass Index (BMI) (kg/m2) (Miranda et al., 2017). Obesity was considered as a BMI ≥ 30 kg/m2 (WHO, 2000).

<u>Insufficient intake of micronutrients</u>

The FFQ data were processed, and the amount of each food item consumed was measured in grams or milliliters per day. Nutrient intake was then determined using Brazilian nutritional composition tables as reference (IBGE, 2011; Universidade de Campinas, 2011).

The mean daily intake of vitamins A, Thiamin (B1), Riboflavin (B2), Niacin (B3), Pyridoxine (B6), Folate (B9), Cobalamin (B12), C, D, and E, and of minerals Iron (Fe), Magnesium (Mg), Zinc (Zn), Selenium (Se), Copper (Cu), Calcium (Ca) and Potassium (K), obtained on FFQ data, were compared and classified as "adequate" or "inadequate", according to the Dietary Reference Intake (DRIs) of the Institute of Medicine. Estimated Average Requirement (EAR) was used for all nutrients investigated here, except for K, which was evaluated as Adequate Intake (AI) (Institute of Medicine, 1997, 1998, 2000, 2001, 2019; Medicine, 2011).

Environmental outcome variables

<u>Environmental footprints from food patterns</u>

The carbon (CFP), water (WFP) and ecological (EFP) footprints of each individual were calculated by multiplying the average amount of each food by footprint coefficients (Garzillo et al., 2019) that quantify, respectively, the emissions of greenhouse gases (expressed in grams of carbon dioxide equivalent (gCO2e)), the use of total water (including the blue, green and gray water, expressed in volume (L)), and the demand from the regenerative capacity of the biosphere (expressed in units of land area (m^2)). All environmental footprints were calculated per gram or milliliter of food, per person, per day.

Exposure assessment

<u>Dietary patterns</u>

In this study, to identify the major dietary patterns and to reduce the complexity of the data, the FFQ food items were first grouped into 27 groups, considering their nutritional composition, the level and intent of processing, according to the NOVA classification (unprocessed and minimally processed foods; processed culinary or food industry ingredients; processed food; and ultra-processed foods) (Monteiro et al., 2016) and the coefficients of environmental footprints (Garzillo et al., 2019).

The evaluation of the applicability of the Principal Components Analysis (PCA) was done through Bartlett's sphericity test (BTS) and Kaiser-Meyer-Olkin (KMO) statistical test. Then, PCA was performed to identify eating patterns, and the number of dietary patterns to retain was determined considering the eigenvalue greater than one, scree test (i.e., identifying the breaking point in the scree plot of components' eigenvalues), and natural interpretability.

Varimax rotation was used to achieve a simple matrix and uncorrelated dietary patterns, and positive factor loading values ≥ 0.25 were used to determine the food groups in each dietary pattern. Lastly, a score for each dietary pattern for every individual based on their intakes of different food groups weighted by corresponding factor loadings was calculated. The labeling of dietary patterns identified was based on the literature and our interpretation of the data.

Covariates

In the first phase of the questionnaire, data on sex (male/female), age (continuous), individual income (continuous), marital status (single/married/divorced or widow(er)), and professional status (employed/student/retired or home duties/unemployed) were collected. The practice of physical activity was investigated from a list of 23 leisure activities and the respective time dedicated to each one (Martínez-González et al., 2005). Participants were classified as physically active, insufficiently active, or inactive, according to the World Health Organization (WHO, 2010).

Statistical analysis

To characterize the study population, absolute and relative frequencies of the socio-economic variables were presented for the total sample and according to dietary patterns and the outcomes investigated in this study. For categorical variables, the Pearson chi-square test was used to identify statistical differences between participants' characteristics. For continuous variables, statistical differences were assessed by the Kruskal-Wallis test, and pairwise comparison of means test with Tukey's method adjustment.

Logistic and linear regression models were performed to evaluate the association between dietary patterns and the components of the global syndemic investigated in this study. Models included factor loadings of the four dietary patterns (model 1) and were then adjusted for sex, age, individual income, and the daily energy intake in kcal (model 2). Analysis for obesity outcome was additionally adjusted for physical activity. All analyses were performed on Stata/SE® 17.0 and adopted a significance level of 5%.

Results

Characterization of the sample

Table 1 shows the descriptive statistics of participants according to the global syndemic components investigated in this study. The sample of this study consisted of 7560 participants from the CUME Study, with 68% being female and 64.21% being white. The average age of participants was 35 ± 8.5 years and their average monthly income was R$ 6108.58 ± 436.49 (approximately US$ 1227).

Women were more likely to obesity and typically had an inadequate micronutrients intake, while men's diet emitted a higher amount of CO_2e, consumed more water and required more productive area. Those between the ages of 30 and 49 are also at higher risk of obesity, insufficient micronutrient intake, and a greater environmental impact. Lower income was associated with obesity and insufficient vitamin intake, whereas environmental footprints increased proportionally with income. Compared to white people, black/brown people's diet showed a higher CFP, WFP and EFP. Regarding marital status, married people's diet was more likely to cause obesity and have a greater environmental impact. Employed participants were at a higher risk for obesity and insufficient intake of vitamins. Compared to students, employed people's diet emitted more CO_2e and required more productive area. The region of Brazil where participants live did not significantly affect the variables investigated here (Table 1).

Dietary patterns

Regarding the dietary patterns, BTS and KMO tests (BTS ≤ 0.001 and KMO = 0.728) indicated that the sample was suitable for the PCA. We identified four dietary patterns (DP), explaining 29% of the data variance. The first pattern, named "Unhealthy-DP", consisted of meats, ultra-processed foods, sweetened beverages and alcoholic beverages. The "Brazilian-DP" comprised rice, beans, culinary ingredients, ultra-processed fats, and white bread. The "Healthy-DP" included eggs, grains and tubers, fruits and natural juice, vegetables, teas and water, nuts, and olive oil. The "Dairy-DP" was composed of milk, cheeses, yogurts, and ultra-processed breads (Table 2).

The Unhealthy-DP factor score was higher among men and those with higher income. The Brazilian-DP factor score was higher among men, older people, those with lower income and unemployed. Healthy-DP factor score increased significantly with age and individual income. The Dairy-DP factor score was higher among women and older people. When differences in mean factor score for dietary patterns were evaluated among Brazil's region, we verified that the Southeast region had a higher mean factor score for Brazilian-DP and Dairy-DP (Table 3).

Overall, the average caloric consumption was 2395.72 ± 11.28 kcal/day, being higher in Unhealthy-DP (2800.82 ± 27.96 kcal/day) and lower in Dairy-DP (2069 ± 18.53). The Unhealthy-DP had the highest mean for protein (142.48 ± 1.85 g/day) and total fat (126.25 ±

1.47 g/day), and the Dairy-DP had the lowest mean for carbohydrate (232.78 ± 2.23 g/day), protein (92.87 ± 0.90 g/day) and total fat (83.29 ± 0.89 g/day). The fiber content was higher on Healthy-DP (33.69 ± 0.39 g/day) (data not shown).

Malnutrition

Figure 1 shows the average BMI and micronutrient intake value for the total sample and according to dietary patterns. The mean BMI among those belonging to Unhealthy-DP (26.09 ± 0.12 kg/m2) was significantly higher than for the total sample (24.87 ± 0.05 kg/m2).

For the total sample, the daily average intake of vitamins and minerals was adequate, except for vitamins D (164.66 ± 1.64 UI/day) and E (8.95 ± 0.06 mg/day), and Ca (846.51 846.51 ± 4.96 mg/day). The Unhealthy-DP had the highest daily averages for vitamins B1 (1.86 ± 0.02 mg), B2 (2.63 ± 0.08 mg), B3 (38.50 ± 0.51 mg), B6 (2.28 ± 0.03 mg), B12 (5.59 ± 0.12 µg), D (210 ± 4.94 UI), as well as Fe (14.25 ± 0.16 mg) and Zn (16.94 ± 0.21 mg). The Brazilian-DP had the highest daily average for vitamin B9 (546.75 ± 5.98 µg). The Healthy-DP had the highest daily averages for vitamins A (1,119.62 ± 13.35 µg), C (347.10 ± 6.80 mg) and E (11.23 ± 0.15 mg) as well as Mg (452.70 ± 4.28 mg), Se (258.65 ± 4.64 µg), Cu (2.05 ± 0.03 µg) and K (4,473.90 ± 40.90 mg). The highest daily average for Ca was observed in Dairy-DP (976.90 ± 10.77 mg) (Figure 1).

The overall prevalence of insufficient intake of vitamins was 12.49% for vitamin A, 13.08% for vitamin B1, 5.65% for vitamin B2, 3.82% for vitamin B3, 11.40% for vitamin B6, 22.87% for vitamin B9, 16.10% for vitamin B12, 9.01% for vitamin C, 94.51% for vitamin D and 80.89% for vitamin E. Regarding insufficient intake of minerals, the prevalence was 16.59%, 32.91%, 15.44%, 2.34%, 6.75%, 54.70% and 29.71% for Fe, Mg, Zn, Se, Cu, Ca and K, respectively (data not shown).

Logistic regression models displayed in Table 4 were performed to analyze the association between dietary patterns and obesity as well as insufficient intake of micronutrients. After conducting an adjusted analysis, it was found that Unhealthy-DP and Brazilian-DP had respective odds of increasing obesity by 45% and 14%.

Regarding micronutrient intake, Unhealthy-DP had the highest odds for insufficient intake of vitamins B9 (18%), C (33%), E (69%), Mg (29%), and Cu (131%). On the other hand, it had the highest protective effect for vitamin B12 (80%) and Zn (46%) intake. Brazilian-DP had the highest odds for insufficient Se (210%) intake, whereas it was protective for vitamins B1 (75%) and B9 (79%) intake. Healthy-DP was protective for the majority of micronutrients investigated in the study, particularly for vitamins C (77%) and E (32%), Fe (42%), Mg (82%), and K (87%). There was no statistically significant result for vitamin B3, zinc, and selenium. Dairy-DP had the highest protective effect for Ca intake (86%) (Table 4).

Environmental footprints from dietary patterns

Figure 2 shows the average values of the environmental footprints investigated in this study for the total sample and according to dietary patterns. The mean CPF among those belonging to Unhealthy-DP (10238.44 ± 148.46) was significantly higher than for the total sample (6713.45 gCOe/person/day). All other dietary patterns showed mean CFP values significantly below the general mean. The mean WFP and EFP for the total sample were 7952.50 liters/person/day and 48.19 m2/person/day, also being significantly higher among those belonging to Unhealthy-DP (10682.86 liters/person/day and 68.15 m2/person/day, respectively).

The results of the linear regression models found that Unhealthy-DP had the highest environmental impact compared to the other three dietary patterns across all three measurements in both crude and adjusted analyses. In adjusted analyses, the CO2e emission of Unhealthy-DP was 122.3%, 85.7%, and 46.7% higher than Brazilian-DP, Healthy-DP, and Dairy-DP, respectively. Additionally, Unhealthy-DP required 49.7%, 9.2%, and 71% more water than Brazilian-DP, Healthy-DP, and Dairy-DP, respectively. Regarding the biosphere's regenerative capacity, Unhealthy-DP required 58.5%, 0.5%, and 30% more bio-productive area than Brazilian-DP, Healthy-DP, and Dairy-DP, respectively (Table 4).

Discussion

As far as we know, this study is the first to examine how dietary patterns relate to the three components of the global syndemic. Based on data from the CUME Study, we identified four distinct dietary patterns and labeled them based on the literature and our interpretation of the data. With that in mind, it was expected that Unhealthy-DP and Dairy-DP would be positively associated with all three components of the global syndemic, Healthy-DP would be negatively associated with the three outcomes, and Brazilian-DP would be negatively associated with environmental footprints and present a null or little association with malnutrition outcomes.

As expected, Unhealthy-DP had the greatest environmental impact for all three metrics used in this study (CFP, WFP, and EFP). This may be explained by its dominant composition of meat and ultra-processed foods. It is well established that animal-source foods require more water and land and emit significantly greater amounts of CO2e (Marlow et al., 2015; Nabipour Afrouzi et al., 2023; Sabaté et al., 2015). Recent literature has demonstrated that ultra-processed foods significantly impacts CO2e emissions, land use, and water consumption (Berardy et al., 2020; J. T. da Silva et al., 2021; Garzillo et al., 2022).

Unhealthy-DP also was positively associated with malnutrition outcomes, increasing 45% the odds of obesity. This dietary pattern consists of food items that are known to contribute to obesity, such as red meats (Luan et al., 2020; Oliveira et al., 2020), ultra-processed foods (Hall et al., 2019; F. M. Silva et al., 2018), sweetened beverages (Oliveira et al., 2020; Santos et al., 2022) and alcoholic beverages (Albani et al., 2018; Souza et al., 2021). The highest odds for insufficient intake of some vitamins and minerals observed for Unhealthy-DP were expected since those are nutrients most commonly found in fresh fruits and vegetables. The protective effect of intake of vitamin B12 and Zn was expected because of the meat composition of this dietary pattern, once vitamin B12 is exclusively found in animal-source food and meat is a great source of zinc (IBGE, 2011; Universidade de Campinas, 2011).

In our study, Brazilian-DP increased the odds of obesity by 14%, which was unexpected as previous literature showed a null or negative association between traditional Brazilian dietary patterns and obesity measurements (De Oliveira Santos et al., 2017; França et al., 2021; Machado Arruda et al., 2016). Studies that investigate dietary patterns on health outcomes are difficult to compare because although they may receive the same name, their composition varies widely (Kac et al., 2007). This is especially true in Brazil, where food culture changes from one region to another, and all of them may be named Brazilian patterns (Kac et al., 2007; Ministério da Saúde, 2014). Although not representative of the Brazilian population, CUME Study's participants live in all 27 states of Brazil, and Brazilian-DP in this study is composed of rice, beans, culinary ingredients, ultra-processed fats, and white bread. In a study conducted with women in the Brazilian state Rio Grande do Sul, a common Brazilian dietary pattern was characterized by cassava, yam, farofa, chicken, egg, fish, potato, black beans, and polenta (França et al., 2021). In a study conducted in the state of São Paulo, the traditional Brazilian dietary pattern was composed of positive factorial loads for beans, rice, margarine, and beef and a negative factor loading for low-fat dairy foods, whole grain bread, and diet sodas (Machado Arruda et al., 2016). Both studies showed a negative association between these dietary patterns and excess weight.

Regarding the environmental impact, Brazilian-DP had the lowest CFP and EFP, and the second lowest WFP out of the four dietary patterns studied, showing the low environmental impacts of Brazilian dietary patterns on CFP, WFP, and EFP. A previous study estimated that the average CFP of the Brazilian diet in 2008-2009 was 4489 gCO2e/person/day (Garzillo et al., 2021), which is 0.33 times lower than the mean CFP for the total sample and 0.20 times lower than the mean CFP for Brazilian-DP in this study. Although belonging to Brazilian-DP, it does not mean that those participants do not consume meat and other food items with higher CFP. Our results show that CFP tends to increase with income, which is consistent with the results of Garzillo et al. Moreover, Garzillo et al. also found that CFP increases with higher levels of education, which may explain the higher CFP observed in our study, given that all participants were university graduates.

Although Brazilian-DP had the lowest environmental impact in this study, international literature suggests there are diets with even lower environmental impacts. While this Brazilain-DP emits 5627.15 gCO2e/person/day, current Indonesian diet, mainly composed of grains, starchy roots, and some animal source food, emits less than 3000 gCO2e/person/day (De Pee et al., 2021). Data from Seguimiento Universidad de Navarra (SUN Cohort) in Spain accounted for 3540 gCO2e/person/day (Fresán et al., 2020). In our study, Brazilian-DP demanded 7384.44 L/person/day of water and 42.61 m2/person/day of land, whereas the Spanish diet demanded only 3753 L/person/day of water and 7.17 m2/person/day (Fresán et al., 2020). On the other hand, data from NHANES Study account 2230 gCO2e/1000 kcal (O'Malley et al., 2023), a result similar to ours. The discrepancies observed may be due to diet composition and different data resources used in these studies, which account for the different food production systems.

Brazilian diet is known for its variety, consisting mainly of unprocessed or minimally processed foods, plant-based food combinations complemented with a minimum of animal source food. If followed properly, it can provide a balanced and nutritious diet rich in vitamins, minerals, bioactive compounds, and fiber, which can help prevent obesity and micronutrient deficiencies. It also promotes a fairer food system, supporting the local economy and respecting the food culture. Additionally, limiting animal-source food consumption reduces the environmental impact on the food system (Ministério da Saúde, 2014). The absence of animal-source food in the Brazilian-DP in our study may mean that its consumption is limited. On the other hand, the lack of fruits and vegetables may mean that the Brazilian diet is not as varied as it should be and is not following Brazilian dietary guidelines.

In this study, Healthy-DP was protective against the inadequacy of micronutrients. It was expected since it is a diversified dietary pattern, composed mainly of fresh fruits and vegetables, a great source of vitamins such as C and E, and minerals such as K (IBGE, 2011; Universidade de Campinas, 2011). Additionally, Dairy-DP had the highest protective effect against Ca inadequacy, which is not surprising, as dairy products are the primary source of this mineral (IBGE, 2011; Universidade de Campinas, 2011). It was not surprising that Healthy-DP had the second lowest CFP, as research has shown that plant-based foods generally have a lower CFP (Berardy et al., 2020; Chapa et al., 2020; Fresán & Sabaté, 2019; Nabipour Afrouzi et al., 2023). However, some results for the environmental impacts of Healthy-DP and Dairy-DP were thought-provoking. Healthy-DP had the second-highest WFP, while Dairy-DP had the lowest WFP. In agreement with our study, Berardy et al. estimated the environmental impacts of food groups and reported a lower water consumption for dairy products and high water consumption for fruits, a major food item in our Healthy-DP. They also account that nuts and seeds, food items also belonging to our Healthy-DP, had the highest water consumption on a protein content basis, probably due to the small edible mass compared to the overall plant biomass.

