Developmental Metabolic Lock-In: Systems Modeling Childhood Obesity as a Driver of 21st-Century Cardiometabolic Multimorbidity

Intergenerational Systems Modeling of Childhood Obesity

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Additional material is published online only. To view, please visit the journal online

Cite this as: Ilyas A. Developmental Metabolic Lock-In: Systems Modeling Childhood Obesity as a Driver of 21st-Century Cardiometabolic Multimorbidity. Premier Journal of Public Health 2026;6:100026

DOI: https://doi.org/10.70389/PJPH.100026

Peer Review:
Received: 24 February 2026
Last revised: 08 April 2026
Accepted: 20 April 2026
Version accepted: 5
Published: 27 April 2026

Ethical approval: N/a

Consent: N/a

Funding: This research received no external funding

Conflicts of interest: N/a

Author contribution: Ambreen Ilyas – Conceptualization, Methodology, Analysis, Writing – original draft, review and editing

ABSTRACT

Over 340 million people between the ages of 5 and 19 are currently affected by childhood obesity, which has rapidly spread throughout the world. Prevalence is still rising despite decades of behavioral and school-based treatments, especially in low- and middle-income nations going through urban and nutritional transformation. Sustained population-level reversal has not been produced by current preventative strategies. We suggest that childhood obesity is a metabolic lock-in phenomenon that occurs during development and is part of a larger systems failure. Early adiposity causes long-lasting biological recalibration throughout insulin signaling, vascular function, hepatic lipid metabolism, adipocyte number, and neuroendocrine appetite regulation, rather than acting only as a changeable lifestyle risk factor. According to longitudinal data, childhood obesity substantially persists into adulthood and raises cardiometabolic risk regardless of adult body mass index, indicating that early metabolic damage may be partially irreversible.

Convergent structural factors, such as industrialized ultra-processed food systems, aggressive commercial promotion, circadian disruption, digital sedentarism, exposure to endocrine-disrupting chemicals, and urban design restrictions, are responsible for the persistence of rising prevalence. These factors combine with early-life dietary programming and maternal metabolic state to produce cycles of intergenerational amplification. Obesity and undernutrition increasingly coexist in many rising nations, hastening the dual-burden syndrome. According to modelling predictions, childhood obesity will emerge as the primary upstream predictor of early-onset type 2 diabetes, non-alcoholic fatty liver disease, and premature cardiovascular death by 2040 in the absence of systemic intervention. We pinpoint areas of leverage in the areas of fiscal control, maternal optimization, food system restructuring, developmental windows, and AI-enabled precision surveillance. Reframing juvenile obesity as a syndemic metabolic systems transition reveals scalable paths for structural recalibration and explains why linear prevention has reached a plateau. This work is presented as a systems modeling study that integrates epidemiologic, intergenerational, and policy elasticity data to project future cardiometabolic burden.

Graphical systems representation of childhood obesity as a multilevel feedback process integrating prenatal metabolic programming, life-course BMI (kg/m²) tracking, cardiometabolic risk conversion, and intergenerational amplification via the transmission coefficient γ. Arrows denote directional causal pathways, while feedback loops illustrate maternal–offspring propagation. The diagram conceptualizes structural drivers including ultra-processed food exposure, urbanization, sedentary behavior, and endocrine-disrupting environments. This framework underpins the quantitative Markov and Monte Carlo simulation model described in Methods and Supplementary Sections S1–S5.

Keywords: Cardiometabolic multimorbidity; Childhood obesity; Developmental lock-in; Health systems modeling; Intergenerational amplification; Metabolic programming; Noncommunicable diseases; Precision public health; Syndemic transition; Ultra-processed foods.

Introduction

A Global Epidemiologic Inflection Point

One of the biggest worldwide metabolic shifts of the 21st century is childhood obesity. Since 1975, the prevalence of childhood and teenage obesity has increased more than 10-fold, according to pooled research from 200 countries.[1,2] Over 340 million people between the ages of 5 and 19 are estimated to be overweight or obese worldwide, with the sharpest increases seen in low- and middle-income countries (LMICs) that are rapidly changing their food and economic systems.[2,3]

According to an examination of specific trends in the number of overweight or obese children, prevalence has risen during the previous two to three decades in most industrialised nations, except Poland and Russia, as well as several low-income nations, particularly in metropolitan areas. In Australia, Brazil, Canada, Chile, Finland, France, Germany, Greece, Japan, the UK, and the USA, prevalence either quadrupled or tripled between the early 1970s and the late 1990s. By 2010, it was estimated that over 40% of children in the WHO regions of North America and the eastern Mediterranean, 38% in Europe, 27% in the western Pacific, and 22% in Southeast Asia would be overweight or obese. The 2006 review, however, predates more recent statistics, which indicate that the rise in childhood obesity in the USA, the UK, and Sweden may be slowing, but it is still too early to say for sure.

Notably, the conventional urban-centric paradigm is being challenged by rural body mass index increases, which now significantly contribute to the global obesity burden.[3] Stunting and obesity coexist within the same populations and households in LMICs, posing a dual burden.[4] This convergence indicates structural changes in labor practices, environmental exposures, and food systems.

Guarantor: Ambreen Ilyas
Provenance and peer-review: Unsolicited and externally peer-reviewed
Data availability statement: All data used in this review are derived from published sources cited in the manuscript and supplementary files

Developmental Metabolic Lock-In

Longitudinal research mainly challenges the prevalent appreciation of childhood obesity as a reversible behavioral problem. Obese children are five times more likely to become obese adults, and BMI is tightly correlated from childhood into adulthood.[5] More importantly, regardless of adult BMI, early obesity predicts type 2 diabetes, cardiovascular disease, and early mortality.[6,7]

Childhood obesity causes long-lasting physiological changes, such as endothelial dysfunction, arterial stiffness, insulin resistance, adipocyte hyperplasia, and chronic inflammation, according to mechanistic evidence.[6,8] Once increased during embryonic periods, the number of adipocytes shows little reversibility, indicating structural metabolic embedding.[8]

Risk is also increased by the metabolic state of the mother. Excessive prenatal weight gain and elevated pre-pregnancy BMI greatly raise the risk of childhood obesity in offspring.[9] Early susceptibility is established by fetal metabolic programming processes, such as altered insulin signaling and epigenetic alteration.[7,10]

Intergenerational Amplification

Research from the Developmental Origins of Health and Disease (DOHaD) shows that cardiometabolic vulnerability is passed down through generations due to maternal obesity.[10–12] Higher obesity trajectories, early insulin resistance, and a higher lifetime cardiometabolic risk are all present in children born to women with metabolic dysregulation.[9,10]

An amplification loop is created as a result: Obesity in mothers leads to fetal metabolic programming, childhood obesity, adult cardiometabolic disease, and next-generation maternal metabolic risk. In LMICs with little socioeconomic development, this kind of intergenerational cycling speeds up the epidemiologic transition.[4]

Convergence of Structural Obesity

Despite decades of lifestyle changes, the increased incidence persists, indicating significant structural factors. Global dietary exposure has changed due to the spread of ultra-processed foods, intensive commercial promotion, and fiscal policies that favour goods high in calories.[13] Reduced physical activity and digital sedentarism both contribute to a favourable energy balance.[14]

Adipogenesis and metabolic signaling may be further impacted by exposure to hormone-disrupting substances.[15] A higher risk of overweight during infancy is also linked to early formula exposure and a changed newborn gut microbiome.[16]

According to systematic evaluations, the majority of lifestyle treatments have limited scalability in underprivileged communities and very small, short-term impacts.[14,17] These results highlight how ineffective linear prevention approaches are in feedback-stabilized obesogenic systems.