Besides that, WFP is often reported as a single value in the literature, but it is composed of three components: green water, blue water, and grey water, being green water the amount of precipitation and soil moisture that is directly consumed in growing crops (Garzillo et al., 2019; Gleick, 2014). Around three-quarters of the global water footprint is green water (Gleick, 2014), which may explain the greater WFP for Healthy-DP. Rainfed agriculture accounts for over 80% of cropland worldwide and produces more than 60% of all cereal grains. Therefore, using green water may not significantly impact the overall water budget (Fekete, 2013; Wilderer, 2010).

Moreover, food items that compound Healthy-DP are less calorically dense (IBGE, 2011; Universidade de Campinas, 2011), which could lead to increased overall food consumption, since environmental impacts were analyzed here for each gram of edible food consumed by CUME Study's participants. On average, participants belonging to Healthy-DP consumed the greatest amount of food (3653.1 ± 22.71 grams of food/person/day), while those on Dairy-DP had the lowest total food intake (2805.44 ± 20.77 grams of food/person/day).

It is worth mentioning that there is currently no food production with zero or negative CFP, WFP, or EFP. Therefore, the negative coefficient values for environmental footprint in Table 4 mean that, for the four dietary patterns being compared, the negative values represent the difference between them. Further research is needed to identify diverse compositions of a traditional Brazilian dietary pattern and their impact on the components of the Global Syndemic.

A strength of our study is that CUME Study uses an online platform, which enabled us to recruit participants from all regions of Brazil. Our sample consisted of individuals with a high level of education, which ensured the reliability of the data since it was self-reported. Also, food consumption data were obtained using a validated FFQ (Azarias et al., 2021), as well as data regarding BMI (Miranda et al., 2017). Although this study uses a highly educated sample, which does not represent the Brazilian population, representativeness is usually unnecessary in analytical epidemiological studies (Richiardi et al., 2013). Thus, the CUME Study provides data that allow the discussion, planning, and implementation of specific interventions in Brazil. Another strength is that we assessed three metrics of the environmental impact of dietary patterns consumed by Brazil's population. We also used environmental impact coefficients that consider the entire life cycle of foods, from “farm to fork.”

A limitation of this study is that, although environmental impact coefficients used in the study were calculated based on food and culinary preparations consumed in Brazil, some of their estimates came from studies conducted in other countries and industry reports. Also, our sample population allowed us to evaluate the outcome of undernutrition, only in terms of insufficient intake of micronutrients, without considering underweight and food safety factors.

Conclusion

For the first time, the relationship between dietary patterns and the three components of the Global Syndemic was explored. In this Brazilian university graduate sample, diet has affected the environment and people’s health. Obesity and micronutrients inadequacy prevalence was high at the same time CFP, WFP and EFP and is higher than the national average and that of other countries.

Our study highlights the need to understand the different compositions of the Brazilian Dietary Pattern and how they may affect the three components of the Global Syndemic. Our results also reveal that the Brazilian diet is not in line with the Brazilian Dietary Guideline, which is negatively affecting the environment and people's health. Therefore, it is important for health services to educate the general population about the importance of following the guidelines for better health and a healthier environment. At the same time, dietary patterns identified here to contribute to poor health and environmental damage can help the government develop policies that incorporate the costs of these effects into the prices of the food.

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Author contributions

Mattar JB: conceptualization, methodology, formal analysis, investigation, writing - original draft and visualization. **Costa MH:** conceptualization, methodology, and writing - review & editing. **Domingos ALG:** conceptualization, investigation, and writing - review & editing. **Hermsdorff HHM:** investigation, resources, writing - review & editing, funding acquisition and project administration. **Pimenta AM:** investigation, resources, data curation, writing - review & editing, funding acquisition and project administration. **Bressan J:** conceptualization, methodology, investigation, resources, writing - review & editing, supervision, funding acquisition and project administration. All authors read and approved the final version of the manuscript. The authors declare no conflict of interest.

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Table 1. Socio-demographic characteristics, according to global syndemic components, baseline CUME study (n = 7560, 2016-2022)

Characteristic	Total n (%)	Obesity n (%)	VII n (%)	MII n (%)	CFP Mean ± sd	WFP Mean ± sd	EFP Mean ± sd
Sex							
Male	2420 (32.01)	380 (40.25)	2328 (31.71)	1454 (30.85)	7676.13 ± 94.5[a]	9106 ± 93.12[a]	54.72 ± 0.62[a]
Female	5140 (67.99)	564 (59.75)	5014 (68.29)	3259 (69.15)	6260.20 ± 56.53[b]	7409.41 ± 53.15[b]	45.11 ± 0.37[b]
P-value	-	**< 0.001**	**0.001**	**0.005**	**-**	**-**	**-**
Age							
20-29	2317 (30.65)	175 (18.54)	2266 (30.86)	1454 (30.85)	6364.07 ± 88.76[a]	7499.17 ± 85.6[a]	44.53 ± 0.54[a]
30-39	3234 (42.78)	382 (40.47)	3156 (42.99)	2046 (43.41)	6811.93 ± 76.36[b]	8020.24 ± 72.7[b]	48.9 ± 0.52[b]
40-49	1388 (18.36)	261 (27.65)	1338 (18.22)	819 (17.38)	7030.4 ± 113.9[b]	,406.16 ± 111.37[c]	51 ± 0.72[b]
50-59	621 (8.21)	126 (13.35)	582 (7.93)	394 (8.36)	6795.77 ± 171.57[a,b]	8277.12 ± 167.7[b,c]	51.86 ± 1.17[b]
P-value	-	**< 0.001**	**< 0.001**	**0.041**	-	-	-
Individual income (minimum wage)*							
< 5	4344 (57.46)	499 (52.86)	4225 (57.55)	2742 (58.18)	6430.43 ± 65.97[a]	7704.42 ± 63.5[a]	45.92 ± 0.42[a]
≥ 5 to < 10	2215 (29.30)	273 (28.92)	2160 (29.42)	1365 (28.96)	7002.66 ± 91.38[b]	8194.37 ± 86.49[b]	50.3 ± 0.61[b]
≥ 10	1001 (13.24)	172 (18.22)	957 (13.03)	606 (12.86)	7301.7 ± 126.73[b]	8493.87 ± 129.1[b]	53.34 ± 0.83[c]
P-value	-	**< 0.001**	**0.008**	0.224	-	-	-
Skin color							
White	4854 (64.21)	579 (61.33)	4722 (64.31)	2993 (63.51)	6532.94 ± 56.85[a]	7813.05 ± 55.95[a]	47.36 ± 0.38[a]
Black/Brown	2614 (34.58)	349 (36.97)	2530 (34.46)	1659 (35.20)	7024.65 ± 94.35[b]	8192.58 ± 88.46[b]	49.55 ± 0.6[b]
Yellow/Indigenous	925 (1.22)	16 (1.69)	90 (1.23)	61 (1.29)	7395.27 ± 560.77[a,b]	8488.7 ± 564.64[a,b]	53.36 ± 3.74[a,b]
P-value	-	0.074	0.439	0.225	-	-	-
Marital status							
Single	3702 (84.97)	390 (41.31)	3604 (49.09)	2311 (49.03)	6569.68 ± 71.79[a]	7798.04 ± 69.27[a]	46.75 ± 0.47[a]
Married	3500 (46.30)	501 (53.07)	3392 (46.20)	2169 (46.02)	6888.26 ± 71.48[b]	8099.86 ± 68.69[b]	49.63 ± 0.47[b]
Divorced/Widow(er)	358 (4.74)	53 (5.61)	346 (4.71)	233 (4.94)	6491.12 ± 227.53[a,b]	8109.01 ± 224.62[a,b]	48.9 ± 1.4[a,b]
P-value	-	**< 0.001**	0.465	0.506	-	-	-
Professional status							
Employed	5611 (74.22)	748 (79.24)	5447 (74.19)	3538 (75.07)	6789.75 ± 56.95[a]	8016.13 ± 54.83[a]	48.74 ± 0.37[a]
Student	1292 (17.09)	103 (10.91)	1265 (17.23)	779 (16.53)	6415.72 ± 122.02[b]	7754.35 ± 118.65[a]	46.29 ± 0.84[b]
Retired/home duties	96 (1.27)	21 (2.22)	94 (1.28)	65 (1.38)	6913.39 ± 494.5[a,b]	7914.73 ± 411.94[a]	48.29 ± 2.5[a,b]
Unemployed	591 (7.42)	72 (7.63)	536 (7.30)	331 (7.02)	6601.82 ± 184.46[a,b]	7778.87 ± 181.81[a]	47.06 ± 1.26[a,b]
P-value	-	**< 0.001**	**0.044**	0.061	-	-	-
Region of Brazil							
North	120 (1.38)	13 (1.38)	102 (1.39)	69 (1.47)	7077.48 ± 467.56[a]	7712.54 ± 424.09[a]	50.55 ± 2.75[a]
North-east	274 (3.16)	33 (3.50)	229 (3.13)	151 (3.21)	7152.16 ± 288.10[a]	8019.95 ± 258.71[a]	52.22 ± 1.87[a]
South-east	7824 (90.18)	839 (89.07)	6605 (90.16)	4208 (89.53)	6680.99 ± 52.17[a]	7952 ± 50.48[a]	48.01 ± 0.34[a]
Mid-west	304 (3.50)	39 (4.14)	258 (3.52)	183 (3.89)	7141.98 ± 275.26[a]	8193.49 ± 268.56[a]	49.95 ± 1.62[a]
South	154 (1.78)	18 (1.91)	132 (1.80)	89 (1.89)	6473.98 ± 281.42[a]	7649.92 ± 265.73[a]	45.49 ± 1.66[a]
P-value	-	0.798	0.253	0.186	-	-	-

P-value was obtained from Pearson chi-squared test for categorical variables, and bold means statistical significance ($p \leq 0.05$). Differences for continuous variables were obtained by Kruskal-Wallis or pairwise comparison of means with Tukey's method adjustment different letters mean statistically significant differences ($p \leq 0.05$). VII: insufficient intake of, at least, one vitamin; MII: insufficient intake of, at least, one mineral; CFP: Carbon Footprint; WFP: Water Footprint; EFP: Ecological Footprint. *Minimum wage (R$ 880.00 in 2016; R$ 954.00 in 2018; R$ 1,045.00 in 2020; R$ 1,212.00 in 2022).

Table 2. Dietary patterns and factor loadings of food groups consumed by CUME Study's participants in baseline (n = 7560, 2016-2022)

Food groups	Dietary patterns				h^2
	Unhealthy	Brazilian	Healthy	Dairy	
Milk	-	-	-	0.4524	0.6854
Cheeses	-	-	-	0.2820	0.7623
Yogurts	-	-	-	0.4280	0.6468
Red meat	0.3990	-	-	-	0.6726
Chicken and fish	0.3223	-	-	-	0.6509
Salt meat	0.2966	-	-	-	0.8127
Sushi	-	-	-	-	0.8869
Egg	-	-	0.3264	-	0.7011
Ultra-processed meets	0.3995	-	-	-	0.6411
Rice and pasta	-	0.4337	-	-	0.5997
Beans	-	0.3084	-	-	0.6701
Grains and tubers	-	-	0.3047	-	0.6277
Fried tubers	-	-	-	-	0.8036
Culinary ingredients	-	0.3655	-	-	0.716
Ultra-processed fats	-	0.2618	-	-	0.7317
Fruits and natural juice	-	-	0.4080	-	0.5694
Vegetables	-	-	0.4553	-	0.5518
Coffee	-	-	-	-	0.8352
Teas and water	-	-	0.3161	-	0.7882
Sweetened beverages	0.2899	-	-	-	0.7121
Fermented alcoholic beverages	0.2743	-	-	-	0.6865
Distilled alcoholic beverages	0.2608	-	-	-	0.7732
Nuts and olive oils	-	-	0.3403	-	0.7532
French bread	-	0.3782	-	-	0.6359
Ultra-processed breads	-	-	-	0.3555	0.7101

Cont.

Food groups	Dietary patterns				h^2
	Unhealthy	Brazilian	Healthy	Dairy	
Preserves (jams)	-	-	-	-	0.9175
Ultra-processed foods	0.3059	-	-	-	0.6775

Table 3. Socio-demographic characteristics, according to dietary patterns, baseline CUME study (n = 7560, 2016-2022)

Characteristic	Total n (%)	Dietary patterns			
		Unhealthy (UDP)	Brazilian (BDP)	Healthy (HDP)	Dairy (DDP)
Sex					
Male	2,420 (32.01)	0.46 ± 0.03[a]	0.39 ± 0.03[a]	0.05 ± 0.03[a]	- 0.14 ± 0.03[a]
Female	5,140 (67.99)	- 0.22 ± 0.02[b]	- 0.19 ± 0.02[b]	- 0.02 ± 0.02[a]	0.07 ± 0.02[b]
Age					
20-29	2,317 (30.65)	- 0.02 ± 0.03[a]	- 0.02 ± 0.03[a]	- 0.15 ± 0.03[a]	0.00 ± 0.02[a,b]
30-39	3,234 (42.78)	0.03 ± 0.03[a]	- 0.06 ± 0.02[a]	- 0.03 ± 0.02[b]	- 0.06 ± 0.02[b]
40-49	1,388 (18.36)	0.02 ± 0.04[a]	0.15 ± 0.04[b]	0.13 ± 0.04[c]	0.07 ± 0.03[a,c]
50-59	621 (8.21)	- 0.13 ± 0.06[a]	0.02 ± 0.06[a,b]	0.39 ± 0.06[d]	0.15 ± 0.05[c]
Individual income*					
< 5	4,344 (57.46)	- 0.06 ± 0.02[a]	0.08 ± 0.02[a]	- 0.05 ± 0.02[a]	0.00 ± 0.02[a]
≥ 5 to < 10	2,215 (29.30)	0.06 ± 0.03[b]	- 0.09 ± 0.03[b]	0.04 ± 0.03[b]	0.02 ± 0.03[a]
≥ 10	1,001 (13.24)	0.16 ± 0.05[b]	- 0.14 ± 0.04[b]	0.13 ± 0.04[b]	- 0.04 ± 0.04[a]
Skin color					
White	4,854 (64.21)	- 0.04 ± 0.02[a]	- 0.07 ± 0.02[a]	0.00 ± 0.02[a]	0.00 ± 0.02[a]
Black/Brown	2,614 (34.58)	0.06 ± 0.03[b]	0.13 ± 0.03[b]	- 0.00 ± 0.03[a]	0.00 ± 0.02[a]
Yellow/Indigenous	925 (1.22)	0.13 ± 0.18[a,b]	0.14 ± 0.16[a,b]	0.04 ± 0.13[a]	- 0.14 ± 0.11[a]
Marital status					
Single	3,702 (84.97)	0.03 ± 0.02[a]	- 0.01 ± 0.02[a]	- 0.05 ± 0.02[a]	0.01 ± 0.02[a]
Married	3,500 (46.30)	- 0.02 ± 0.02[a]	0.01 ± 0.02[a]	0.03 ± 0.02[b]	- 0.01 ± 0.02[a]
Divorced/Widow(e)	358 (4.74)	- 0.09 ± 0.08[a]	0.00 ± 0.07[a]	0.17 ± 0.08[b]	0.07 ± 0.07[a]
Professional status					
Employed	5,611 (74.22)	0.02 ± 0.02[a]	- 0.03 ± 0.02[a]	0.01 ± 0.02[a,b,c]	- 0.02 ± 0.02[a]
Student	1,292 (17.09)	- 0.03 ± 0.04[a]	0.04 ± 0.04[a]	- 0.04 ± 0.04[b]	0.04 ± 0.03[a]
Retired/home duties	96 (1.27)	- 0.45 ± 0.12[b]	- 0.24 ± 0.13[a]	0.37 ± 0.14[c]	0.15 ± 0.12[a]
Unemployed	591 (7.42)	- 0.02 ± 0.07[a]	0.25 ± 0.07[b]	- 0.02 ± 0.06[a,b,c]	0.08 ± 0.05[a]
Region of Brazil					
North	120 (1.38)	- 0.03 ± 0.17[a]	- 0.23 ± 0.13[a,b,c]	- 0.06 ± 0.13[a]	- 0.11 ± 0.11[a,b,c]
North-east	274 (3.16)	0.08 ± 0.10[a]	- 0.14 ± 0.09[a,b,c]	0.25 ± 0.10[a]	- 0.03 ± 0.08[b]
South-east	7,824 (90.18)	- 0.01 ± 0.02[a]	0.03 ± 0.02[b]	- 0.01 ± 0.02[a]	0.02 ± 0.01[a,b]
Mid-west	304 (3.50)	0.10 ± 0.09[a]	- 0.29 ± 0.08[c]	0.10 ± 0.09[a]	- 0.33 ± 0.07[c]
South	154 (1.78)	- 0.03 ± 0.11[a]	- 0.24 ± 0.11[a,b,c]	- 0.26 ± 0.12[a]	- 0.08 ± 0.11[a,b,c]

Differences were obtained by Kruskal-Wallis or pairwise comparation of means with Tukey's method adjust, and different letters mean statistically significant differences ($p \leq 0.05$). *Minimum wage (R$ 880.00 in 2016; R$ 954.00 in 2018; R$ 1,045.00 in 2020; R$ 1,212.00 in 2022).

Table 4. Regression models for evaluating the association of dietary patterns on components of the global syndemic (obesity, insufficient intake of micronutrients and environmental footprints) in baseline CUME Study participants (n = 7560, 2016-2022)

Outcome	Dietary patterns Coefficient* (95% confidence interval)							
	Unhealthy (UDP)		Brazilian (BDP)		Healthy (HDP)		Dairy (DDP)	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Obesity	1.27 (1.22 – 1.33)	1.45 (1.33 – 1.58)	1.10 (1.05 – 1.15)	1.14 (1.06 – 1.22)	0.91 (0.86 – 0. 95)	1.00 (0.92 – 1.08)	1.03 (0.97 – 1.08)	1.10 (1.02 – 1.17)
Yes[a]								
Insufficient intake								
Vitamin A[a]	0.63 (0.59 – 0.67)	0.42 (0.36 – 0. 48)	0.74 (0.69 – 0.79)	0.56 (0.51 – 0.62)	0.20 (0.18 – 0.22)	0.15 (0.13 – 0.17)	0.33 (0.30 – 0.36)	0.29 (0.27 – 0.33)
Vitamin B1[a]	0.15 (0.12 – 0.17)	0.41 (0.33 – 0.52)	0.13 (0.11 – 0.15)	0.25 (0.20 – 0.30)	0.16 (0.14 – 0.19)	0.40 (0.33 – 0.49)	0.21 (0.18 – 0.25)	0.37 (0.33 – 0.49)
Vitamin B2[a]	0.12 (0.09 – 0.15)	0.21 (0.15 – 0.29)	0.39 (0.34 – 0.47)	0.60 (0.47 – 0.77)	0.17 (0.14 – 0.20)	0.32 (0.25 – 0.43)	0.13 (0.10 – 016)	0.19 (0.15 – 0.25)
Vitamin B3[a]	0.06 (0.04 – 0.08)	0.29 (0.19 – 0.44)	0.38 (0.31 – 0.46)	1.43 (1.06 – 1.92)	0.28 (0.23 – 0.34)	1.24 (0.94 – 1.64)	0.28 (0.23 – 0.34)	0.79 (0.59 – 1.06)
Vitamin B6[a]	0.28 (0.24 – 0.32)	0.82 (0.66 – 1.02)	0.21 (0.18 – 0.24)	0.42 (0.35 – 0.51)	0.14 (0.12 – 0.16)	0.30 (0.25 – 0.37)	0.40 (0.35 – 0.46)	0.67 (0.58 – 0.78)
Vitamin B9[a]	0.58 (0.54 – 0.62)	1.18 (1.02 – 1.37)	0.14 (0.12 – 0.16)	0.21 (0.18 – 0.24)	0.16 (0.14 – 0.18)	0.26 (0.23 – 0.30)	0.48 (0.44 – 0.52)	0.64 (0.58 – 0.71)
Vitamin B12[a]	0.16 (0.14 – 0.18)	0.20 (0.17 – 0.23)	1.26 (1.18 – 1.35)	1.51 (1.35 – 1.69)	0.54 (0.50 – 0.58)	0.64 (0.57 – 0.73)	0.20 (0.17 – 0.22)	0.21 (0.19 – 0.24)
Vitamin C[a]	1.01 (0.95 – 1.09)	1.33 (1.13 – 1.55)	0.73 (0.67 – 0.79)	0.85 (0.75 – 0.96)	0.26 (0.23 – 0.29)	0.33 (0.28 – 0.39)	0.56 (0.51 – 0.61)	0.69 (0.62 – 0.78)
Vitamin D[a]	0.55 (0.52 – 0.59)	0.67 (0.60 – 0.74)	1.35 (1.26 – 1.46)	1.59 (1.44 – 1.75)	0.65 (0.61 – 0.70)	0.79 (0.71 – 0.87)	0.65 (0.61 – 0.70)	0.73 (0.67 – 0.79)
Vitamin E[a]	0.72 (0.69 – 0.75)	1.69 (1.54 – 1.86)	0.69 (0.66 – 0.73)	1.18 (1.10 – 1.26)	0.35 (0.33 – 0.38)	0.68 (0.62 – 0.73)	0.74 (0.70 – 0.78)	1.11 (1.04 – 1.19)
Iron[a]	0.23 (0.20 – 0.26)	1.12 (0.92 – 1.37)	0.28 (0.25 – 0.31)	0.79 (0.68 – 0.93)	0.21 (0.19 – 0.24)	0.58 (0.49 – 0.68)	0.60 (0.54 – 0.66)	1.13 (0.99 – 1.29)
Magnesium[a]	0.51 (0.47 – 0.54)	1.29 (1.12 – 1.49)	0.58 (0.54 – 0.62)	1.02 (0.91 – 1.14)	0.12 (0.11 – 0.13)	0.18 (0.16 – 0.21)	0.38 (0.35 – 0.41)	0.64 (0.58 – 0.71)
Zinc[a]	0.18 (0.16 – 0.20)	0.54 (0.44 – 0.66)	0.60 (0.56 – 0.66)	1.71 (1.47 – 2.00)	0.30 (0.27 – 0.33)	1.04 (0.89 – 1.22)	0.28 (0.25 – 0.31)	0.60 (0.51 – 0.69)
Selenium[a]	0.05 (0.30 – 0.07)	0.13 (0.08 – 0.22)	1.01 (0.87 – 1.18)	3.10 (2.26 – 4.26)	0.23 (0.18 – 0.29)	0.76 (0.54 – 1.07)	0.40 (0.30 – 0.54)	0.93 (0.65 – 1.33)
Copper[a]	0.29 (0.24 – 0.34)	2.31 (1.71 – 3.11)	0.22 (0.18 – 0.26)	0.81 (0.63 – 1.04)	0.10 (0.08 – 0.12)	0.42 (0.32 – 0.53)	0.36 (0.30 – 0.43)	1.04 (0.85 – 1.28)
Calcium[a]	0.42 (0.39 – 0.44)	0.53 (0.48 – 0.59)	0.78 (0.74 – 0.82)	0.92 (0.85 – 0.99)	0.48 (0.45 – 0.51)	0.55 (0.50 – 0.60)	0.14 (0.13 – 0.16)	0.14 (0.13 – 0.16)
Potassium[a]	0.48 (0.45 – 0.52)	1.07 (0.92 – 1.25)	0.48 (0.44 – 0.51)	0.74 (0.65 – 0.83)	0.10 (0.08 – 0.11)	0.13 (0.11 – 0.16)	0.35 (0.32 – 0.38)	0.55 (0.49 – 0.62)
Environmental data								
CFP[b]	2145.82 (2062.65 – 2228.99)	803.42 (680.09 – 926.74)	-121.33 (-179.30 – -63.36)	-983.02 (-1086.64 – -879.40)	432.92 (383.53 – 482.30)	-689.21 (-804.99 – -573.42)	283.73 (214.66 – 352.80)	-375.37 (-463.86 – -286.88)
WFP[b]	1879.49 (1809.02 – 1949.96)	843.32 (741.13 – 945.50)	248.90 (192.54 – 305.26)	-419.22 (-504.32 – -334.11)	941.87 (889.68 – 994.06)	78.02 (-13.29 – 169.34)	-99.19 (-168.65 – -29.74)	-599.08 (-676.77 – -521.38)
EFP[b]	13.36 (12.77 – 13.95)	7.33 (6.52 – 8.14)	-0.37 (-0.79 – 0.05)	-4.29 (-4.98 – -3.61)	5.19 (4.85 – 5.54)	0.04 (-0.61 – 0.69)	0.79 (0.34 – 1.25)	-2.21 (-2.73 – -1.68)

Model 1: multiple regression models, considering all four dietary patterns; Model 2: model 1 adjusted for sex, age, income and total energy (kcal); analysis for obesity was additionally adjusted for physical activity. *Odds Ratio (OR) for logistic regression; [a]Logistic regression model; [b]Linear regression model. CFP: Carbon footprint (gCO2eq/person/day); WFP: Water footprint (liters/person/day); EFP: Ecological footprint (m^2/person/day).

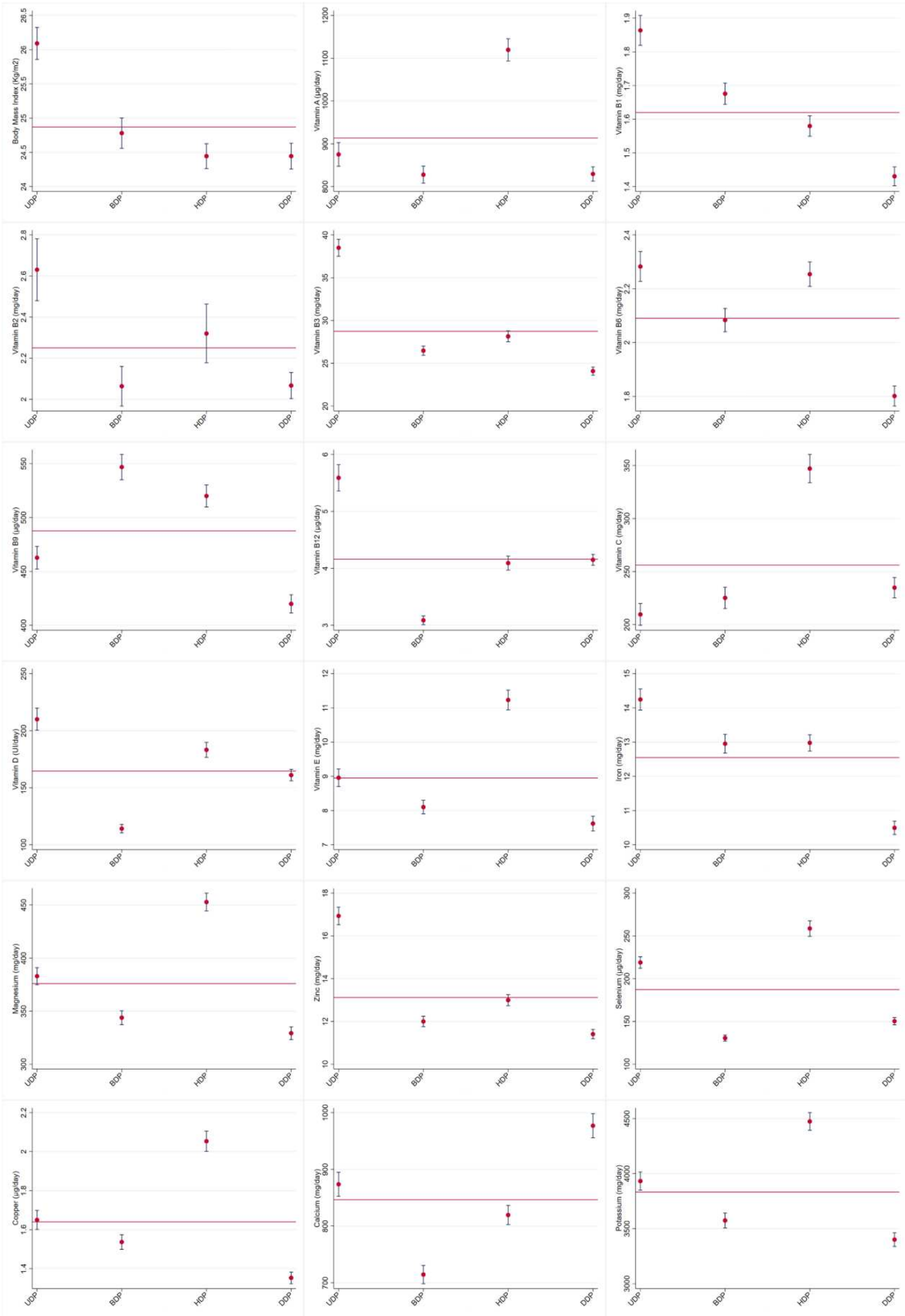

Figure 1. Average value for Body Mass Index (Kg/m^2) and micronutrient intake (mg or µg/person/day) for the total sample (red line) and according to dietary patterns (UDP: Unhealthy dietary pattern; BDP: Brazilian dietary pattern; HDP: Healthy dietary pattern; DDP: Dairy dietary pattern).

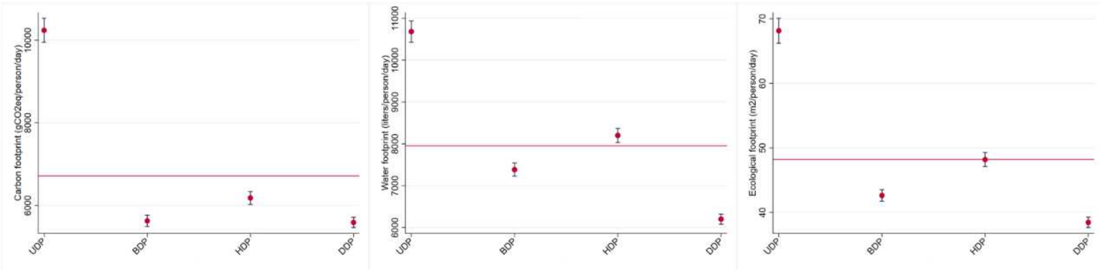

Figure 2. Average value of the environmental footprints (Carbon footprint (gCO2e/person/day); Water footprint (liters/person/day); Ecological footprint (m^2/person/day)) for the total sample (red line) and according to dietary patterns (UDP: Unhealthy dietary pattern; BDP: Brazilian dietary pattern; HDP: Healthy dietary pattern; DDP: Dairy dietary pattern).

The interaction between chronic ambient $PM_{2.5}$ exposure and physical activity on BMI in a Brazilian prospective cohort (CUME Study)

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Abstract
Epidemiological data on the association between fine particulate matter ($PM_{2.5}$) and obesity indicators in adults are limited. We aimed to assess the association of long-term exposure to $PM_{2.5}$ on Body Mass Index (BMI) in a Brazilian graduate cohort. We gathered data on anthropometric measurements, food intake, physical activity, and personal cofounder data from the Cohort of Universities of Minas Gerais (CUME Study), and used census-tract-level cofounder variables from Brazilian census data. We also obtained secondary data on $PM_{2.5}$ from the Atmospheric Composition Analysis Group. We evaluated the main and interaction effects of $PM_{2.5}$ with physical activity and total kilocalories consumed on BMI, using multi-level mixed-effects linear models. We found no main effect between $PM_{2.5}$ and BMI. However, we did observe a significant interaction effect between $PM_{2.5}$ and physical activity on BMI. For example, after covariate adjustment, BMI was significantly higher among physically inactive individuals exposed to 15-30 µg/m3 $PM_{2.5}$, compared to those who were insufficiently active. We also found that compared to physically active individuals, those who were inactive had a significantly higher BMI when exposed to ≥ 15 µg/m3 $PM_{2.5}$. We conclude that the effects of physical inactivity on BMI are larger among those exposed to higher chronic ambient $PM_{2.5}$ concentrations.

Key-words

Air pollution. Body Mass Index. Obesity. Long-term effects.

Introduction

Obesity is a major public health concern worldwide, as it is linked to several diseases such as type 2 diabetes, cardiovascular disease, some cancers, and increased mortality. Its prevalence has nearly tripled over the past few decades around the world (WHO, 2020) and in Brazil (Malta et al., 2017). According to the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL), 24.3% of the Brazilian population have obesity in 2023 (Brasil. Ministério da Saúde, 2023).

Obesity is a multifactorial disease, and research indicates that genetic factors and its complex gene-gene and gene-environmental interactions, socioeconomic, behavioral and environmental factors are the main determinants of this disease (Blüher, 2019; Hermsdorff & Bressan, 2019; WHO, 2020). Recently, air pollution has been considered as one of the possible environmental factors contributing to obesity (An et al., 2018).

Air pollution poses one of the greatest environmental risks to human health. Currently, 99% of the global population breathes air that exceeds the air quality guidelines set by the World Health Organization (WHO, 2022). In this context, ambient fine particulate matter (PM2.5) has emerged as a major air pollutant. Its size, which is less than 2.5 micrometers in diameter, is directly associated with its ability to cause health problems. This is because PM2.5 can not only lodge in the alveolar region of the lower respiratory system but can also access the bloodstream (US EPA, 2023).

Although most studies on the health effects of PM2.5 focus on cardiovascular and pulmonary disease, cancer (Busch et al., 2023), and prenatal exposure on early childhood growth (Clarke et al., 2022), recent literature is linking PM2.5 exposure to obesity indicators. Furthermore, the current research in this area focuses on the child and adolescent populations, whereas studies among adults are mixed and inconclusive. Thus, this study aimed to test the hypothesis that long-term exposure to PM2.5 is positively associated with longitudinal changes in Body Mass Index (BMI) in a Brazilian graduate sample.

Methods

CUME Study

The Cohort of Universities of Minas Gerais (CUME Study) is an ongoing prospective open cohort study which aims to evaluate the impact of the Brazilian dietary pattern and nutritional transition on the incidence of non-communicable diseases. This study included adults (18 to 59 years old) who have graduated from Brazilian public universities.

Data has been collected biennially since 2016 through an online questionnaire. Participants complete the questionnaire based on their respective monitoring time. Alumni from seven Federal Universities in Minas Gerais State, Brazil, were invited to participate in the study via email. The email contains a link that directs them to the most appropriate questionnaire for their follow-up time.