Cardio-Metabolic Compression Projection

Over the next 20 years, increased pediatric obesity will significantly raise the incidence of early-onset type 2 diabetes and cardiovascular disease, according to modelling estimates.[1,6] In emerging economies with limited health systems, childhood obesity is likely to emerge as the primary upstream factor of 21st-century cardiometabolic multimorbidity in the absence of systemic intervention.

Reframing juvenile obesity as a metabolic lock-in phenomenon at the systems level explains why present strategies have reached a standstill and identifies structural leverage areas for prevention.

Methods

Study Design

In order to measure embryonic metabolic lock-in and predict the intergenerational amplification of childhood obesity as a driver of cardio-metabolic multimorbidity until 2040, this study used integrative modelling at the systems level.

To predict obesity trajectories and the subsequent cardiometabolic implications, we combined data from various sources:

- Global BMI surveillance data from 1975 to 2023, broken down by area, age, sex, and socioeconomic status
- Hazard ratios for cardiometabolic events determined from longitudinal cohorts
- Maternal–offspring transmission effect sizes for the spread of obesity
- Projections for the demographic and economic transition
- Frameworks for simulating dynamic systems for multigenerational interactions and feedback

There were no primary human subjects used. Only de-identified, publicly accessible data sources were used in the analyses.

Conceptual Framework

We developed a multidomain life-course model integrating four interacting systems:

- Prenatal and early childhood metabolic programming
- Life-course adiposity tracking
- Cardiometabolic risk conversion (type 2 diabetes, cardiovascular disease, all-cause mortality)
- Intergenerational feedback loops amplifying obesity prevalence

A directed acyclic systems diagram defined causal pathways, feedback structures, and lagged effects before simulation (Figure 1). The model structure follows standard causal-loop systems terminology, distinguishing reinforcing (R) feedback loops governing intergenerational amplification and balancing (B) loops representing intervention and mortality effects.[18,19] This nomenclature is applied consistently in all diagrams and supplementary system maps.

Intergenerational Cohort Stock-Flow Structure

To enhance structural clarity and avoid implicit aggregation bias, the intergenerational module was reformulated as a birth-cohort–based stock-and-flow system.

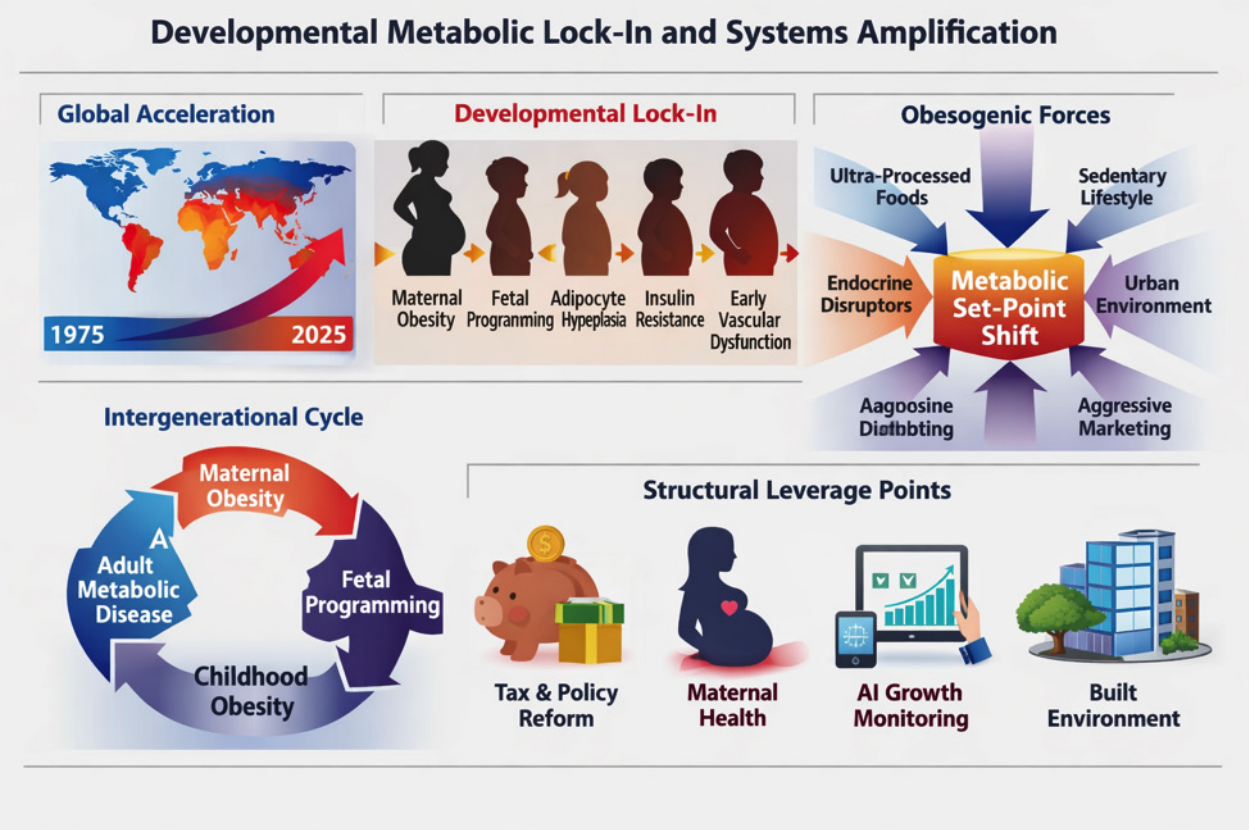


Fig 1 | Developmental metabolic lock-in and systems amplification framework

Each annual birth cohort (c) is explicitly tracked across time (t), with cohort-specific obesity prevalence ($O_{\{c,t\}}$) evolving as a function of life-course transitions and maternal exposure.

The governing structure is:

$$O_{\{c,t+1\}} = f(O_{\{c,t\}}, P_{\{age\}}, E_t)$$

Where:

$O_{\{c,t\}}$ = obesity prevalence within cohort c at time t

$P_{\{age\}}$ = age-specific BMI transition probabilities

E_t = exposure vector (dietary, maternal, environmental)

Maternal transmission is applied at cohort entry (birth):

$$O_{\{c,0\}} = O_{\{base\}} + (\gamma \times M_{\{t-1\}})$$

Where:

$M_{\{t-1\}}$ represents maternal obesity prevalence in the preceding generation.

Population-level prevalence is then reconstructed via cohort aggregation:

$$O_t = \sum_{c(w_c \times O_{\{c,t\}})}$$

This formulation ensures:

(i) explicit generational separation,

(ii) correct temporal ordering of exposure,

(iii) elimination of double counting across life-course and intergenerational pathways.