The baseline questionnaire (Q_0) consists of two parts. The first part includes questions related to lifestyle, sociodemographic, anthropometric, biomedical, and clinical data, individual and family morbidity, and personal examination history. The second part consists of filling out the semi-quantitative Food Frequency Questionnaire (FFQ), which has been validated for the study population (Azarias et al., 2021). Follow-up questionnaires assessed changes in food consumption, lifestyle, and disease incidence over two (Q_2), four (Q_4), and six (Q_6) years. The study's detailed methodologies have been published elsewhere (Domingos et al., 2018).

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the ethics committees of the universities involved (UFVJM, UNIFAL, UFJF, UFLA, UFMG, UFOP, and UFV; protocol no. 44483415.5.2005.5108, 44483415.5.2002.5148, 2615738/2018, 2676682, 2491366/18, 2565240/2018, and 596741-0/2013, respectively). All participants read and agreed to the online informed consent form before answering the questionnaire.

Sample

Between 2016 and 2022, a total of 8694 individuals completed the Q_0 questionnaire, and 5440 were excluded for various reasons (Supplemental Figure 1). Therefore, only 3254 individuals composed the sample of this study.

Outcome variable: Body Mass Index (BMI)

Self-reported data on participants' weight (kg) and height (m) were validated in a subsample of the cohort (Miranda et al., 2017) and used to calculate the BMI (kg/m2) on baseline and follow-up questionnaires. BMI was considered a continuous variable in all modeling.

Exposure assessment: PM2.5, physical activity, and total energy intake

At baseline, participants were asked to provide their residential address, which was then geocoded using both Google Maps and the OpenStreetMap plugin on QGIS® (version 3.22.14).

Global estimates of ground-level ambient PM2.5 were obtained from the Atmospheric Composition Analysis Group (ACAG), gridded at 0.01° x 0.01° (1 x 1 km) (ACAG, 2023). We linked the PM2.5 data to the assigned latitude and longitude coordinates that represent each participant's housing unit, using QGIS® (3.22.14) and the WGS 84 Geographic Coordinate System (EPSG 4326). Annual PM2.5 concentrations was averaged for the prior 5 years for each participant included in the sample. PM2.5 exposure was treated as a continuous variable in all regression models.

The level of physical activity was assessed from a list of 23 leisure activities and the respective time dedicated to each one was collected from baseline questionnaire (Martínez-González et al., 2005). Participants were classified as physically active, insufficiently active, or inactive, according to the World Health Organization's (WHO, 2010) recommendations in the Physical Activity Compendium.

Food consumption was evaluated at baseline by FFQ consisting of 144 food items, distributed among eight food groups. Each participant reported the frequency and the portion size for each food item consumed in prior 12-months. These data were then computed and the consumption of each food was transformed into grams or milliliters per day. Nutrient intake was determined using Brazilian tables of the nutritional composition of foods as a reference (IBGE, 2011; Universidade de Campinas, 2011). Further, energy intake, in kilocalories (kcal), was standardized using z-score to eliminate the problem of different scales. This variable was considered continuous in all modeling.

Covariates

At baseline, we collected sociodemographic data such as age, individual income, and professional status. Additionally, we asked participants whether they perceived the presence of open public spaces for physical activity near their homes. Perception of the presence of a public space was recorded as a binary variable (yes/no). Age and individual income were considered as continuous variables, whereas professional status was categorized into four categories: (1) employed, (2) student, (3) retired or home duties, and (4) unemployed.

Publicly available secondary data on Normalized Difference Vegetation Index (NDVI) were obtained from NASA (NASA, 2023). The data are available in the form of monthly averages, gridded at a resolution of 0.1° x 0.1° (10 x 10 km). Similar to the PM2.5 data, the NDVI data was averaged for the prior 5 years before each participant's conclusion of baseline questionnaire. The NDVI data was then linked to their geocoded address on QGIS® (version

3.22.14) using the WGS 84 Geographic Coordinate System (EPSG 4326). NDVI was fit as a continuous variable in regression models.

Other covariates include data from the Brazilian Census obtained from the Brazilian Institute of Geography and Statistics (IBGE, 2010). Data on per capita income (continuous), and the situation of the census tract (categorical: urban, peri-urban, or rural) were collected at the census tract level. Data on the total number of houses, existence of street identification, street lighting, paved street, paved sidewalk, curb, and manhole were collected to compute an urbanization score of each census tract. The urbanization score was analyzed as a continuous variable. The population density at the census tract level (quintiles) was calculated on QGIS® (3.22.14), using the geobr package (version 1.7.0) (Pereira et al., 2019) obtained on RStudio® (1.3.959).

Analyses were additionally adjusted by post-enrollment PM2.5 data. To this end, we updated participant addresses if reported differently in follow-up questionnaires. The annual PM2.5 data, obtained from ACAG, were averaged for each participant's follow-up time, and treated as a continuous confounding variable in the full adjusted regression models.

Statistical analyses

Categorical and continuous variables for baseline characteristics of participants were summarized by frequency, and mean and standard deviation (±SD), respectively.

To assess the relationship between chronic $PM_{2.5}$ exposure at baseline on longitudinal BMI, a Directed Acyclic Graph (DAG) was created based on a theoretical framework to identify potential confounding factors (Figure 1). The DAG revealed three causal pathways that could be explored to investigate the effect of PM2.5 on BMI. These pathways include the main effect of $PM_{2.5}$ on BMI, the interaction effect of PM2.5 and physical activity on BMI, and the interaction effect of $PM_{2.5}$, physical activity, and kilocalories (kcal) intake on BMI. Thus, multi-level mixed-effects linear models were performed to estimate the main and interaction effects of $PM_{2.5}$ on BMI. For each causal pathway, five different models were applied to the total sample and sex-stratified groups. The first is a crude model with a random effect for participants' identification variable (id). The second model was adjusted for age, individual income, professional status, the presence of public space for physical activity practice near participants' home and census tract level data, such as per capita income, rate of urbanization, situation of the census tract and population density, with a random effect for id. The third model further adjusted the second model for post-enrollment $PM_{2.5}$. As a sensitivity analysis, the fourth and fifth models are, respectively, the second and third models with an additional random effect for the federative unity (state) that participants live in (adding a random effect for state did not affect results). Physical activity and kcal intake were considered adjustment variables when their interaction was not being assessed. All analyses were performed on STATA/SE® (version 17) software, with an α value of 5%.

Results

The study included 3254 participants (Table 1), of which 65.54% were female and the average age was 34.8 ± 7.7 years. The average follow-up time was 3.5 ± 1.7 years. At baseline, the average BMI was 24.83 ± 4.6 kg/m2 (n = 3254). After two years of follow-up (n = 3023), the average BMI increased to 25.2 ± 4.7 kg/m2. BMI increased further to 25.56 ± 5 kg/m2 and 25.7 ± 5 kg/m2 after four (n = 1572) and six (n = 870) years of follow-up, respectively. The average five-year PM2.5 exposure at baseline was 12.95 ± 2.76 μg/m^3.

The crude and adjusted main effects models indicate no significant main effect of $PM_{2.5}$ exposure on BMI (Table 2). However, the assessment of the second causal pathway showed that there was a significant multiplicative interaction effect between $PM_{2.5}$ exposure and the practice of physical activity on BMI (Table 3). This interaction effect is visualized in Figure 2, which we estimated by calculating the predictive margins of physical activity on the linear prediction of BMI at particular values of $PM_{2.5}$. The effect of a lack of physical activity on higher BMI was more pronounced among individuals exposed to higher $PM_{2.5}$ exposure. On adjusted analyses, for example, participants who were physically inactive and exposed to 15-30 μg/m3 $PM_{2.5}$ had higher BMI compared to those who were insufficiently active. Additionally, physically inactive individuals who were exposed to ≥ 15 μg/m3 $PM_{2.5}$ had a higher BMI than their physically active counterparts. This adverse effect of physical inactivity on BMI was not apparent at lower levels of $PM_{2.5}$ exposure (Figure 2).

The results for the third causal pathway showed no interaction between PM2.5 or physical activity and energy intake. Nevertheless, the results do support the interaction effect between PM2.5 and physical activity (Supplementary Table 3). Sensitivity analyses were performed and it was discovered that the inclusion of post-enrollment PM2.5 exposure or the additional random effect for the state did not alter the results for any of the three causal pathways (Supplementary Tables 1, 2 and 3).

Discussion

In the present study, we assessed the relationship between chronic ambient PM2.5 exposure on BMI assessed prospectively in the CUME cohort. A DAG was created to identify the minimal sufficient adjustment for estimating the total effect of air pollution on BMI. Furthermore, the DAG identified three potential causal pathways in this relationship, all of which were evaluated in our epidemiological analysis.

Although no main effect between PM2.5 and BMI was observed, an interaction effect between PM2.5 and physical activity on BMI was observed. Specifically, there was no effect of physical activity on BMI among those exposed to lower PM2.5 concentrations, but the effects of physical inactivity on BMI were more pronounced among those exposed to higher PM2.5 concentrations. This suggests that the effect of PM2.5 on BMI may depend on lifestyle factors.

Studies on the association between PM2.5 and BMI in literature are inconsistent and mostly conducted among children and adolescents (Tamayo-Ortiz et al., 2021; Tong et al., 2022). Nevertheless, recent literature is already beginning to present results for adults. A prospective cohort of 3,902,440 U.S. veterans found that an increase of 10 µg/m3 in average annual PM2.5 concentration raised the risk of developing obesity by 1.08 and resulted in a 4.54 kg increase in body weight after a median follow-up of 8.1 years (Bowe et al., 2021). Their results suggest a longer-term effect of PM2.5 exposure on BMI, which may partially explain no significant main effect of PM2.5 found in our study, which had a mean of 3.54 years of follow-up.

Another recent prospective cohort, conducted with American midlife women, investigated the association between exposure to air pollution and body weight, BMI, waist circumference and body composition in a group of 1,654 middle-aged women. The authors found that an increase of 4.5 µg/m3 in PM2.5 concentration was associated with 4.53% rise in fat mass, 1.1% increase in the proportion of fat mass, and 0.39% decrease in lean mass. Similar to our study, they observed that associations between PM2.5 and body size and composition measures were attenuated in participants who engaged in more physical activity (Wang et al., 2022). The interaction effect between physical activity and PM2.5 exposure on obesity was also assessed in a Chinese nationwide representative sample. The results indicated that the benefits of physical activity on obesity were attenuated as PM2.5 increased, showing that reducing PM2.5 exposure can enhance the benefits of physical activity in combating obesity (Guo et al., 2022).

The interaction between air pollution and physical activity on obesity must be analyzed carefully. On one hand, greater physical activity taken outdoor may increase exposure to air pollution. On the other hand, higher air pollution levels can lead to physical inactivity (Gray et al., 2018). Nevertheless, both studies, as well as ours, present results according to participant's physical activity level, showing, therefore, that both physical inactivity and air pollution together are harmful to body composition.

In this study, we did not find an association between the three-way interaction effect of PM2.5, physical activity, and energy intake on BMI. In contrast, a study demonstrated an association between traffic-related pollutants, including $PM_{2.5}$, with higher consumption of fast food and trans-fat among adolescents. This suggests that air pollution exposure may contribute to unhealthy eating habits that lead to obesity (Chen et al., 2019). The different results may be due to a longer-term effect captured in Chen et al. study and not in ours, as their follow-up time was about 4-8 years; the population studied, once results of air pollution on obesity are more consistent in adolescents than in adults (Tamayo-Ortiz et al., 2021); or the way food consumption was assessed. Here we analyzed the daily energy intake, while Chen et al. evaluated qualitatively fast food and specific nutrient consumption, such as trans-fat, mainly present in unhealthy foods associated with obesity (Louzada et al., 2019; Mattar et al., 2022).

To the best of our knowledge, this is the first prospective cohort study to evaluate the interaction effect between $PM_{2.5}$, physical activity, and energy intake on long-term BMI in Brazilian adults. In addition, data from the CUME Project allow the discussion, planning, and implementation of specific interventions in Brazil, since participants are from different locations in Brazil and their high level of education ensures that participants are comparable. Although the use of BMI has its limitations, such as not accounting for body composition, it remains a valuable tool due to its strong correlation with the risk of various disabilities. It is also a recognized and recommended epidemiological indicator for diagnosing obesity (WHO, 2000). Additionally, the highly educated cohort in our study may not be generalizable to Brazilians who are of lower educational attainment with a higher prevalence of social and environmental vulnerability.

Conclusion

In this Brazilian graduate sample, after a mean of 3.54 years of follow-up time, BMI was influenced by the level of physical activity among individuals exposed to high ($> 15\mu g/m^3$) PM2.5 concentrations. To confirm our findings and our hypothesis that there is an association between air pollution and obesity, additional longitudinal studies with an extended follow-up period, a wider range of air pollutants, and measurements of body composition are necessary.

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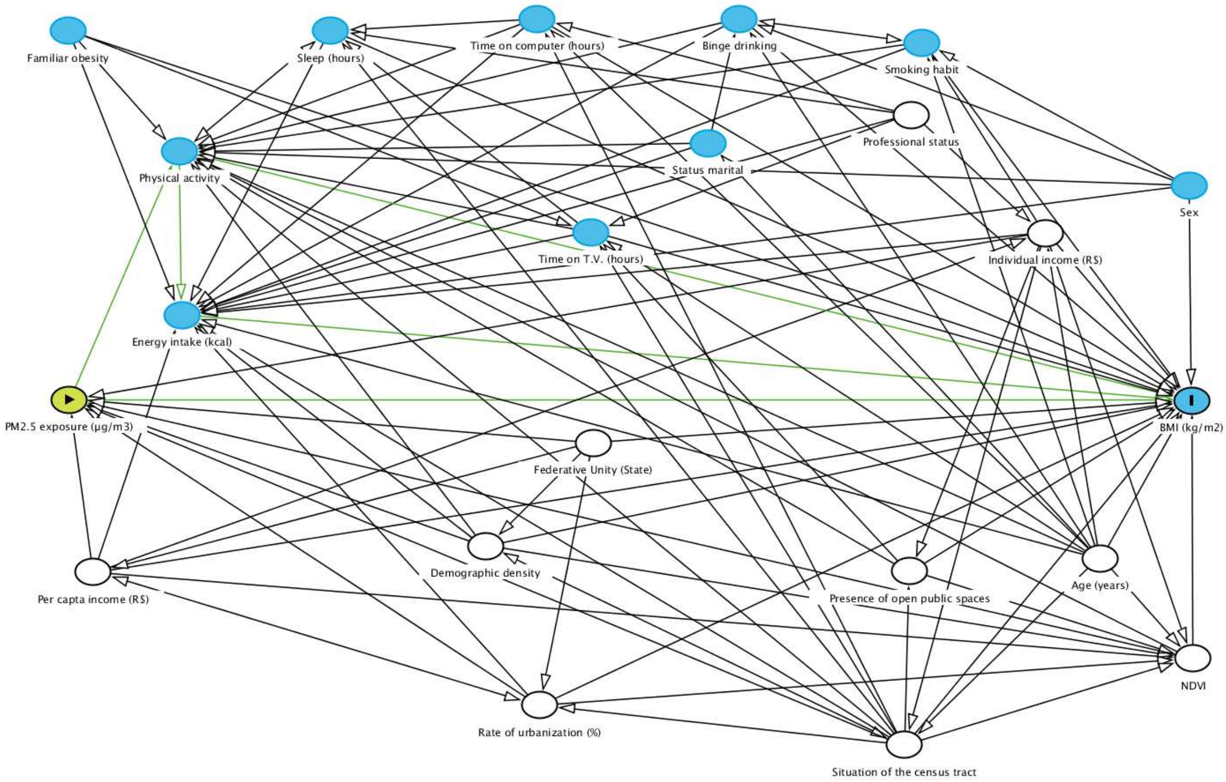


Figure 1. Directed acyclic graph (DAG) designed to identify potential confounders on the relationship between $PM_{2.5}$ exposure at baseline and long-term BMI, CUME Study. BMI: Body Mass Index; NDVI: Normalized Difference Vegetation Index. Blue variables: ancestor of outcome, no bias suggested. White variables: adjusted variables to control bias. Green line: causal path.

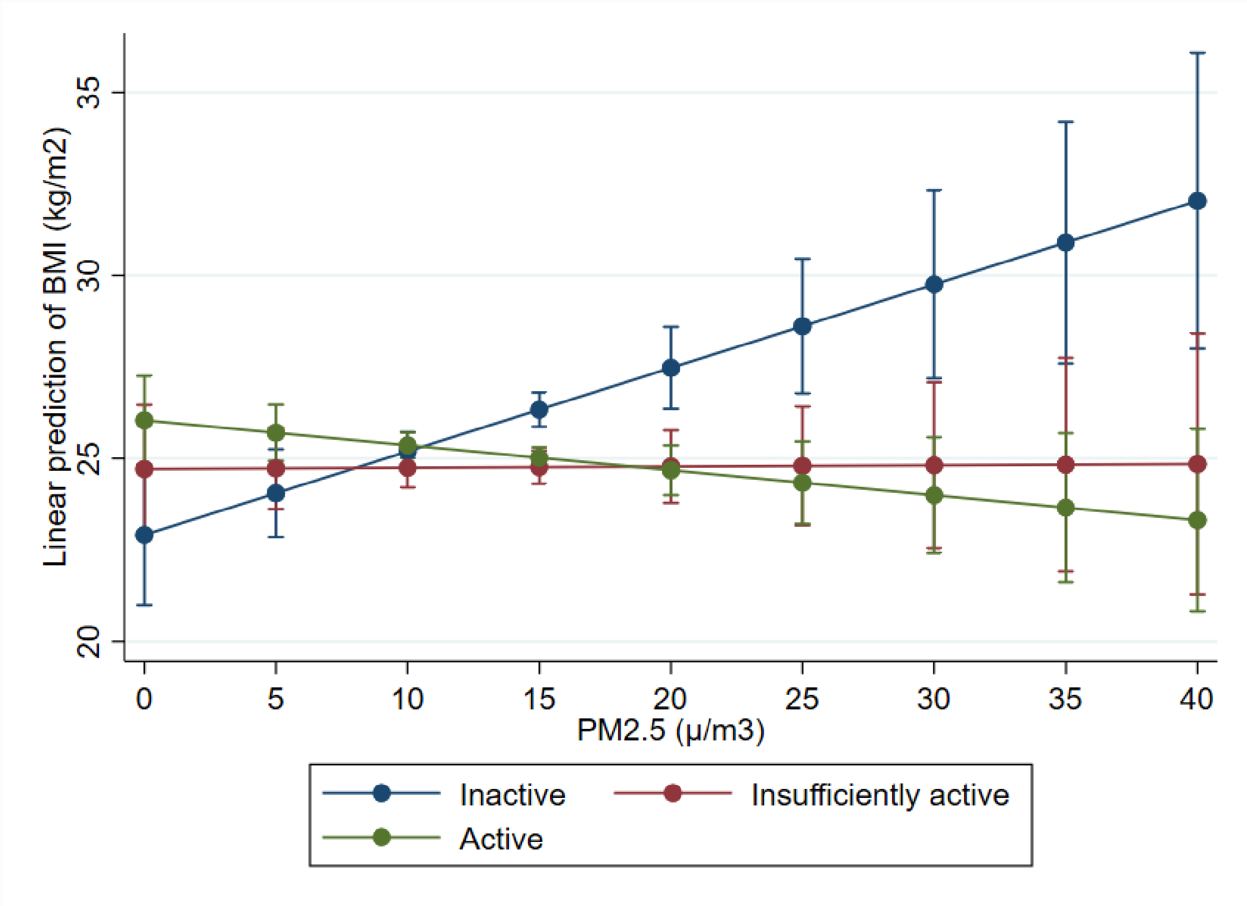


Figure 2. Predictive means of Body Mass Index (Kg/m^2), according to physical activity level at particular values of $PM_{2.5}$.

Table 1. Baseline characteristics of CUME Project Participants, 2016-2022

Baseline characteristics	Total sample size *n = 3,254*
[a]Sex	
Female	2,136 (65.64%)
[b]Age (years)	34.7 ± 7.7
[a]Professional status	
Employed	2427 (74.59%)
Student	580 (17.82%)
Retired/home duties	21 (0.65%)
Unemployed	226 (6.95%)
[b]Individual income (R$)	5578.21 ± 10380.89
[b]Body Mass Index (kg/m^2)	24.83 ± 4.61
[a]Physical activity	
Inactive	782 (24.03%)
Insufficiently active	639 (19.64%)
Active	1833 (56.33%)
[b]Daily energy intake (kcal)	2390.53 ± 952.92
[a]Presence of open public space	
Yes	2619 (80.49%)
[b]$PM_{2.5}$ exposure (μg/m^3)	12.95 ± 2.76
[b]NDVI	0.35 ± 0.40
[b]Per capita income at census tract level (R$)	1736.96 ± 1227.82
[b]Rate of urbanization (%)	83.2 ± 17.4
[a]Situation of the census tract	
Urban	3152 (98.16%)
Peri urban	33 (1.03%)
Rural	26 (0.81%)
[a]Demographic density	
1st quintile	573 (17.89%)
2nd quintile	611 (19.08%)
3rd quintile	642 (20.04%)
4th quintile	705 (22.01%)
5th quintile	672 (20.98%)

[a]Categorical variables, data are absolute frequency (relative frequency). [b]Continuous variables, data are mean ± standard deviations (SD). $PM_{2.5}$: Fine Particulate Matter; NDVI: Normalized Difference Vegetation Index.

Table 2. Direct effect of $PM_{2.5}$ exposure at baseline on long-term Body Mass Index in CUME Project participants, 2016-2022

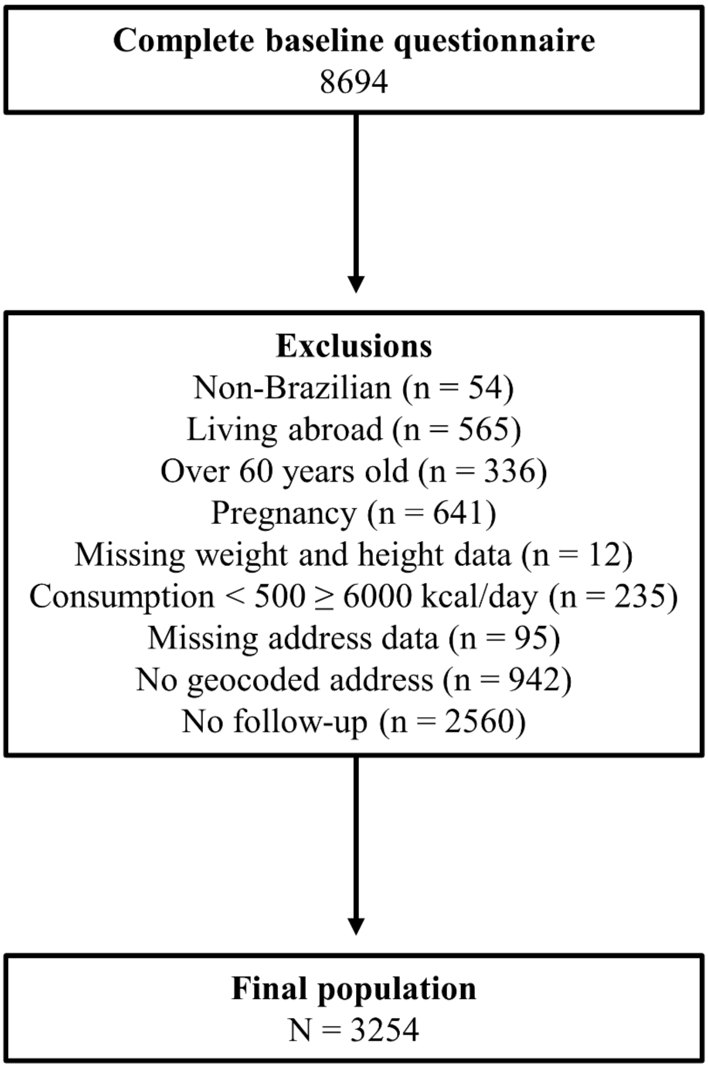
	Model 1	Model 2
	Coefficient (95%CI)	**Coefficient (95%CI)**
$PM_{2.5}$ (μg/m^3)	-0.02 (-0.07, 0.04)	0.01 (-0.06, 0.08)
Physical activity		
Inactive		*-ref-*
Insufficiently active		**-1.07 (-1.57, -0.57)**
Active		**-0.68 (-1.08, -0.27)**
Total Energy (Kcal)		**0.58 (0.41, 0.74)**
Age		**0.16 (0.14, 0.17)**
Individual income (R$)		-0.01 (-0.24, 0.23)
Professional situation		
Employed		*-ref-*
Student		0.11 (-0.34, 0.56)
Retired/home duties		1.81 (-0.13, 3.75)
Unemployed		0.10 (-0.56, 0.75)
Per capita income (R$)		-0.11 (-0.31, 0.09)
Presence of public space		**-0.44 (-0.86, -0.01)**
NDVI		-0.17 (-0.70, 0.36)
Urbanization rate		-0.10 (-0.32, 0.12)
Census tract		
Urban area		*-ref-*
Peri-urban area		-0.06 (-1.79, 1.67)
Rural area		0.39 (-1.82, 2.60)
Population density		
1º Quintile		*-ref-*
2º Quintile		0.17 (-0.41, 0.75)
3º Quintile		0.16 (-0.42, 0.74)
4º Quintile		-0.31 (-0.91, 0.28)
5º Quintile		0.00 (-0.62, 0.63)

Model 1: crude analysis, with random effect for participants' identification variable (ID). Model 2: Model 1, adjusted for physical activity, total kcal intake, age, individual income, professional status, the presence of open public space, per capita income, rate of urbanization, situation of the census tract and demographic density. Bold results mean statistical significance with an α value of 5%.

Table 3. Interaction effect of $PM_{2.5}$ exposure and physical activity at baseline on long-term Body Mass Index in CUME Project participants, 2016-2022

	Model 1	Model 2
	Coefficient (95%CI)	**Coefficient (95%CI)**
$PM_{2.5}$ (µg/m^3)	**0.13 (0.01, 0.26)**	**0.23 (0.08, 0.38)**
Physical activity		
Inactive		*-ref-*
Insufficiently active	1.07 (-1.19, 3.34)	1.80 (-0.76, 4.37)
Active	1.57 (-0.41 – 3.56)	**3.13 (0.92, 5.35)**
$PM_{2.5}$ ## Physical activity		
Inactive	*-ref-*	*-ref-*
Insufficiently active	-0.16 (-0.33, 0.01)	**-0.22 (-0.42, -0.03)**
Active	**-0.18 (-0.34, -0.03)**	**-0.30 (-0.47, -0.13)**
Total Energy (Kcal)		**0.58 (0.42, 0.75)**
Age		**0.16 (0.15, 0.17)**
Individual income (R$)		-0.02 (-0.25, 0.22)
Professional situation		
Employed		*-ref-*
Student		0.11 (-0.34, 0.55)
Retired/home duties		1.78 (-0.16, 3.72)
Unemployed		0.09 (-0.56, 0.74)
Per capita income (R$)		-0.11 (-0.31, 0.09)
Presence of public space		**-0.45 (-0.87, -0.02)**
NDVI		-0.15 (-0.68, 0.38)
Urbanization rate		-0.11 (-0.33, 0.12)
Census tract		
Urban area		*-ref-*
Peri-urban area		-0.00 (-1.72, 1.72)
Rural area		0.41 (-1.79, 2.62)
Population density		
1º Quintile		*-ref-*
2º Quintile		0.17 (-0.41, 0.75)
3º Quintile		0.18 (-0.39, 0.76)
4º Quintile		-0.29 (-0.88, 0.30)
5º Quintile		0.01 (-0.61, 0.64)

Model 1: crude analysis, with random effect for participants' identification variable (ID). Model 2: Model 1, adjusted for total kcal intake, age, individual income, professional status, the presence of open public space, per capita income, rate of urbanization, situation of the census tract and demographic density. ##: interaction symbol. Bold results mean statistical significance with an α value of 5%.



Supplementary figure 1. Fluxogram of the study.

Supplementary table 1. Direct effect of $PM_{2.5}$ exposure at baseline on long-term Body Mass Index in CUME Project participants

	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
$PM_{2.5}$ (µg/m^3)			
Total sample	0.00 (-0.08, 0.08)	0.01 (-0.06, 0.08)	0.00 (-0.08, 0.08)
Male	0.05 (-0.06, 0.16)	0.05 (-0.04, 0.15)	0.05 (-0.06, 0.16)
Female	-0.08 (-0.18, 0.03)	-0.06 (-0.16, 0.03)	-0.08 (-0.18, 0.03)
Physical activity			
Inactive	*-ref-*	*-ref-*	*-ref-*
Insufficiently active			
Total sample	**-1.07 (-1.57, -0.57)**	**-1.07 (-1.57, -0.57)**	**-1.07 (-1.57, -0.57)**
Male	**-0.87 (-1.68, -0.06)**	**-0.88 (-1.69, -0.07)**	**-0.87 (-1.68 -0.06)**
Female	**-1.09 (-1.71 -0.47)**	**-1.08 (-1.70, -0.47)**	**-1.09 (-1.71, -0.47)**
Active			
Total sample	**-0.68 (-1.08, -0.27)**	**-0.68 (-1.08, -0.27)**	**-0.68 (-1.08, -0.27)**
Male	-0.59 (-1.23, 0.04)	-0.60 (-1.23, 0.04)	-0.59 (-1.23, 0.04)
Female	**-0.76 (-1.27 -0.26)**	**-0.76 (-1.26, -0.25)**	**-0.76 (-1.27, -0.26)**
Total Energy (Kcal)			
Total sample	**0.58 (0.42, 0.75)**	**0.58 (0.41, 0.74)**	**0.58 (0.42, 0.75)**
Male	**0.44 (0.20, 0.68)**	**0.43 (0.19, 0.68)**	**0.44 (0.20, 0.68)**
Female	**0.41 (0.19, 0.63)**	**0.41 (0.19, 0.62)**	**0.41 (0.19, 0.63)**
Age			
Total sample	**0.16 (0.15, 0.17)**	**0.16 (0.14, 0.17)**	**0.16 (0.15, 0.17)**
Male	**0.12 (0.10, 0.15)**	**0.12 (0.09, 0.15)**	**0.12 (0.10, 0.15)**
Female	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**
Individual income (R$)			
Total sample	-0.01 (-0.25, 0.22)	-0.01 (-0.24, 0.23)	-0.01 (-0.25, 0.22)
Male	-0.27 (-0.88, 0.34)	-0.27 (-0.88, 0.34)	-0.27 (-0.88, 0.34)
Female	-0.10 (-0.36, 0.16)	-0.10 (-0.36, 0.16)	-0.10 (-0.36, 0.16)
Professional situation			
Employed	*-ref-*	*-ref-*	*-ref-*
Student			
Total sample	0.12 (-0.33, 0.57)	0.11 (-0.34, 0.56)	0.12 (-0.33, 0.57)
Male	-0.34 (-1.10, 0.42)	-0.35 (-1.11, 0.42)	-0.34 (-1.10, 0.42)
Female	0.44 (-0.11, 0.99)	0.42 (-0.13, 0.97)	0.44 (-0.11, 0.99)
Retired/home duties			
Total sample	1.80 (-0.15, 3.74)	1.81 (-0.13, 3.75)	1.80 (-0.15, 3.74)
Male	**-5.70 (-11.40, -0.01)**	-5.68 (-11.37, 0.02)	**-5.70 (-11.40, -0.01)**
Female	**2.89 (0.80, 4.98)**	**2.91 (0.82, 5.00)**	**2.89 (0.80, 4.98)**
Unemployed			
Total sample	0.10 (-0.55 0.76)	0.10 (-0.56, 0.75)	0.10 (-0.55, 0.76)
Male	-0.22 (-1.39, 0.94)	-0.22 (-1.38, 0.95)	-0.22 (-1.39, 0.94)
Female	0.51 (-0.27, 1.28)	0.49 (-0.28, 1.26)	0.51 (-0.27, 1.28)
Per capita income (R$)			
Total sample	-0.11 (-0.31, 0.09)	-0.11 (-0.31, 0.09)	-0.11 (-0.31, 0.09)
Male	0.17 (-0.11, 0.46)	0.17 (-0.11, 0.46)	0.17 (-0.11, 0.46)
Female	**-0.35 (-0.61, -0.09)**	**-0.35 (-0.61, -0.09)**	**-0.35 (-0.61, -0.09)**
Public space for PA			
Total sample	**-0.44 (-0.86, -0.01)**	**-0.44 (-0.86, -0.01)**	**-0.44 (-0.86, -0.01)**
Male	-0.16 (-0.85, 0.52)	-0.15 (-0.83, 0.53)	-0.16 (-0.85, 0.52)
Female	**-0.64 (-1.16, -0.11)**	**-0.64 (-1.16, -0.12)**	**-0.64 (-1.16, -0.11)**
NDVI			
Total sample	-0.16 (-0.69, 0.37)	-0.17 (-0.70, 0.36)	-0.16 (-0.69, 0.37)
Male	0.06 (-0.74, 0.87)	0.05 (-0.75, 0.85)	0.06 (-0.74, 0.87)
Female	-0.31 (-0.98, 0.36)	-0.32 (-0.99, 0.35)	-0.31 (-0.98, 0.36)
Urbanization rate			
Total sample	-0.10 (-0.33, 0.12)	-0.10 (-0.32, 0.12)	-0.10 (-0.33, 0.12)
Male	-0.01 (-0.35, 0.33)	-0.01 (-0.35, 0.33)	-0.01 (-0.35, 0.33)
Female	-0.10 (-0.38, 0.18)	-0.10 (-0.38, 0.18)	-0.10 (-0.38, 0.18)

Cont.