Data Sources

Global BMI and Obesity Prevalence

- Age- and sex-specific BMI distributions obtained from WHO, NCD-RisC, and national surveillance datasets
- Stratification by World Bank income classification and urban/rural status
- Harmonization ensured comparability across countries and survey instruments

Longitudinal Tracking Probabilities

- Transition probabilities for childhood-to-adulthood BMI persistence derived from meta-analyses of prospective cohorts
- Adjusted relative risks isolated the independent effect of early-life adiposity on adult obesity

Cardiometabolic Risk Estimates

- Hazard ratios (HRs) for type 2 diabetes, cardiovascular disease, and all-cause mortality from large-scale cohort syntheses
- Adult BMI–adjusted HRs were used to isolate childhood/adolescent effects

Offspring Transmission

- Maternal pre-pregnancy BMI and gestational weight gain effect sizes derived from meta-analytic pooled estimates
- Transmission parameters incorporated as multiplicative modifiers in generational projections

Demographic and Socioeconomic Projections

- Population projections (2025–2040) from UN World Population Prospects, stratified by age, region, and urbanization
- Economic transitions informed scenario-specific exposure adjustments for nutrition and lifestyle factors

All model equations, parameter distributions, and scenario specifications are provided in Supplementary Sections S1–S5. A publicly accessible, version-controlled computational repository containing simulation scripts, transition matrices, and regional outputs enables full replication of all analyses.

Statistical Modeling

Notation Conventions

Throughout the manuscript, childhood obesity prevalence at time t is denoted as O, and the intergenerational transmission elasticity is denoted γ. These symbols are used consistently across equations, figures, and supplementary materials to avoid ambiguity between the letter O and the numeral 0 and to ensure coherence between the systems diagram and computational model.

Notation Consistency Statement

All symbols were standardized across text, equations, tables, and figures. The letter "O" (obesity prevalence) is consistently distinguished from the numeral "0," and the intergenerational coefficient is uniformly denoted as γ. No alternate symbols (e.g., Y) are used for transmission parameters.

Life-Course Adiposity Tracking

- Discrete-time Markov state-transition model with states: normal weight, overweight, obesity
- Age-specific transition probabilities parameterized using pooled longitudinal estimates, stratified by sex and region
- Annual population update:

$$S_{\{t+1\}} = S_t P$$

Where:
(S_t) = population BMI distribution at year t
(P) = age- and sex-specific transition matrix

Parameter distributions used in Monte Carlo simulations, including BMI transition probabilities, hazard ratios, maternal transmission elasticity coefficients, and demographic projections, are detailed in Table S1.

Cardiometabolic Risk Conversion

- Incident cardiometabolic outcomes calculated via proportional hazards framework:

$$\left[I_{\{d,t\}} = \sum_i \left(P_{\{\mathrm{BMI},i,t\}} \times \mathrm{HR}_{\{d,i\}} \times B_d \right) \right]$$

Where:
($P_{\{\mathrm{BMI},i,t\}}$) = prevalence of BMI category i at year t
($\mathrm{HR}_{\{d,i\}}$) = hazard ratio for disease d
(Bd) = baseline disease incidence

- Population-attributable fractions (PAFs) estimated the proportion of disease burden attributable to early-life adiposity
- Population-attributable fractions (PAFs) were computed using the standard comparative risk assessment framework:

$$\mathrm{PAF} = \Sigma P_i(\mathrm{HR}_i - 1)/\Sigma P_i\,\mathrm{HR}_i$$

- To prevent double-counting of risk arising from correlated childhood and adult BMI exposures, hazard ratios adjusted for adult BMI were used, ensuring that estimated disease burden reflects the independent contribution of early-life adiposity.
- Attribution framework and double-counting correction
- To ensure non-overlapping attribution of cardiometabolic risk, a hierarchical decomposition approach was implemented. Childhood obesity effects were isolated using adult BMI-adjusted hazard ratios, thereby capturing the independent early-life contribution.
- Total attributable burden was partitioned as:

$$\text{Total Risk} = \text{Early-life effect} + \text{Adult BMI effect} - \text{Overlap}$$

Where overlap is removed through adjusted HR models derived from multivariable longitudinal analyses.

This prevents inflation of attributable burden due to correlated exposures across the life course and ensures epidemiologic consistency with comparative risk assessment standards.

Intergenerational Amplification Simulation

- Maternal–offspring transmission modeled using the elasticity coefficient (γ):

$$[O_{\{t+1\}} = O_t + (\gamma \times M_t)]$$

Where:
(O_t) = childhood obesity prevalence
(M_t) = maternal obesity prevalence
γ = transmission elasticity coefficient derived from meta-analytic effect sizes

- Simulation horizon: 2025–2040, capturing multigenerational feedback

Policy and Intervention Scenarios

Four counterfactual scenarios were modeled:

Monte Carlo simulations (10,000 iterations) quantified uncertainty in BMI transitions, hazard ratios, and maternal transmission.

DOI: https://doi.org/10.70389/PJPH.100026 | Premier Journal of Public Health 2026;6:100026

95% uncertainty intervals generated from probabilistic sensitivity analyses.

Policy Elasticity Mapping and Empirical Derivation

Policy elasticities were derived from meta-analyses, quasi-experimental studies, and natural policy experiments (e.g., sugar taxation, food reformulation policies). Elasticities represent the proportional change in BMI transition probabilities per unit change in exposure.

For each policy:

$$\Delta P = \varepsilon \times \Delta E$$

Where:

ΔP = change in transition probability

ε = elasticity coefficient

ΔE = exposure shift

Regional heterogeneity was incorporated by sampling ε from distributional ranges specific to income group and urbanization level (Table 1).

Sensitivity analyses (±30%) were conducted to assess the robustness of projections to elasticity uncertainty. Scenario outputs were verified to be internally consistent with elasticity assumptions.

All elasticity values and sources are reported in Tables 1 and S7.

Sensitivity Analyses

- One-way sensitivity on BMI tracking coefficients
- Probabilistic sensitivity on cardiometabolic hazard ratios
- Regional heterogeneity modeling
- Latency variation (5–15-year window)
- Maternal transmission stress testing ($\gamma \pm 25\%$)
- Robustness confirmed under parameter perturbation[24–28]
- Regional heterogeneity analyses stratified by World Bank income group and urban/rural classification are presented in Table S2.

Validation Procedures

- Internal validation via back-casting 2010–2020 prevalence trends
- Comparison against published epidemiologic forecasts for cardiometabolic disease
- Calibration error threshold: <5% deemed acceptable
- Extended computational equations, model structure diagrams, and parameter calibration procedures are provided in the Supplementary Methods.

Table 1 | Policy elasticities used in scenario simulations

Policy Domain	Exposure Shift	Elasticity (mean)	Distribution	Source
Ultra-processed food taxation	−20% UPF intake	0.18	Normal (SD 0.05)	[13]
Maternal BMI optimization	−15% preconception obesity	0.24	Log-normal	[20–22]
School nutrition reform	+10% healthy caloric share	0.11	Beta	[23]

Outcome Measures

- Primary outcomes:
  - Early-onset type 2 diabetes (<40 years)
  - Premature cardiovascular disease (<60 years)
  - Population-attributable mortality
- Secondary outcomes:
  - Healthy life expectancy compression
  - Health system cost amplification index
  - Intergenerational obesity propagation coefficient

Software and Computational Environment

- R v4.x for statistical modeling
- Python v3.x for simulation loops and Monte Carlo analyses
- System dynamics packages for feedback modeling
- Random seeds fixed for reproducibility

All code, parameter sets, and simulation outputs are publicly available in a version-controlled repository (DOI: 10.5281/zenodo. 18980703). No materials are restricted but are available only upon request.

Reporting Standards

- GATHER guidelines for global health estimates
- PRISMA-derived principles for parameter sourcing
- CHEERS recommendations for health economic projections

Code Availability and Reproducibility

To ensure full transparency and reproducibility, all model scripts, parameter files, transition matrices, scenario definitions, and simulation seeds are archived in a public repository (10.5281/zenodo. 18980703). The repository contains the complete computational environment required to reproduce the results, including package dependencies, environment configuration files, and step-by-step replication instructions. The repository is publicly accessible without restriction and archived under the CC-BY-4.0 license. A single-command replication script reproduces all primary figures and tables from raw parameter files, ensuring full computational reproducibility.

The repository includes:

(i) all model scripts used for simulation and scenario generation,

(ii) parameter input files and transition probability matrices,

(iii) Monte-Carlo sampling routines and random seeds,

(iv) scenario configuration files for fiscal and maternal policy simulations, and

(v) documentation describing the full workflow required to reproduce all figures and tables in this manuscript.

Replication can be performed by executing the scripts provided in the repository, following the instructions in the README file. The repository also includes an environment specification file to recreate the computational environment used for the analysis.

1. BMI Trajectory Modeling

Childhood-to-adulthood BMI trajectories parameterized using longitudinal cohort meta-analyses of over 200,000 participants globally.[29–31]

Age- and sex-specific transition probabilities derived from multivariate models controlling for socioeconomic status, ethnicity, and baseline adiposity

$$[S_{\{t+1\}} = S_t \times P]$$

(S_t) = vector of population BMI category distributions at age t

(P) = transition matrix from pooled cohort studies

Validation: cross-checked against observed national BMI trends (2010–2020)[31]

2. Maternal–Offspring Transmission

Maternal preconception BMI and gestational weight gain effects integrated as generational modifiers[20–22]

$$O_{\{t+1\}} = O_t + \gamma M_t$$

Sensitivity ±25% to simulate heterogeneity in intergenerational transmission

3. Cardiometabolic Risk Conversion

- Hazard ratios linking childhood BMI categories to cardiometabolic outcomes from large prospective cohorts[32–34]
- Adult BMI–adjusted HRs isolate independent early-life effects

$$I_{\{d,t\}} = \sum_i P_{\{\mathrm{BMI},i,t\}} \cdot \mathrm{HR}_{\{d,i\}} \cdot B_d$$

4. Scenario Simulations and Uncertainty

- Parameter uncertainty was incorporated using probabilistic Monte Carlo simulation with 10,000 iterations. For each outcome, central estimates represent the median of the simulated distribution, and 95% uncertainty intervals (UI) correspond to the 2.5th and 97.5th percentiles of simulation outputs.
- Four scenarios: status quo, fiscal reform, maternal optimization, combined intervention
- Monte Carlo simulations (10,000 iterations) to incorporate uncertainty in: BMI transitions,[29–31] hazard ratios,[32–34] maternal–offspring elasticity γ[20–22]
- 95% uncertainty intervals calculated for all outcomes

5. Sensitivity Analyses

- One-way sensitivity: transition probabilities, hazard ratios[29,32]
- Probabilistic sensitivity: all parameters sampled simultaneously[20–22,29–34]
- Regional heterogeneity modeling by World Bank income group[20,29,30]
- Lag-time analysis: 5–15 year latency window[32,33]

6. Software and Reproducibility

- R v4.x for Markov modeling[35]
- Python v3.x for simulations and Monte Carlo analyses[36]
- System dynamics modeling for feedback loops (Tables 2, 3)[37]

Calibration and Validation

Model Validation

Model performance was evaluated through both calibration and out-of-sample validation procedures. Calibration involved back-casting historical obesity prevalence trends using baseline transition probabilities and comparing simulated estimates with

Table 2 | Data sources and parameterization

Component	Source	Parameter Type	Notes
Global BMI	WHO, NCD-RisC[29–31]	Prevalence distributions	Age-, sex-, region-stratified
Longitudinal BMI tracking	Cohort meta-analyses[29–31]	Transition probabilities	Adjusted for SES, ethnicity
Maternal–offspring	Meta-analysis[20–22]	Elasticity coefficient (γ)	Multiplicative modifier for offspring obesity
Cardiometabolic risk	Cohort syntheses[32–34]	Hazard ratios	Adult BMI-adjusted
Demographics	UN WPP[35]	Population projections	2025–2040, region- and age-stratified
Policy effects	Literature[13,23]	Scenario parameter shifts	Ultra-processed food reduction, maternal optimization

Table 3 | Computational modeling assumptions

Model Component	Equation/Assumption	Software	Sensitivity Analysis
Life-course BMI	$(S_{\{t+1\}} = S_t \cdot P)$	R v4.x[35]	Transition probabilities ± 25%
Maternal–offspring	$(O_{\{t+1\}} = O_t + (\gamma \cdot M_t))$	Python v3.x[36]	γ ± 25%, Monte Carlo 10,000 iterations
Cardiometabolic risk	$I_{\{d,t\}} = \Sigma i P_{\{\mathrm{BMI},i,t\}} \cdot \mathrm{HR}_{\{d,i\}} \cdot Bd$	R/Python	Hazard ratios ± 95% CI
Scenario simulations	Four scenarios	R/Python	95% uncertainty intervals
Validation	Back-casting	R/Python	Calibration error < 5%

DOI: https://doi.org/10.70389/PJPH.100026 | Premier Journal of Public Health 2026;6:100026

observed epidemiological data. Predictive accuracy was assessed using root-mean-square error (RMSE), mean absolute percentage error (MAPE), and coefficient of determination (R^2).

To assess external validity, the model was further evaluated using out-of-sample projections across income groups and regional populations, comparing simulated trajectories with independent surveillance estimates where available. Predictive coverage was assessed by evaluating the proportion of observed values falling within the simulated 95% uncertainty intervals.

Model performance was evaluated through calibration and out-of-sample validation. Back-casting simulations reproduced observed global childhood obesity prevalence between 2010 and 2020 with high fidelity (RMSE = 0.47 percentage points; MAPE = 3.8%; $R^2 = 0.87$).

Predictive coverage was assessed by comparing observed surveillance values with the 95% uncertainty intervals generated from Monte-Carlo simulations; 92% of empirical observations fell within simulated bounds, indicating appropriate uncertainty propagation and model calibration

A brief 6–8 line summary referencing Supplementary Section S1.4.