	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
Census tract			
Urban area	*-ref-*	*-ref-*	*-ref-*
Peri-urban area			
Total sample	-0.06 (-1.78, 1.67)	-0.06 (-1.79, 1.67)	-0.06 (-1.78, 1.67)
Male	-0.81 (-3.57, 1.95)	-0.80 (-3.56, 1.95)	-0.81 (-3.57, 1.95)
Female	0.43 (-1.70, 2.57)	0.42 (-1.71, 2.56)	0.43 (-1.70, 2.57)
Rural area			
Total sample	0.38 (-1.83, 2.59)	0.39 (-1.82, 2.60)	0.38 (-1.83, 2.59)
Male	1.30 (-2.10, 4.70)	1.31 (-2.09, 4.71)	1.30 (-2.10, 4.70)
Female	0.16 (-2.64, 2.95)	0.17 (-2.63, 2.96)	0.16 (-2.64, 2.95)
Population density			
1º Quintile	*-ref-*	*-ref-*	*-ref-*
2º Quintile			
Total sample	0.18 (-0.40, 0.76)	0.17 (-0.41, 0.75)	0.18 (-0.40, 0.76)
Male	0.82 (-0.03, 1.67)	0.80 (-0.05, 1.64)	0.82 (-0.03, 1.67)
Female	-0.12 (-0.87, 0.64)	-0.12 (-0.87, 0.63)	-0.12 (-0.87, 0.64)
3º Quintile			
Total sample	0.16 (-0.42, 0.74)	0.16 (-0.42, 0.74)	0.16 (-0.42, 0.74)
Male	0.25 (-0.59, 1.10)	0.25 (-0.60, 1.09)	0.25 (-0.59, 1.10)
Female	0.10 (-0.65, 0.85)	0.09 (-0.65, 0.84)	0.10 (-0.65, 0.85)
4º Quintile			
Total sample	-0.30 (-0.89, 0.30)	-0.31 (-0.91, 0.28)	-0.30 (-0.89, 0.30)
Male	-0.30 (-1.18, 0.58)	-0.32 (-1.20, 0.56)	-0.30 (-1.18, 0.58)
Female	-0.29 (-1.05, 0.47)	-0.31 (-1.07, 0.46)	-0.29 (-1.05, 0.47)
5º Quintile			
Total sample	0.02 (-0.61, 0.64)	0.00 (-0.62, 0.63)	0.02 (-0.61, 0.64)
Male	0.45 (-0.47, 1.38)	0.44 (-0.48, 1.37)	0.45 (-0.47, 1.38)
Female	-0.12 (-0.93, 0.68)	-0.14 (-0.94, 0.66)	-0.12 (-0.93, 0.68)
Post-enrollment $PM_{2.5}$ (μ/m³)			
Total sample	0.01 (-0.03, 0.05)		0.01 (-0.03, 0.05)
Male	-0.00 (-0.07, 0.06)		-0.00 (-0.07, 0.06)
Female	0.02 (-0.03, 0.06)		0.02 (-0.03, 0.06)

Model 3: model 2 with an additional adjustment for post-enrollment PM2.5. Model 4: model 2 with an additional random effect for the federative unity (state) that participants live in. Model 5: model 3 with an additional random effect for the federative unity (state) that participants live in. Bold results mean statistical significance with an α value of 5%.

Supplementary table 2. Interaction effect of $PM_{2.5}$ exposure and physical activity at baseline on long-term Body Mass Index in CUME Project participants

	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
$PM_{2.5}$ (μg/m^3)			
Total sample	**0.22 (0.07, 0.37)**	**0.23 (0.08, 0.38)**	**0.22 (0.07, 0.37)**
Male	**0.31 (0.10, 0.52)**	**0.30 (0.10, 0.51)**	**0.31 (0.10, 0.52)**
Female	0.10 (-0.10, 0.31)	0.12 (-0.08, 0.32)	0.10 (-0.10, 0.31)
Physical activity			
Inactive	*-ref-*	*-ref-*	*-ref-*
Insufficiently active			
Total sample	1.81 (-0.76, 4.37)	1.80 (-0.76, 4.37)	1.81 (-0.76, 4.37)
Male	**3.69 (0.07, 7.32)**	3.62 (-0.00, 7.24)	**3.69 (0.07, 7.32)**
Female	0.31 (-3.13, 3.76)	0.37 (-3.08, 3.81)	0.31 (-3.13, 3.76)
Active			
Total sample	**3.13 (0.92, 5.35)**	**3.13 (0.92, 5.35)**	**3.13 (0.92, 5.35)**
Male	**3.33 (0.20, 6.46)**	**3.32 (0.19, 6.44)**	**3.33 (0.20, 6.46)**
Female	2.84 (-0.14, 5.81)	2.84 (-0.13, 5.81)	2.84 (-0.14, 5.81)
$PM_{2.5}$ ## Physical activity			
Inactive	*-ref-*	*-ref-*	*-ref-*
Insufficiently active			
Total sample	**-0.23 (-0.42, -0.03)**	**-0.22 (-0.42, -0.03)**	**-0.23 (-0.42, -0.03)**
Male	**-0.34 (-0.61, -0.08)**	**-0.34 (-0.61 -0.07)**	**-0.34 (-0.61, -0.08)**
Female	-0.11 (-0.38, 0.15)	-0.12 (-0.38, 0.15)	-0.11 (-0.38, 0.15)
Active			
Total sample	**-0.30 (-0.47, -0.13)**	**-0.30 (-0.47, -0.13)**	**-0.30 (-0.47, -0.13)**
Male	**-0.30 (-0.53, -0.07)**	**-0.30 (-0.53, -0.06)**	**-0.30 (-0.53, -0.07)**
Female	**-0.28 (-0.51, -0.05)**	**-0.28 (-0.51, -0.05)**	**-0.28 (-0.51, -0.05)**
Total Energy (Kcal)			
Total sample	**0.59 (0.43, 0.75)**	**0.58 (0.42, 0.75)**	**0.59 (0.43, 0.75)**
Male	**0.46 (0.22, 0.70)**	**0.45 (0.21, 0.69)**	**0.46 (0.22, 0.70)**
Female	**0.41 (0.19, 0.63)**	**0.41 (0.19, 0.62)**	**0.41 (0.19, 0.63)**
Age			
Total sample	**0.16 (0.15, 0.17)**	**0.16 (0.15, 0.17)**	**0.16 (0.15, 0.17)**
Male	**0.12 (0.10, 0.15)**	**0.12 (0.10, 0.15)**	**0.12 (0.10, 0.15)**
Female	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**
Individual income (R$)			
Total sample	-0.02 (-0.25, 0.22)	-0.02 (-0.25, 0.22)	-0.02 (-0.25, 0.22)
Male	-0.27 (-0.88, 0.33)	-0.27 (-0.87, 0.34)	-0.27 (-0.88, 0.33)
Female	-0.10 (-0.36, 0.16)	-0.10 (-0.36, 0.16)	-0.10 (-0.36, 0.16)
Professional situation			
Employed	*-ref-*	*-ref-*	*-ref-*
Student			
Total sample	0.12 (-0.33, 0.57)	0.11 (-0.34, 0.55)	0.12 (-0.33, 0.57)
Male	-0.33 (-1.09, 0.43)	-0.34 (-1.09, 0.42)	-0.33 (-1.09, 0.43)
Female	0.43 (-0.12, 0.98)	0.42 (-0.13, 0.96)	0.43 (-0.12, 0.98)
Retired/home duties			
Total sample	1.77 (-0.17, 3.70)	1.78 (-0.16, 3.72)	1.77 (-0.17, 3.70)
Male	**-5.76 (-11.43, -0.08)**	**-5.73 (-11.41, -0.06)**	**-5.76 (-11.43, -0.08)**
Female	**2.84 (0.75, 4.93)**	**2.86 (0.77, 4.95)**	**2.84 (0.75, 4.93)**
Unemployed			
Total sample	0.10 (-0.55, 0.75)	0.09 (-0.56, 0.74)	0.10 (-0.55, 0.75)
Male	-0.23 (-1.38, 0.93)	-0.22 (-1.37, 0.94)	-0.23 (-1.38, 0.93)
Female	0.50 (-0.27, 1.27)	0.48 (-0.29, 1.25)	0.50 (-0.27, 1.27)
Per capita income (R$)			
Total sample	-0.11 (-0.30, 0.09)	-0.11 (-0.31, 0.09)	-0.11 (-0.30, 0.09)
Male	0.17 (-0.11, 0.46)	0.17 (-0.11, 0.46)	0.17 (-0.11, 0.46)
Female	**-0.35 (-0.61, -0.09)**	**-0.35 (-0.61, -0.09)**	**-0.35 (-0.61, -0.09)**

Cont.

	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
Public space for PA			
Total sample	**-0.45 (-0.87, -0.02)**	**-0.45 (-0.87, -0.02)**	**-0.45 (-0.87, -0.02)**
Male	-0.21 (-0.90, 0.47)	-0.20 (-0.88, 0.48)	-0.21 (-0.90, 0.47)
Female	**-0.63 (-1.16, -0.11)**	**-0.64 (-1.16, -0.11)**	**-0.63 (-1.16, -0.11)**
NDVI			
Total sample	-0.14 (-0.67, 0.39)	-0.15 (-0.68, 0.38)	-0.14 (-0.67, 0.39)
Male	0.09 (-0.72, 0.89)	0.07 (-0.73, 0.88)	0.09 (-0.72, 0.89)
Female	-0.31 (-0.98, 0.36)	-0.32 (-0.99, 0.35)	-0.31 (-0.98, 0.36)
Urbanization rate			
Total sample	-0.11 (-0.33, 0.11)	-0.11 (-0.33, 0.12)	-0.11 (-0.33, 0.11)
Male	-0.03 (-0.37, 0.31)	-0.03 (-0.37, 0.32)	-0.03 (-0.37, 0.31)
Female	-0.10 (-0.38, 0.18)	-0.10 (-0.38, 0.179)	-0.10 (-0.38, 0.18)
Census tract			
Urban area	*-ref-*	*-ref-*	*-ref-*
Peri-urban area			
Total sample	0.00 (-1.72, 1.73)	-0.00 (-1.72, 1.72)	0.00 (-1.72, 1.73)
Male	-0.78 (-3.53, 1.97)	-0.77 (-3.52, 1.98)	-0.78 (-3.53, 1.97)
Female	0.47 (-1.67, 2.60)	0.46 (-1.67, 2.59)	0.47 (-1.67, 2.60)
Rural area			
Total sample	0.40 (-1.80, 2.61)	0.41 (-1.79, 2.62)	0.40 (-1.80, 2.61)
Male	1.35 (-2.04, 4.74)	1.36 (-2.03, 4.75)	1.35 (-2.04, 4.74)
Female	0.18 (-2.61, 2.97)	0.19 (-2.60, 2.98)	0.18 (-2.61, 2.97)
Population density			
1º Quintile	*-ref-*	*-ref-*	*-ref-*
2º Quintile			
Total sample	0.18 (-0.40, 0.76)	0.17 (-0.41, 0.75)	0.18 (-0.40, 0.76)
Male	0.80 (-0.05, 1.64)	0.77 (-0.07, 1.62)	0.80 (-0.05, 1.64)
Female	-0.09 (-0.85, 0.66)	-0.10 (-0.85, 0.66)	-0.09 (-0.85, 0.66)
3º Quintile			
Total sample	0.19 (-0.39, 0.77)	0.18 (-0.39, 0.76)	0.19 (-0.39, 0.77)
Male	0.28 (-0.57, 1.12)	0.27 (-0.58, 1.11)	0.28 (-0.57, 1.12)
Female	0.13 (-0.62, 0.88)	0.12 (-0.62, 0.87)	0.13 (-0.62, 0.88)
4º Quintile			
Total sample	-0.28 (-0.87, 0.32)	-0.29 (-0.88, 0.30)	-0.28 (-0.87, 0.32)
Male	-0.28 (-1.16, 0.60)	-0.30 (-1.18, 0.58)	-0.28 (-1.16, 0.60)
Female	-0.28 (-1.04, 0.48)	-0.30 (-1.06, 0.47)	-0.28 (-1.04, 0.48)
5º Quintile			
Total sample	0.03 (-0.60, 0.65)	0.01 (-0.61, 0.64)	0.03 (-0.60, 0.65)
Male	0.47 (-0.45, 1.40)	0.46 (-0.46, 1.38)	0.47 (-0.45, 1.40)
Female	-0.12 (-0.92, 0.68)	-0.13 (-0.93, 0.67)	-0.12 (-0.92, 0.68)
Post-enrollment $PM_{2.5}$ (μ/m^3)			
Total sample	0.01 (-0.03, 0.05)		0.01 (-0.03, 0.05)
Male	-0.00 (-0.07, 0.06)		-0.00 (-0.07, 0.06)
Female	0.02 (-0.03, 0.06)		0.02 (-0.03, 0.06)

Model 3: model 2 with an additional adjustment for post-enrollment PM2.5. Model 4: model 2 with an additional random effect for the federative unity (state) that participants live in. Model 5: model 3 with an additional random effect for the federative unity (state) that participants live in. Bold results mean statistical significance with an α value of 5%.

Supplementary table 3. Interaction effect of $PM_{2.5}$ exposure, physical activity and total energy intake (kcal) at baseline on long-term Body Mass Index in CUME Project participants

	Model 1	Model 2	Model 3	Model 4	Model 5
	Coefficient (95%CI)	**Coefficient (95%CI)**	**Coefficient (95%CI)**	**Coefficient (95%CI)**	**Coefficient (95%CI)**
$PM_{2.5}$ (µg/m^3)					
Total sample	**0.15 (0.02, 0.28)**	**0.24 (0.09, 0.39)**	**0.23 (0.08, 0.39)**	**0.24 (0.09, 0.39)**	**0.23 (0.08, 0.39)**
Male	**0.27 (0.08, 0.46)**	**0.35 (0.13, 0.56)**	**0.35 (0.12, 0.57)**	**0.35 (0.13, 0.56)**	**0.35 (0.12, 0.57)**
Female	0.02 (-0.16, 0.19)	0.13 (-0.08, 0.33)	0.11 (-0.10, 0.32)	0.13 (-0.08, 0.33)	0.11 (-0.10, 0.32)
Physical activity					
Inactive	*-ref-*	*-ref-*	*-ref-*	*-ref-*	*-ref-*
Insufficiently active					
Total sample	1.52 (-0.72, 3.76)	1.87 (-0.70, 4.43)	1.87 (-0.70, 4.44)	1.87 (-0.70, 4.43)	1.87 (-0.70, 4.44)
Male	2.91 (-0.55, 6.36)	3.67 (-0.14, 7.48)	3.70 (-0.11, 7.51)	3.67 (-0.14, 7.48)	3.70 (-0.11, 7.51)
Female	-0.10 (-3.07, 2.86)	0.39 (-3.07, 3.85)	0.34 (-3.13, 3.80)	0.39 (-3.07, 3.85)	0.34 (-3.13, 3.80)
Active					
Total sample	1.84 (-0.12, 3.79)	**3.32 (1.10, 5.54)**	**3.32 (1.10, 5.54)**	**3.32 (1.10, 5.54)**	**3.32 (1.10, 5.54)**
Male	2.85 (-0.07, 5.77)	**4.19 (0.85, 7.53)**	**4.18 (0.84, 7.52)**	**4.19 (0.85, 7.53)**	**4.18 (0.84, 7.52)**
Female	1.29 (-1.44, 4.02)	3.01 (-0.01, 6.03)	3.01 (-0.02, 6.04)	3.01 (-0.01, 6.03)	3.01 (-0.02, 6.04)
$PM_{2.5}$ ## Physical activity					
Inactive	*-ref-*	*-ref-*	*-ref-*	*-ref-*	*-ref-*
Insufficiently active					
Total sample	**-0.19 (-0.36 -0.02)**	**-0.23 (-0.42, -0.03)**	**-0.23 (-0.42, -0.03)**	**-0.23 (-0.42, -0.03)**	**-0.23 (-0.42, -0.03)**
Male	**-0.28 (-0.54, -0.03)**	**-0.33 (-0.61, -0.05)**	**-0.33 (-0.61, -0.05)**	**-0.33 (-0.61, -0.05)**	**-0.33 (-0.61, -0.05)**
Female	-0.07 (-0.30, 0.16)	-0.12 (-0.39, 0.15)	-0.12 (-0.39, 0.15)	-0.12 (-0.39, 0.15)	-0.12 (-0.39, 0.15)
Active					
Total sample	**-0.20 (-0.35, -0.05)**	**-0.31 (-0.48, -0.14)**	**-0.31 (-0.48, -0.14)**	**-0.31 (-0.48, -0.14)**	**-0.31 (-0.48, -0.14)**
Male	**-0.26 (-0.48, -0.04)**	**-0.34 (-0.59, -0.10)**	**-0.34 (-0.59, -0.10)**	**-0.34 (-0.59, -0.10)**	**-0.34 (-0.59, -0.10)**
Female	-0.19 (-0.40, 0.02)	**-0.30 (-0.54, -0.07)**	**-0.30 (-0.54, -0.07)**	**-0.30 (-0.54, -0.07)**	**-0.30 (-0.54, -0.07)**
Total Energy (Kcal)					
Total sample	0.98 (-0.72, 2.68)	1.28 (-0.58, 3.15)	1.29 (-0.58, 3.16)	1.28 (-0.58, 3.15)	1.29 (-0.58, 3.16)
Male	0.47 (-2.13, 3.06)	1.81 (-1.14, 4.77)	1.80 (-1.16, 4.75)	1.81 (-1.14, 4.77)	1.80 (-1.16, 4.75)
Female	1.76 (-0.52, 4.05)	1.47 (-0.94, 3.89)	1.49 (-0.93, 3.91)	1.47 (-0.94, 3.89)	1.49 (-0.93, 3.91)

Cont.