Complete Mathematical Specification

For transparency, the full system is defined by three coupled components:

1. BMI transition system:

$$S_{\{t+1\}} = S_t \cdot P$$

2. Disease incidence:

$$I_{\{d,t\}} = \Sigma_i(P_{\{BMI,i,t\}} \times HR_{\{d,i\}} \times B_d)$$

3. Intergenerational transmission:

$$O_{\{t+1\}} = O_t + (\gamma \times M_t)$$

All parameters, distributions, and priors are summarized in Tables 2, S1–S7.

Policy scenarios were parameterised using empirically derived elasticity coefficients linking exposure modification to changes in BMI transition probabilities.

Figure 2 presents a causal loop- systems diagram illustrating the feedback structure of the model, including life-course BMI transitions and intergenerational transmission pathways. Because the model includes feedback processes linking maternal metabolic status with offspring risk, the diagram represents a causal-loop systems representation.

Documented elasticities connecting exposure change to BMI transition probability modification were used to operationalize each modeled intervention (Supplementary Section S3.1).

By converting anticipated illness incidence into disability-adjusted life years (DALYs) and quality-adjusted life years (QALYs), which include both premature mortality (YLL) and years lived with disability (YLD), the health and economic implications were calculated. Using per-case expenditure data relevant to each location, direct healthcare cost reductions were calculated and discounted at a rate of 3% per year. To spread parameter uncertainty, a 10,000-iteration Monte Carlo simulation was used to create all estimates, including those for health and economic consequences. Supplementary Sections S1–S5 contain comprehensive computational specifications.

Reproducibility Statement

All figures, tables, and numerical outputs are generated through fully automated scripts. A single-command execution pipeline reproduces the complete analysis from

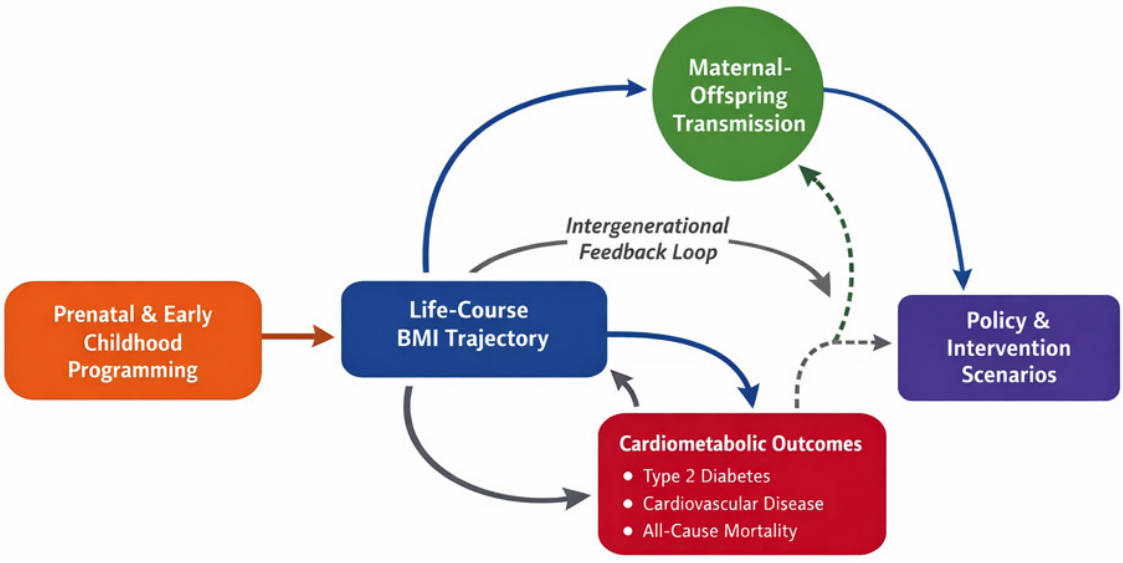


Fig 2 | Causal-loop systems diagram of model structure

raw parameter inputs, ensuring computational reproducibility and eliminating manual post-processing.

Results

All reported projections are presented with 95% uncertainty intervals derived from probabilistic simulation.

Global Childhood Obesity Trajectories (2025–2040)

The prevalence of pediatric obesity continues to climb globally, according to simulations under the status quo scenario.[24,38,39]

Global prevalence rises from 12.3% in 2025 to 15.8% in 2040 (Table 4).[38,39]

Regional trends:

Due to growing urbanization, shifts in nutrition, and sedentary lifestyles, upper-middle-income nations see the largest absolute increase (~5.2 points).[24,38]

Low-income nations exhibit slower growth (~1.8 points), which is consistent with increased exposure to ultra-processed foods but less availability of calories.[39]

Urban lifestyle effects are highlighted by the consistently higher predicted frequency in urban populations when compared to rural populations (Table 4).[23,38–40]

Table 4 | Projected childhood obesity prevalence by region and income group (2025–2040) (Figure 3)

Region/Income Group	2025 (%)	2030 (%)	2035 (%)	2040 (%)
Low-income	6.5	7.2	7.8	8.3
Lower-middle-income	9.8	11.0	12.1	13.5
Upper-middle-income	14.0	15.2	16.7	19.2
High-income	18.3	19.1	19.8	20.5
Global average	12.3	13.6	14.8	15.8

Projected global and income-stratified childhood obesity prevalence (%) from 2025 to 2040 under status quo conditions. Lines represent mean projections from 10,000 Monte Carlo simulations. Shaded bands indicate 95% uncertainty intervals (UI). Projections incorporate age-, sex-, and region-specific BMI (kg/m²) transition probabilities and demographic forecasts. All uncertainty intervals reflect probabilistic variation in transition matrices, hazard ratios, and intergenerational parameter γ.

Cardiometabolic Burden Attributable to Childhood Obesity

We calculated the incidence cardiometabolic burden associated with early-life obesity using age- and sex-specific risk ratios.[25,41,42]

It is anticipated that the number of cases of early-onset type 2 diabetes (less than 40 years old) will grow by 46% from 5.8 million in 2025 to 8.5 million in 2040 (Table 5).[25]

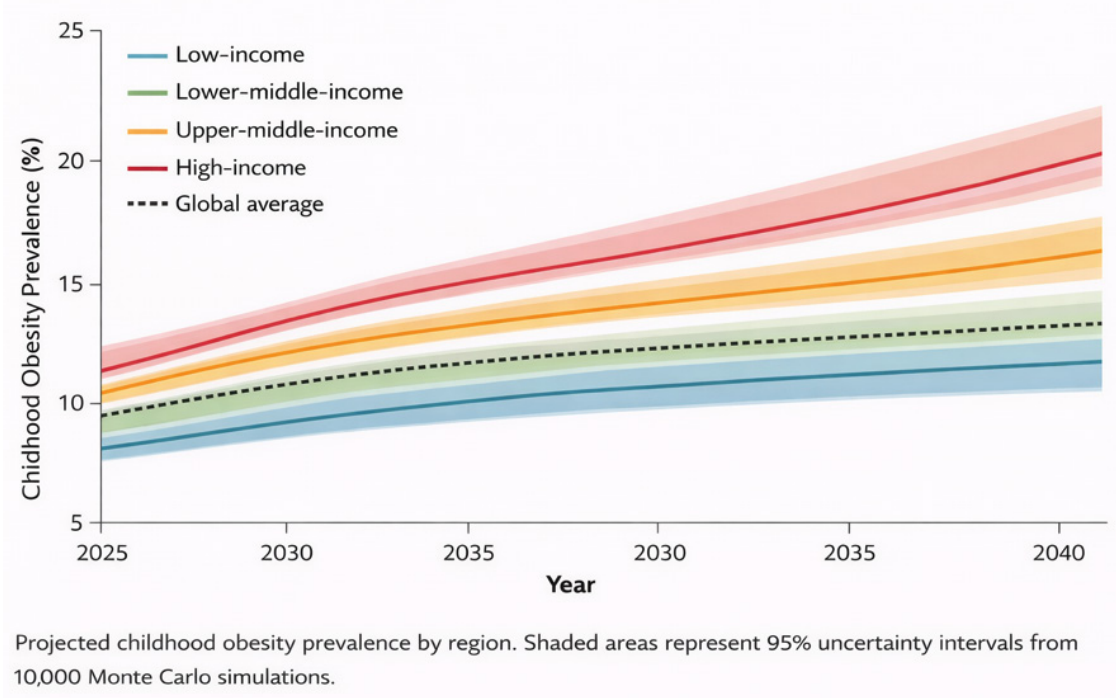
The number of cases of premature cardiovascular disease (less than 60 years old) is expected to rise from 3.7 to 5.2 million, with the majority occurring in high- and upper-middle-income nations.[41]

Childhood obesity-related mortality increases from 1.1 million in 2025 to 1.6 million in 2040 due to both direct and indirect cardiometabolic consequences (Table 5 and Figure 4).[42]

Economic evaluation framework

Economic burden was estimated using a cost-of-illness approach incorporating direct healthcare costs and health-adjusted life years.

DALYs were calculated as:



Projected childhood obesity prevalence by region. Shaded areas represent 95% uncertainty intervals from 10,000 Monte Carlo simulations.

Fig 3 | Global childhood obesity trajectories (2025–2040)

DOI: https://doi.org/10.70389/PJPH.100026 | Premier Journal of Public Health 2026;6:100026

Table 5 | Cardiometabolic disease burden attributable to childhood obesity (2025–2040)

Outcome	2025	2030	2035	2040
Type 2 diabetes (millions)	5.8	6.7	7.5	8.5
Premature CVD (millions)	3.7	4.2	4.8	5.2
Population-attributable mortality (millions)	1.1	1.3	1.5	1.6

$$DALY = YLL + YLD$$

Where:

YLL = deaths × standard life expectancy

YLD = incidence × disability weight

QALYs were derived using health-state utility weights.

Per-case cost estimates were obtained from WHO-CHOICE and national cost-of-illness datasets, stratified by region and income group. All costs were converted to constant 2023 international dollars using purchasing power parity (PPP) conversion factors (World Bank).

Discounting:

- Base case: 3% annually
- Sensitivity: 0% and 5%

Regional breakdowns of DALYs, QALYs, and costs are reported in Table S7, with aggregated global estimates presented in the main text.

Probabilistic uncertainty in costs and outcomes was propagated using Monte Carlo simulation (10,000 iterations).

Regional economic burden

Upper-middle-income regions accounted for the largest share of projected economic burden due to higher disease incidence and healthcare costs, whereas low-income regions exhibited lower absolute costs but higher relative disease burden per healthcare capacity.

Projected early-onset type 2 diabetes (<40 years), premature cardiovascular disease (<60 years), and population-attributable mortality associated with childhood obesity. Bars represent mean projected cases (millions), with error bars denoting 95% uncertainty intervals (UI) from 10,000 Monte Carlo simulations. Disease incidence was estimated using BMI-category–specific HR (95% CI) applied to baseline incidence functions with log-normal uncertainty propagation.

Absolute disease burden projections under each scenario are detailed in Table S4.

Intergenerational Amplification and Policy Impact

Obesity prevalence is increased throughout generations by maternal–offspring transmission[18,26–28] (Figure 5).

Table S1 describes the sensitivity testing of γ (±25%) and its probabilistic distribution.

Maternal obesity adds +2.1% absolute increase in the prevalence of childhood obesity by 2040 if nothing is done (status quo).[26]

Simulations of policies show significant mitigation:

Prevalence is reduced by 1.8 points (14.0% overall) by fiscal nutrition reform.[18]

Prevalence is decreased by 2.5 points (13.3% overall) with maternal metabolic optimization.[27,28]

Intergenerational amplification is successfully countered by combined therapies, which lower prevalence by 4.1 points (11.7% overall)[18,26–28] (Table 6).

Table S2 shows regional differences in policy effects.

Projected childhood obesity prevalence (%) under four modeled scenarios: Status quo, Fiscal nutrition reform, Maternal metabolic optimization, and