	Model 1 Coefficient (95%CI)	Model 2 Coefficient (95%CI)	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
$PM_{2.5}$ ## Kcal					
Total sample	0.01 (-0.12, 0.14)	-0.02 (-0.16, 0.13)	-0.02 (-0.16, 0.13)	-0.02 (-0.16, 0.12)	-0.02 (-0.16, 0.13)
Male	0.03 (-0.17, 0.23)	-0.06 (-0.29, 0.16)	-0.06 (-0.29, 0.16)	-0.06 (-0.29, 0.16)	0.06 (-0.29, 0.16)
Female	-0.05 (-0.23, 0.13)	-0.04 (-0.23, 0.14)	-0.05 (-0.24, 0.14)	-0.04 (-0.23, 0.14)	-0.05 (-0.24, 0.14)
Physical activity ## Kcal					
Inactive	*-ref-*	*-ref-*	*-ref-*	*-ref-*	*-ref-*
Insufficiently active					
Total sample	-0.18 (-2.49, 2.14)	0.49 (-2.15, 3.13)	0.58 (-2.06, 3.22)	0.49 (-2.15, 3.13)	0.58 (-2.06, 3.22)
Male	1.94 (-1.51, 5.38)	1.80 (-2.07, 5.67)	2.02 (-1.85, 5.90)	1.80 (-2.07, 5.67)	2.02 (-1.85, 5.90)
Female	-1.96 (-5.07, 1.16)	-1.24 (-4.88, 2.41)	-1.23 (-4.88, 2.42)	-1.24 (-4.88, 2.41)	-1.23 (-4.88, 2.42)
Active					
Total sample	-0.90 (-2.91, 1.10)	-1.32 (3.55, 0.92)	-1.32 (-3.56, 0.92)	-1.32 (-3.55, 0.92)	-1.32 (-3.56, 0.92)
Male	-0.32 (-3.27, 2.63)	-1.71 (-5.09, 1.68)	-1.68 (-5.06, 1.71)	-1.71 (-5.09, 1.68)	-1.68 (-5.06, 1.71)
Female	-1.15 (-3.98, 1.67)	-0.91 (-3.96, 2.14)	-0.93 (-3.98, 2.12)	-0.91 (-3.96, 2.14)	-0.93 (-3.98, 2.12)
$PM_{2.5}$ ## Physical activity ## kcal					
Inactive	*-ref-*	*-ref-*	*-ref-*	*-ref-*	*-ref-*
Insufficiently active					
Total sample	-0.03 (-0.20, 0.15)	-0.08 (-0.28, 0.12)	-0.09 (-0.29, 0.12)	-0.08 (-0.28, 0.12)	-0.09 (-0.29, 0.12)
Male	-0.18 (-0.43, 0.08)	-0.16 (-0.46, 0.13)	-0.18 (-0.47, 0.11)	-0.16 (-0.46, 0.13)	-0.18 (-0.47, 0.11)
Female	0.11 (-0.13, 0.35)	0.05 (-0.23, 0.33)	0.05 (-0.23, 0.33)	0.05 (-0.23, 0.33)	0.05 (-0.23, 0.33)
Active					
Total sample	0.02 (-0.13, 0.18)	0.05 (-0.12, 0.23)	0.05 (-0.12, 0.23)	0.05 (-0.12, 0.23)	0.05 (-0.12, 0.23)
Male	-0.01 (-0.24, 0.21)	0.07 (-0.18, 0.33)	0.07 (-0.19, 0.33)	0.07 (-0.18, 0.33)	0.07 (-0.19, 0.33)
Female	0.02 (-0.20, 0.24)	0.01 (-0.22, 0.25)	0.01 (-0.22, 0.25)	0.01 (-0.22, 0.25)	0.01 (-0.22, 0.25)
Age					
Total sample		**0.16 (0.15, 0.17)**	**0.16 (0.15, 0.17)**	**0.16 (0.15, 0.17)**	**0.16 (0.15, 0.17)**
Male		**0.12 (0.10, 0.15)**	**0.12 (0.10, 0.15)**	**0.12 (0.10, 0.15)**	**0.12 (0.10, 0.15)**
Female		**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**	**0.18 (0.16, 0.20)**
Individual income (R$)					
Total sample		-0.03 (-0.26, 0.21)	-0.03 (-0.27, 0.20)	-0.03 (-0.26, 0.21)	-0.03 (-0.27, 0.20)
Male		-0.31 (-0.91, 0.30)	-0.31 (-0.91, 0.29)	-0.31 (-0.91, 0.30)	-0.31 (-0.91, 0.29)
Female		-0.09 (-0.35, 0.17)	-0.09 (-0.36, 0.17)	-0.09 (-0.35, 0.17)	-0.09 (-0.36, 0.17)

Cont.

	Model 1 Coefficient (95%CI)	Model 2 Coefficient (95%CI)	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
Professional situation					
Employed		*-ref-*	*-ref-*	*-ref-*	*-ref-*
Student					
Total sample		0.09 (-0.35, 0.54)	0.11 (-0.34, 0.56)	0.09 (-0.35, 0.54)	0.11 (-0.34, 0.56)
Male		-0.38 (-1.14, 0.37)	-0.38 (-1.14, 0.38)	-0.38 (-1.14, 0.37)	-0.38 (-1.14, 0.38)
Female		0.42 (-0.13, 0.97)	0.44 (-0.11, 0.98)	0.42 (-0.13, 0.97)	0.44 (-0.11, 0.98)
Retired/home duties					
Total sample		1.66 (-0.28, 3.59)	1.64 (-0.30, 3.57)	1.66 (-0.28, 3.59)	1.64 (-0.30, 3.57)
Male		**-5.81 (-11.45, -0.17)**	**-5.84 (-11.48, -0.20)**	**-5.81 (-11.45, -0.17)**	**-5.84 (-11.48, -0.20)**
Female		**2.76 (0.68, 4.85)**	**2.74 (0.66, 4.83)**	**2.76 (0.68, 4.85)**	**2.74 (0.66, 4.83)**
Unemployed					
Total sample		0.07 (-0.58, 0.72)	0.08 (-0.57, 0.73)	0.07 (-0.58, 0.72)	0.08 (-0.57, 0.73)
Male		-0.28 (-1.44, 0.87)	-0.30 (-1.45, 0.85)	-0.28 (-1.44, 0.87)	-0.30 (-1.45, 0.85)
Female		0.48 (-0.30, 1.25)	0.49 (-0.28, 1.26)	0.48 (-0.30, 1.25)	0.49 (-0.28, 1.26)
Per capita income (R$)					
Total sample		-0.10 (-0.30, 0.09)	-0.10 (-0.30, 0.09)	-0.10 (-0.30, 0.09)	-0.10 (-0.30, 0.09)
Male		0.16 (-0.12, 0.44)	0.16 (-0.12, 0.44)	0.16 (-0.12, 0.44)	0.16 (-0.12, 0.44)
Female		**-0.34 (-0.60, -0.08)**	**-0.34 (-0.60, -0.08)**	**-0.34 (-0.60, -0.08)**	**-0.34 (-0.60, -0.08)**
Public space for PA					
Total sample		**-0.47 (-0.89, -0.05)**	**-0.47 (-0.90, -0.05)**	**-0.47 (-0.89, -0.05)**	**-0.47 (-0.90, -0.05)**
Male		-0.21 (-0.89, 0.47)	-0.22 (-0.90, 0.46)	-0.21 (-0.89, 0.47)	-0.22 (-0.90, 0.46)
Female		**-0.66 (-1.18, -0.14)**	**-0.66 (-1.18, -0.13)**	**-0.66 (-1.18, -0.14)**	**-0.66 (-1.18, -0.13)**
NDVI					
Total sample		-0.16 (-0.69, 0.37)	-0.15 (-0.67, 0.38)	-0.16 (-0.68, 0.37)	-0.15 (-0.67, 0.38)
Male		0.09 (-0.71, 0.89)	0.11 (-0.69, 0.90)	0.09 (-0.71, 0.89)	0.11 (-0.69, 0.90)
Female		-0.33 (-1.00, 0.34)	-0.32 (-0.99, 0.35)	-0.33 (-1.00, 0.34)	-0.32 (-0.99, 0.35)
Urbanization rate					
Total sample		-0.11 (-0.33, 0.11)	-0.11 (-0.33, 0.11)	-0.11 (-0.33, 0.11)	-0.11 (-0.33, 0.11)
Male		-0.02 (-0.36, 0.32)	-0.02 (-0.36, 0.32)	-0.02 (-0.36, 0.32)	-0.02 (-0.36, 0.32)
Female		-0.09 (-0.37, 0.18)	-0.10 (-0.38, 0.18)	-0.09 (-0.37, 0.18)	-0.10 (-0.38, 0.18)

Cont.

	Model 1 Coefficient (95%CI)	Model 2 Coefficient (95%CI)	Model 3 Coefficient (95%CI)	Model 4 Coefficient (95%CI)	Model 5 Coefficient (95%CI)
Census tract					
Urban area		*-ref-*	*-ref-*	*-ref-*	*-ref-*
Peri-urban area					
Total sample		-0.08 (-1.81, 1.64)	-0.08 (-1.80, 1.64)	-0.08 (-1.81, 1.64)	-0.08 (-1.80, 1.64)
Male		-0.94 (-3.90, 1.82)	-0.95 (-3.71, 1.81)	-0.94 (-3.70, 1.82)	-0.95 (-3.71, 1.81)
Female		0.43 (-1.70, 2.56)	0.44 (-1.69, 2.57)	0.43 (-1.70, 2.56)	0.44 (-1.69, 2.57)
Rural area					
Total sample		0.47 (-1.73, 2.67)	0.46 (-1.75, 2.66)	0.47 (-1.73, 2.67)	0.47 (-1.75, 2.66)
Male		1.31 (-2.06, 4.69)	1.28 (-2.10, 4.66)	1.31 (-2.06, 4.69)	1.28 (-2.10, 4.66)
Female		0.31 (-2.47, 3.10)	0.30 (-2.48, 3.09)	0.31 (-2.47, 3.10)	0.30 (-2.48, 3.09)
Population density					
1º Quintile		*-ref-*	*-ref-*	*-ref-*	*-ref-*
2º Quintile					
Total sample		0.20 (-0.38, 0.78)	0.21 (-0.37, 0.79)	0.20 (-0.38, 0.78)	0.21 (-0.37, 0.79)
Male		0.75 (-0.09, 1.60)	0.77 (-0.07, 1.62)	0.75 (-0.09, 1.60)	0.77 (-0.07, 1.62)
Female		-0.07 (-0.83, 0.68)	-0.07 (-0.82, 0.68)	-0.07 (-0.83, 0.68)	-0.07 (-0.82, 0.68)
3º Quintile					
Total sample		0.22 (-0.36, 0.80)	0.23 (-0.35, 0.80)	0.22 (-0.36, 0.80)	0.23 (-0.35, 0.80)
Male		0.27 (-0.57, 1.11)	0.28 (-0.56, 1.12)	0.27 (-0.57, 1.11)	0.28 (-0.56, 1.12)
Female		0.13 (-0.62, 0.88)	0.13 (-0.61, 0.88)	0.13 (-0.62, 0.88)	0.13 (-0.61, 0.88)
4º Quintile					
Total sample		-0.26 (-0.85, 0.33)	-0.25 (-0.84, 0.35)	-0.26 (-0.85, 0.33)	-0.25 (-0.84, 0.35)
Male		-0.27 (-1.15, 0.60)	-0.26 (-1.13, 0.62)	-0.27 (-1.15, 0.60)	-0.26 (-1.13, 0.62)
Female		-0.30 (-1.06, 0.46)	-0.28 (-1.05, 0.48)	-0.30 (-1.06, 0.46)	-0.28 (-1.05, 0.48)
5º Quintile					
Total sample		0.01 (-0.61, 0.63)	0.02 (-0.60, 0.65)	0.01 (-0.61, 0.63)	0.02 (-0.60, 0.65)
Male		0.45 (-0.47, 1.37)	0.47 (-0.46, 1.39)	0.45 (-0.47, 1.37)	0.47 (-0.46, 1.39)
Female		-0.16 (-0.96, 0.64)	-0.14 (-0.94, 0.66)	-0.16 (-0.96, 0.64)	-0.14 (-0.94, 0.66)
Post-enrollment $PM_{2.5}$					
Total sample			0.01 (-0.03, 0.05)		0.01 (-0.03, 0.05)
Male			-0.00 (-0.06, 0.06)		-0.00 (-0.06, 0.06)
Female			0.02 (-0.03, 0.06)		0.02 (-0.03, 0.06)

Model 1: crude analysis, with random effect for participants' identification variable (ID). Model 2: model 1, adjusted for age, individual income, professional status, the presence of open public space, per capita income, rate of urbanization, situation of the census tract and demographic density. Model 3: model 2 with an additional adjustment for post-enrollment $PM_{2.5}$. Model 4: model 2 with an additional random effect for the federative unity (state) that participants live in. Model 5: model 3 with an additional random effect for the federative unity (state) that participants live in. Bold results mean statistical significance with an α value of 5%.

Understanding the complexity of obesity through predictive models based on the exposome approach

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Abstract

Obesity is a complex issue that has been studied extensively. However, the understanding of its determinants is spread across various areas of knowledge. Therefore, this study aims to investigate the determinants of obesity under an exposome approach. Cross-sectional data was collected from the CUME study, which is a prospective cohort conducted with Brazilian university graduates. The data included anthropometric, food intake, lifestyle, and socioeconomic factors. Additionally, secondary data on $PM_{2.5}$ were obtained from the Atmospheric Composition Analysis Group, while normalized difference vegetation index data was obtained from NASA. Brazilian census data was also collected. Five tree-based algorithms were used to predict obesity using the Caret package on RStudio® (4.3.3). The algorithms included Random Forest, Rpart/CART, c5.0, Bagging, and Boosting. The data set used for training and testing comprised 70% and 30% of the sample, respectively. The under-sampling technique was performed to improve the balance of the dataset. Accuracy was used as the primary criterion to determine the best-fitting model. Each model underwent 10-fold cross validation. The Boosting model showed the best performance, and it was used to build the graph of the importance of variables to predict obesity. The findings of the study revealed that having an unhealthy dietary pattern is the most significant predictor of obesity, followed by age, mother's obesity, TV usage, per capita income of the census tract they live, sibling's obesity, $PM_{2.5}$ exposure, having a Brazilian dietary pattern, father's obesity, and individual income. Despite the influence of family obesity, most of the variables that predicted obesity in this sample were modifiable factors. Based on these findings, the study suggests that public policy actions to prevent obesity should focus on modifiable factors, including environmental factors like improving the most economically disadvantaged census sectors and controlling air pollution.

Keywords: Body Mass Index; Artificial Intelligence; Machine Learning; Classification algorithm.

Introduction

Obesity is a chronic and complex disease that can impair health. It is related to the incidence of other non-communicable diseases, such as diabetes, cardiovascular diseases, and cancers (WHO, 2024). Its prevalence has reached pandemic proportions (Swinburn et al., 2019). Projections suggest that obesity will affect almost two billion people by 2035, increasing its global prevalence from 16% to 24% (WHO, 2024; World Obesity Federation, 2023). In Brazil, the prevalence of obesity increased by an average of 0.63 percentage points per year from 2006 to 2019, reaching 24.3% of the Brazilian population in 2023 (Brasil. Ministério da Saúde, 2023).

Owed to its significant threat to public health, obesity has been widely studied. However, due to its complexity and various associated factors, its understanding is organized across different areas of expertise. Studies on the determinants of obesity demonstrate that genetics, environment, social factors, and lifestyle choices are all linked to obesity (Drewnowski et al., 2020; Hermsdorff & Bressan, 2019; WHO, 2024).

To effectively tackle the issue of obesity, we need to gain a deeper understanding of its complexity. We cannot rely on a reductionist approach that isolates the effects of individual factors. Instead, we should explore analytical tools that allow us to evaluate multiple stressors simultaneously. Such emergent approaches can help us better comprehend the problem of obesity and take appropriate actions to control it. (McHale et al., 2018). The exposome approach, which looks at life-course environmental exposures from the prenatal period onwards (Wild, 2005), can help aggregate different data types into a single analysis, making it a more comprehensive way to study obesity. Thus, this study aimed to determine the predictors of obesity under an exposome approach, using machine learning models to predict and gain insights about the most important predictors of obesity.

Methods

CUME Study

This study used data from the Cohort of Universities of Minas Gerais (CUME Study). It is an ongoing prospective open cohort study that aims to evaluate the impact of the Brazilian dietary pattern and nutritional transition on the incidence of non-communicable diseases (Domingos et al., 2018).

Alumni from seven Federal Universities in Minas Gerais, Brazil participated in the study. Once registered, participants had access to the first phase of the baseline questionnaire.

It included questions related to lifestyle, socio-demographic, anthropometric, biomedical, and clinical data, individual and family morbidity, and personal examination history. One week after completing the first phase, participants had access to the second part of the questionnaire. It consisted of a semi-quantitative Food Frequency Questionnaire (FFQ), validated for the study population (Azarias et al., 2021), and questions related to their dietary habits.

The study was conducted following the guidelines of the Declaration of Helsinki and approved by the ethics committees of the universities involved (UFVJM, UNIFAL, UFJF, UFLA, UFMG, UFOP, and UFV; protocol no. 44483415.5.2005.5108, 44483415.5.2002.5148, 2615738/2018, 2676682, 2491366/18, 2565240/2018, and 596741-0/ 2013, respectively). All participants read and agreed to the online informed consent form before answering the questionnaire.

Outcome variable: obesity

Self-reported data on participants' weight (kg) and height (m) were validated in a subsample of the cohort (Miranda et al., 2017) and used to calculate the Body Mass Index (BMI). Obesity was considered as a BMI $\geq$ 30 kg/m2 (WHO, 2000), and used as a binary variable on the models.

Exposure variables, according to the exposome approach

The familial obesity was reported by participants. The analyses included binary variables to indicate the presence of obesity in the participants' mothers, fathers, siblings, and grandparents.

Sex, age, skin color, physical activity, and sedentary activities were reported by participants and considered as internal factors. Sex, daily time spent on TV, computer, and sleeping were considered binary variables. Age was treated as a continuous variable. Skin color and physical activity were transformed into dummy variables to create binary variables for each category.

The perception of public open space for physical activity, income, marital status, and professional status were reported by participants and considered as general external factors. The presence of a public open space was modeled as a binary variable. Income was treated as a continuous variable. Dummy variables were created for each category of marital and professional status to represent them as binary variables.

Municipality data were also considered as general external factors. Those included data from the Brazilian census obtained from the Brazilian Institute of Geography and Statistics (IBGE, 2010). Data on per capita income (continuous), and the situation of the census tract (binary, as urban or no-urban) were collected at census tract level. An urbanization score was computed for each census tract (continuous). Its calculation involved data on the total number of houses, existence of street identification, street lighting, paved street, paved sidewalk, curb, and manhole. The population density at census tract level (quintiles) was calculated on QGIS® (3.22.14), using geobr package (version 1.7.0) (Pereira et al., 2019) obtained on RStudio® (1.3.959).

Dietary patterns, eating habits, tobacco and alcohol use, air pollution and Normalized Difference Vegetation Index (NDVI) were considered as specific external factors. Dietary patterns were identified through the application of Principal Component Analysis on the FFQ food items. The coefficient of each dietary pattern identified was modeled as continuous variable. Participants were asked if they tend to skip breakfast, have their lunch outside of home, eat the visible fat from the meat and have less than three meals per day. All those eating habits variables were considered as binary in the models.

Participants were also asked to identify themselves as former smokers, active smokers, or non-smokers. Dummy variables were created for each category to represent them as binary variables. For alcohol exposure, a binary variable was created based on the frequency of alcohol abuse behavior (National Institute on Alcohol Abuse and Alcoholism, 2015).

Participants were asked to provide their home address, which was then geocoded using Google Maps and the OpenStreetMap plugin on QGIS® (version 3.22.14). The coordinates assigned for their home addresses were used to link data on air pollution, measured as $PM_{2.5}$ exposure, and NDVI.

Global estimates of ground-level ambient PM2.5 were obtained from the Atmospheric Composition Analysis Group (ACAG, 2023). Annual PM2.5 concentrations was averaged for the prior five years for each participant included in the sample. Public available secondary data on NDVI were obtained from NASA (NASA, 2023). NDVI data were also averaged for the prior five years before each participant's inclusion in the sample. PM2.5 and NDVI data were treated as continuous variables in the models.

Supervised learning

Five tree-based algorithms were used on RStudio® (4.3.2) to predict obesity using the Caret package. The algorithms included Random Forest, Rpart/CART, c5.0, Bagging, and Boosting. The sample was divided into a training set of 70% and a testing set of 30%. Due to the unbalanced data, a probability-weighted split was also executed, through under-sampling technique.

Performance metrics were obtained for all models from both the test and training datasets. Accuracy was used as the primary criterion to determine the best-fitting model. Additionally, Kappa index, sensitivity and specificity were also considered. Each model underwent 10-fold cross validation.

Results

The study included a total of 6,384 participants, out of which 4,373 (68.5%) were females. The participants had an average age of 35 (± 8.52) years. Obesity was observed in 777 (12.17%) of the participants, and 1,492 (23.37%) of them had at least one family member with obesity (Table 1).

Most of the participants were physically active, white, single, employed, non-smokers, and lived in urban areas. When it came to dietary habits, less than half of them showed risky behaviors. The average NDVI was 0.38 (± 0.39), and the average $PM_{2.5}$ exposure was 13.04 (± 2.77), as shown in Table 1.

Table 2 presents the performance metrics of the algorithms. The Boosting model outperformed the other models in terms of accuracy, Kappa Index, sensitivity, and specificity.

According to the graph created using the Boosting algorithm (Figure 1), the most important predictor for obesity is having an unhealthy dietary pattern (100%). The next important variables include age (84.2%), mother's obesity (49.3%), TV usage (33.5%), per capita income of the census tract where they live (21%), sibling's obesity (20.8%), PM2.5 exposure (19.8%), having a Brazilian dietary pattern (19.4%), father's obesity (14.1%), and individual income (14.1%).

Discussion

As far as we know, this study is the first to use the exposome approach to predict obesity in Brazilian adults. Based on the characteristics and objectives of this study, the evaluated exposures are recognized as significant predictors of obesity. Therefore, they were selected as exposure factors. Our primary aim was to examine all these factors collectively to determine which ones are the most critical in predicting obesity.

An unhealthy dietary pattern composed of red meats (Luan et al., 2020; Oliveira et al., 2020), ultra-processed foods (Hall et al., 2019; Silva et al., 2018), sweetened beverages (Oliveira et al., 2020; Santos et al., 2022), and alcoholic beverages (Albani et al., 2018; Souza et al., 2021) is well recognized to be a predictor of obesity. A study conducted by our team evaluated the association between dietary patterns and obesity among participants of the CUME Study. The study found that the unhealthy dietary pattern and the Brazilian dietary pattern had respective odds of increasing obesity by 45% and 14%, (not published). These findings are consistent with the results of the study.

The influence of genetic factors on obesity is widely recognized (Bell et al., 2005; Rankinen et al., 2006; Yu et al., 2020). Genome-wide association studies are considered the most effective method to investigate this link (Van Der Klaauw & Farooqi, 2015). However, collecting biological samples may not be feasible in some cases. In such cases, studying familial obesity may be a viable alternative.

Our results reveal the importance of mother's, sibling's, and father's obesity to predict obesity. While we did not come across any research that examines the impact of family obesity on adults, studies conducted with children have demonstrated the significant effect of parental obesity on their children's risk of developing obesity (Moschonis et al., 2022). Another study found a stronger association between maternal weight and child obesity compared to paternal weight (Whitaker et al., 2010). This corroborates our results, which found that mother's obesity had a greater impact than father's obesity.

Age, sex, and socioeconomic condition are also well-established in the literature to be related to obesity (Congdon, 2019; Drewnowski et al., 2020; Schumann & Moura, 2015; WHO, 2000). Here we do not just confirm those data, but we also provide their level of importance in predicting obesity.

Exposure to $PM_{2.5}$ is linked to cardiovascular, cerebrovascular, and respiratory morbidity and mortality (WHO, 2023). However, the effect of $PM_{2.5}$ on obesity is a recent and controversial topic. A systematic review analyzed 16 papers on the effects of air pollution on obesity, of which four were related to $PM_{2.5}$ and found null or mixed results for this association (An et al., 2018). Our team conducted a study which found that long-term exposure to $PM_{2.5}$ and physical activity have an interaction effect on BMI (not published), emphasizing the significance of modifiable factors in predicting obesity. While the existing literature on the association between PM2.5 and obesity is ambiguous, our results indicate that PM2.5 plays a significant role in predicting obesity.

Conclusion

Based on these findings, the study suggests that public policy actions to prevent obesity should focus on modifiable factors, including environmental factors like improving the most economically disadvantaged census tracts and controlling air pollution.

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Table 1. Characteristics of CUME Study participants included in this study, 2016-2022.

Participants characteristics	Total sample size n = 6,384
Sex	
Female	4,373 (68.5%)
Obesity	
Yes	777 (12.17%)
Physical activity	
Physically active	3,618 (56.67%)
Insufficiently active	1,282 (20.08%)
Inactive	1,484 (23.25%)
Dietary pattern	
Healthy dietary pattern	1,694 (26.54%)
Brazilian dietary pattern	1,741 (27.27%)
Unhealthy dietary pattern	1,357 (21.26%)
Dairy dietary pattern	1,592 (24.94%)
Family obesity	
Mother obesity	995 (15.59%)
Father obesity	711 (11.14%)
Sibling obesity	623 (9.76%)
Grandparent obesity	747 (11.70%)
Color	
White	4,086 (64%)
Not white	2,298 (36%)
Marital status	
Single	3,158 (49.47%)
Married	2,863 (44.85%)
Divorced/Widower	363 (5.69%)
Professional status	
Employed	4,700 (73.62%)
Student	1,124 (17.61%)
Retired / Home duties	79 (1.4%)
Unemployed	481 (7.53)
Tobacco use	
Never smoke	5,062 (79.29%)
Former smoker	736 (11.53%)
Smoker	586 (9.18%)
Binge drinking	
Yes	2,56 (40.19%)
Skip breakfast	
Yes	3,130 (49.03%)
Meals per day	
≤ 3	1,439 (22.54%)
Consume visible fat from meat	
Yes	1,588 (24.87%)
Have lunch at home	
No	1,691 (26.49%)
Census tract	
Urban	6,270 (98.21%)

Table 1. Cont.

Participants characteristics	Total sample size n = 6,384
Presence of an open public space for physical activity	
No	1,260 (19.74%)
Age	35.02 ± 8.52
Individual income (R$)	5,988.93 ± 38,348.69
Daily hours on TV	1.85 ± 1.82
Daily hours on computer	5.5 ± 2.73
Sleep duration	9.86 ± 1.39
Urbanization rate (%)	82.83 ± 17.55
Per capita income at census level tract (R$)	1,692.98 ± 1,1991.86
NDVI	0.38 ± 0.39
$PM_{2.5}$ exposure ($\mu g/m^3$)	13.04 ± 2.77

Table 2. Performance metrics of algorithms used to predict obesity in participants in the CUME Study, 2016-2022

Algorithms	Accuracy	Kappa	Sensitivity	Specificity
Random Fores	0.87	0.00	0.99	0.00
Rpart/CART	0.64	0.13	0.65	0.61
C5.0	0.67	0.17	0.67	0.65
Bagging	0.66	0.18	0.65	0.70
Boosting	0.71	0.23	0.71	0.69

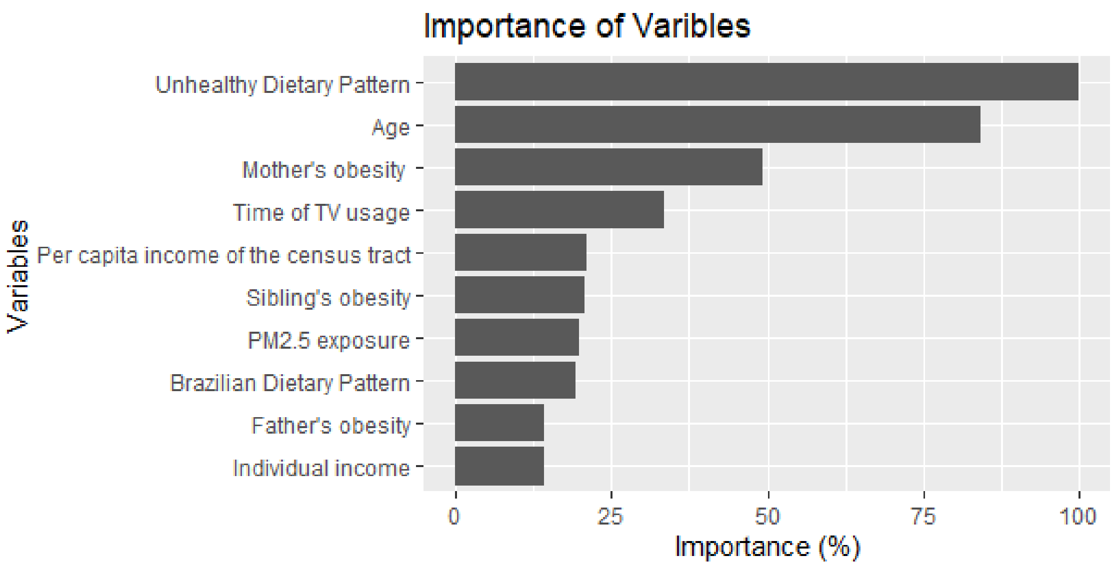

Figure 1. Importance of variables to predict obesity in CUME Study participants, 2016-2022.

6. FINAL CONSIDERATIONS

As far as we know, this study is the first to associate Brazilian dietary patterns with the three components of the global syndemic; to evaluate the interaction effect between $PM_{2.5}$, physical activity, and energy intake on long-term BMI in Brazilian adults; and to use the exposome approach to predict obesity in Brazilian adults.

The importance of this study for public health falls on highlighting the interaction between diet, climate change, socio-environmental factors, undernutrition and obesity. However, the characteristics of CUME Study participants do not allow us to evaluate undernutrition as underweight and food insecurity measures. Furthermore, some of the estimates for the coefficients of the environmental impact of the foods came from studies conducted in other countries and industry reports. Also, data on $PM_{2.5}$ exposure was not directly measured, and data on the municipality are from the Brazilian census conducted in 2010.

Despite these limitations, data from the CUME Study allow the discussion, planning, and implementation of specific interventions in Brazil. The data are validated, and participants are from different locations in Brazil. Furthermore, their high level of education ensured the reliability of the data since it was self-reported.

This study employed two distinct approaches to explore the problem of obesity. The first approach used epidemiological modeling to investigate the relationship between Brazilian dietary patterns and obesity, as well as the impact of long-term exposure to $PM_{2.5}$ on changes in BMI over time. The second approach relied on predictive modeling and accounted for internal and external factors to predict obesity. Although these approaches serve different purposes, both can provide valuable insights for public health.

The epidemiological modeling framework aims to estimate the association between exposure and outcome, based on retrospective and prospective events. Providing insights into long-term trends, it is valuable for predicting the trajectory of disease, evaluating intervention strategies, and helping policy makers make informed decisions. However, it is important to note that they may not always consider the complex interactions between different exposures. So, in order to accurately evaluate an outcome, it can be very complex and the accuracy of predictions can vary based on epidemiological assumptions.

On the other hand, the predictive modeling framework is designed to anticipate an outcome or its trajectory based on historical data, statistical analysis, and computational methods. Unlike epidemiological modeling, predictive modeling takes into account the interaction between all variables included in the model, providing the most important factors to predict an outcome, regardless of other exposures. This allows policymakers to make real-time decisions based on timely predictions.

Although the accuracy of predictive models can be sensitive to noise on the dataset, we have explored all possibilities in order to run our predictive models.

We tested five different models to identify the one that best fits with the dataset. We closely evaluated the performance metrics for each of these models. Initially, we tried four different data partitions and compared the accuracy and Kappa index for each one to determine the best-fitting model. We also executed a test for a probability-weighted split for all partitions of all models.

In the under-sampling technique, a random subset of samples from the class with more instances is selected to match the number of samples from the other class. Using this technique, there is the risk to lose relevant information from the left-out samples.

In the over-sampling technique, a random subset of samples from the minority class is duplicated to match the number of samples from the other class. This technique may overfitting the model, leading to an overestimation of the model's performance.

The ROSE and SMOTE techniques are hybrid methods that combine under-sampling of the majority class with the generation of additional data from the minority class to match the number of samples in each class.

In theory, hybrid techniques may appear to be a superior option, but none of the models performed well with them. Under-sampling, although it may lead to the loss of important information, proved to be the technique that better suited the models, other than boosting.

It's important to note that the CUME Study data might not be the best option for conducting predictive models due to its small sample size and low prevalence of the outcome. However, this open prospective cohort offers a promising dataset for future investigations since new participants are added every two years.

On the other hand, the data used in this study has its advantages. Primary and individual data are ideal for epidemiological modeling and are generally more reliable. Both modeling techniques depend on the quality and precision of the data. The environmental and census tract level data also add value to the dataset. Although personal and environmental data are from different sources and measures, predictive modeling is capable of identifying an interaction between these different data sources.

Finally, although the predictive modeling approach may seem like a black box that is difficult to interpret, the graph displaying the importance of the variables shows that the results obtained through this modeling are consistent with the results obtained through the epidemiological modeling.

Moreover, we conducted a sensitivity analysis by closely evaluating the metrics, running different methods, and comparing them. We observed that the variables on the graph of the importance of variables were very similar across all the models we tried.

The most interesting finding was that the factors identified were modifiable factors, such as diet, physical activity, income, sedentary activities, and exposure to $PM_{2.5}$. Hence, the results reinforce the significance of this research in guiding policymakers regarding activities that could help prevent obesity.

Policies related to food production and retail must take into account the impact they have on both human and planetary health. Governments should not only be concerned about air quality to prevent respiratory diseases but also to ensure that air pollution does not aggravate the obesity risk associated with unhealthy diets and sedentarism. In addition, it is important to identify the variables that influence obesity at the census tract level and take measures to improve them as a policy matter.

7. CONCLUSION

This study revealed that the Brazilian diet does not adhere to the Brazilian Dietary Guidelines, which negatively impacts people's health and the environment. If aligned with the recommendations, the Brazilian dietary pattern may be more balanced and the best option for good nutrition at the same time it is environmentally friendly. Also, there seems to be an association between air pollution exposure and obesity, which depends on lifestyle factors like physical activity, although further studies on this topic are still necessary. Finally, the exposome approach has revealed that while genetics may play a role in obesity, the modifiable factors at individual and environmental levels are the most significant in predicting obesity.

This study highlights the importance of public policy actions to incorporate the costs of the effects of diets on human and planetary health, aligning Brazilian’s diet to the Brazilian Dietary Guideline, to control air pollution at the same time to increase the physical activity the Brazilian population and to improve the living of those who live in the most economically disadvantaged census sectors of Brazil.

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