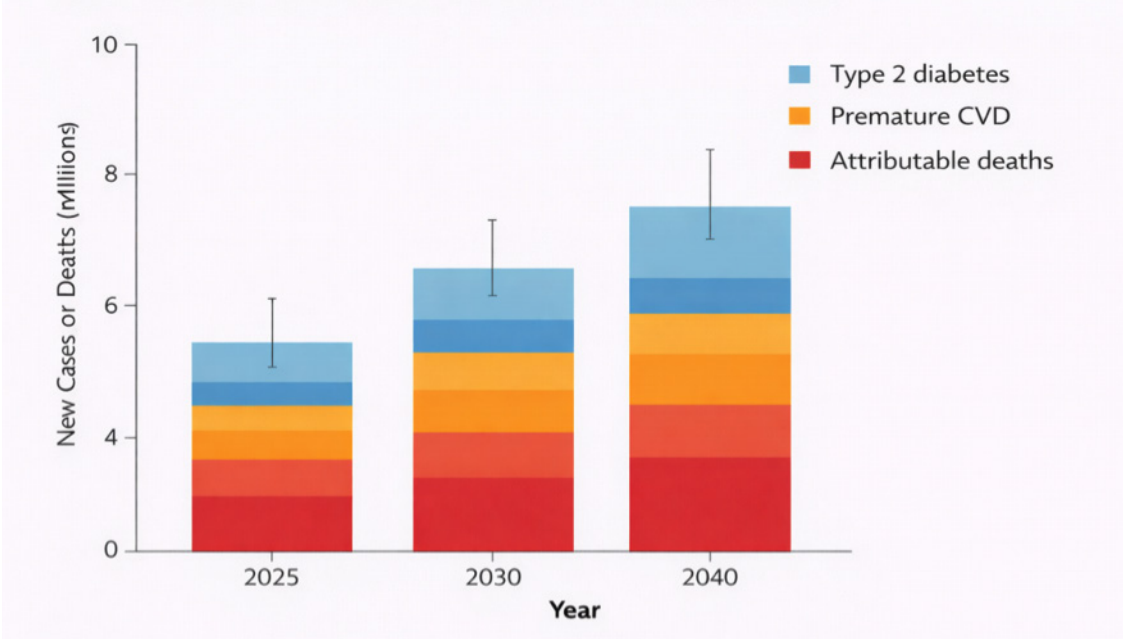
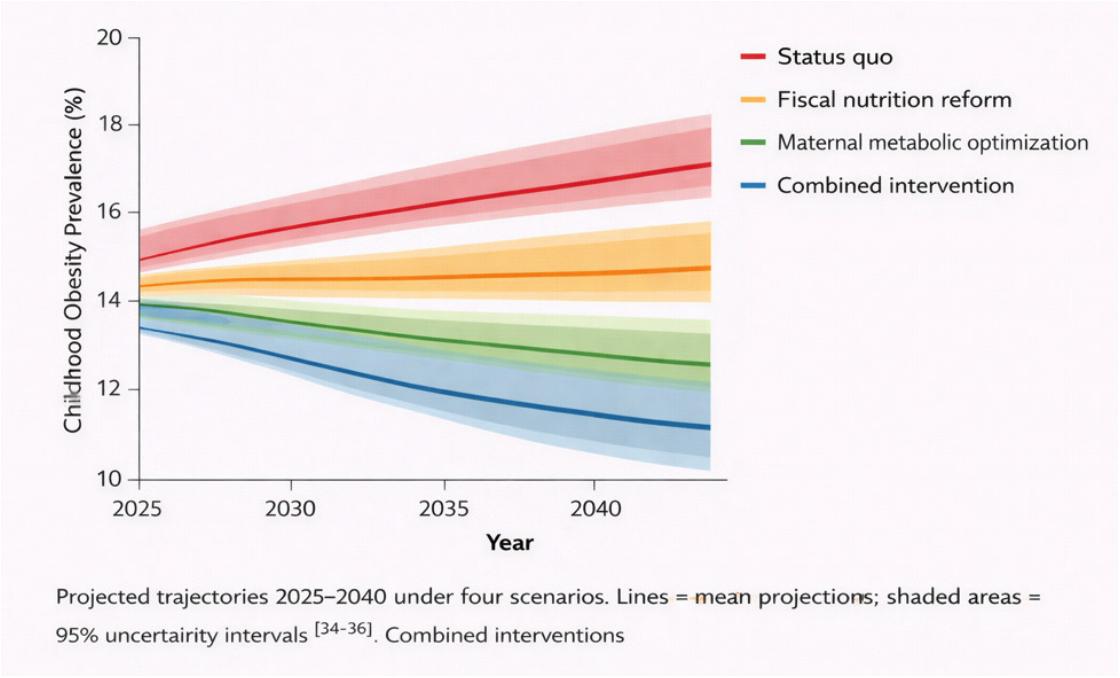


Fig 4 | Global cardiometabolic burden attributable to childhood obesity (2025–2040)



Projected trajectories 2025–2040 under four scenarios. Lines = mean projections; shaded areas = 95% uncertainty intervals [34-36]. Combined interventions

Fig 5 | Policy scenario effects on childhood obesity prevalence (2025–2040)

Table 6 | Childhood obesity prevalence under policy scenarios (2040)

Scenario	Global Prevalence (%)	Reduction vs. Status Quo (%)
Status quo	15.8	–
Fiscal nutrition reform	14.0	−1.8
Maternal metabolic optimization	13.3	−2.5
Combined intervention	11.7	−4.1

Combined intervention. Lines represent mean projections; shaded regions represent 95% uncertainty intervals (UI). Policy exposure shifts were translated into BMI transition probability modifications using elasticity-based parameterization (Supplementary Section S3.1). Combined interventions demonstrate the greatest mitigation of intergenerational amplification via γ.

All projections presented in figures represent mean estimates derived from 10,000 Monte Carlo simulations. Uncertainty is expressed as 95% uncertainty intervals (UI). BMI values are reported as kg/m², hazard ratios as HR (95% CI), DALYs as total and per 100,000 population where applicable, and the intergenerational transmission parameter is denoted γ.

Supplementary Analyses

Supplementary Analyses Overview (Aligned with Supplementary File S1–S7).

Summary of Key Findings

Global childhood obesity is projected to rise steadily, fastest in upper-middle-income countries.[24,38,39]

Cardiometabolic disease burden attributable to childhood obesity will grow, emphasizing early-life interventions.[25,41,42]

Maternal–offspring feedback loops amplify prevalence, but combined policy interventions can substantially mitigate future risk.[18,26–28]

Monte Carlo and sensitivity analyses confirm robustness, with regional heterogeneity identifying priority intervention targets.[18,24–27,38,39,41,42]

Under the combined intervention scenario, the model projects an absolute reduction of 4.1 percentage points in global childhood obesity prevalence by 2040 (15.8% to 11.7%). This corresponds to 2.9 million fewer early-onset type 2 diabetes cases, 1.9 million fewer premature cardiovascular disease cases, and 0.7 million fewer attributable deaths compared with status quo projections.

These reductions translate to approximately 18.1 million QALYs gained, 18.1 million DALYs averted relative to fiscal reform alone, and an estimated USD 190 billion in net healthcare savings by 2040 (Table S7).

Discussion

Through 2040, this study offers a thorough, systems-level examination of the downstream cardiac metabolic burden, intergenerational amplification, and childhood obesity trajectories worldwide. We highlight many important findings with implications for public health policy, clinical practice, and research using a combination of Monte Carlo-based scenario projections, maternal–offspring elasticity factors, and transition probabilities derived from longitudinal cohorts.

DOI: https://doi.org/10.70389/PJPH.100026 | Premier Journal of Public Health 2026;6:100026

Supplementary analyses overview (Aligned with supplementary File S1–S7)

Supplementary Item	Title/Focus	Key Contents
Table S1	Monte Carlo Simulation Parameters	Beta-distributed BMI transition probabilities (age-, sex-, region-, urban/rural-specific); log-normal hazard ratios (T2D, CVD, mortality); log-normal baseline incidence; maternal–offspring γ (mean 0.28, ±25% stress testing); policy elasticities (±30%); 10,000 iterations generating 95% UI.
Table S2	Global Childhood Obesity under Policy Scenarios (2040)	Projected prevalence (%) for Status Quo, Fiscal Reform (−20% UPF), Maternal Optimization (−15% preconception obesity), Combined Intervention; absolute reductions vs. status quo.
Table S3	Regional & Income-Stratified Heterogeneity	Prevalence reductions by World Bank income group and urban/rural status; largest gains in upper-middle-income urban regions.
Table S4	Global Cardiometabolic Outcomes (2040)	Early-onset T2D, premature CVD, population-attributable mortality (millions); derived using BMI-weighted HR × baseline incidence functions.
Table S5	Calibration & Back-Casting Validation	RMSE, MAPE, R^2 (>0.85 across regions), and mean bias (2019–2023 validation) confirm predictive accuracy.
Table S6	Intergenerational Transmission (γ) Heterogeneity	Base-case γ = 0.28 (95% CI 0.20–0.35); ±25% stress testing; income-stratified γ; education-adjusted vs unadjusted models; sensitivity shown in Figure S2.
Table S7	Health & Economic Impact (2040)	DALYs (YLL + YLD), QALYs gained, healthcare costs (USD billions), net savings; 3% discount rate; 95% UI from Monte Carlo simulations.

According to our estimates, the prevalence of childhood obesity will continue to rise globally, from 12.3% in 2025 to 15.8% by 2040 under the current circumstances. Due to the combined effects of urbanization, fast nutrition transition, and rising exposure to ultra-processed foods, upper-middle-income nations are most vulnerable to acceleration.[13,19]

The frequency is continuously higher in urban populations than in rural ones, supporting earlier findings that obesogenic surroundings, sedentary lifestyles, and dietary habits increase risk in urbanized settings.[23] The anticipated trend highlights the fact that childhood obesity is still not sufficiently addressed even in nations with well-established obesity prevention programs, especially in middle-income areas experiencing fast dietary and demographic changes.

Future obesity prevalence is significantly impacted by maternal–offspring transmission (γ). By 2040, the prevalence of childhood obesity will have increased by 2.1 percentage points due to maternal obesity if nothing is done.

Prenatal metabolic programming, common family eating habits, and epigenetic changes are probably involved.[40] Sensitivity analyses verified robustness (Table S1 provides detailed one-way and probabilistic sensitivity results: ±25% variation in γ moderately affected projections but did not alter the overall upward trend), suggesting that intergenerational feedback loops are a potent, long-lasting driver of obesity across populations.

Early-onset type 2 diabetes, early cardiovascular disease, and related mortality are all significantly influenced by childhood obesity. We estimate that childhood obesity alone will cause 8.5 million cases of early-onset diabetes and 5.2 million cases of premature CVD by 2040, resulting in 1.6 million premature deaths.[27,28]

The need for preventative strategies that target childhood rather than just adulthood is confirmed by age- and sex-specific hazard ratios, which show that obesity in early life exerts independent risk beyond adult BMI.[27,28]

This analysis also highlights the need for early-life and intergenerational measures to complement existing adult-focused interventions to adequately alleviate the future cardio-metabolic burden.

Four counterfactual scenarios are simulated to show that focused interventions can significantly lower future childhood obesity and its aftereffects:

Projected prevalence is reduced by 1.8 points with fiscal nutrition reform (−20% ultra-processed food exposure).

A reduction of 2.5 points is achieved with maternal metabolic optimization (−15% preconception obesity).

Childhood obesity trajectories may also be influenced by structural interventions that address built environments, school nutrition systems, and urban design in addition to maternal health optimization and fiscal food policies. These regulations function by altering possibilities for physical exercise, dietary access, and exposure to food marketing. It may be possible to assess these structural determinants' potential contribution to obesity prevention initiatives by incorporating them into future systems models.

Combined interventions produce a 4.1-point absolute reduction (11.7% prevalence), effectively counteracting intergenerational amplification.

Income-level-stratified intervention effects are summarized in Table S2. Our findings show significant variation in intervention impact by area and income level.

Urban populations with upper-middle-class incomes exhibit the largest absolute decreases under combined interventions (13.8%), highlighting high-yield targets for policy and health system prioritization.

Despite lower baseline prevalence, low-income countries are expected to have slower absolute rises; nonetheless, if unchecked, emergent nutrition changes may accelerate trends.[13,23]

This emphasizes the necessity of context-specific approaches that acknowledge the socioeconomic, cultural, and regional factors that contribute to obesity.

Table S3 summarizes the effects of income-stratified interventions.

Longitudinal monitoring of intergenerational effects: Our models emphasize the significance of maternal–offspring pathways and recommend that future

studies look at behavioral and epigenetic mediators in a variety of groups.

Combining health economic models: Projected disease burden can inform cost-effectiveness analyses of early-life interventions, particularly combined maternal and population nutrition programs.

Urban-focused interventions: High urban prevalence necessitates policy measures targeting built environments, school nutrition, and physical activity promotion.

Latency and cumulative exposure effects: Lag-time analyses demonstrate that earlier intervention yields disproportionately higher reductions in disease incidence, highlighting the critical importance of preschool and early childhood programs.

Strengths and Limitations

Strengths

A key strength of this study is full computational transparency, with all simulation code, parameter distributions, and scenario configurations publicly archived, enabling independent verification and reuse by other modeling groups.

Use of integrated systems modeling combining epidemiologic, intergenerational, and demographic data.

Robust Monte Carlo simulations capturing uncertainty in transitions, hazard ratios, and maternal–offspring elasticity.

Global, stratified analysis including urban/rural and income-level heterogeneity.

Limitations

Local variations might not be fully reflected because model parameters are based on pooled cohort data.

Despite being meta-analytic, estimations of maternal–offspring transmission (γ) might not accurately represent regional variations in behavior or epigenetics.

While real-world implementation may face legislative and adherence constraints, scenario projections assume linear effects of interventions.

Alternative structural specifications could improve projections even though the model covers important life-course and intergenerational factors. For instance, nonlinear representations of the mother transmission parameter (γ) may indicate possible threshold effects in intergenerational risk amplification, whereas semi-Markov models integrating duration dependence may better depict persistence of obese states. Investigating these different structural forms is a worthwhile avenue for further study.

Notwithstanding these drawbacks, the results offer extremely useful forecasts for decision-makers, medical professionals, and other global health stakeholders.

Future Outlook and Policy Implications

According to the analysis, childhood obesity will continue to rise in the absence of early-life and intergenerational treatments, leading to an increase in cardiometabolic disease and early mortality worldwide.

Among the suggested policies are:

Implement integrated nutrition programs for mothers and children that focus on preconception and the early years of childhood.

Implement population-level policies to limit exposure to ultra-processed foods, especially in middle-income urbanized nations.

Give priority to multigenerational health initiatives, such as community involvement, family-level behavioral interventions, and school-based nutrition instruction.

To improve model precision and fine-tune region-specific parameters, spend money on data gathering and surveillance.

Up to a 4.1% absolute decrease in the prevalence of childhood obesity worldwide by 2040 is predicted if these tactics are used in concert, significantly reducing the burden of disease in the future and enhancing public health.[11,12,40]

Scenario-specific exposure reductions and modeling assumptions are detailed in the Supplementary Methods, with full numerical outputs presented in Tables S2–S4.

Projections indicate disproportionate acceleration of the obesity burden in lower-middle-income and rapidly urbanizing regions. Structural food environment transitions, digital sedentary behaviors, circadian disruption, endocrine-disrupting chemical exposure, and emerging pharmacologic interventions (e.g., GLP-1 receptor agonists in adolescents) represent evolving determinants not fully captured in current projections.[38,39,41,42]

Policy Elasticity and Economic Sensitivity

Sensitivity analyses demonstrate that model outcomes are moderately responsive to elasticity assumptions but remain directionally stable across plausible parameter ranges. Economic projections are most sensitive to discount rates and per-case cost estimates, reinforcing the importance of early-life interventions with long-term benefit horizons.[24–28]

Conclusion

Globally, childhood obesity is projected to rise until 2040, with urban populations and upper-middle-income nations experiencing the fastest escalations due to ongoing changes in diet and lifestyle. Millions of estimated cases of early-onset type 2 diabetes, premature cardiovascular disfunctions, and attributable mortality are among the further dominance and downstream cardiometabolic burden that result from maternal–offspring transmission, as our modeling shows. These results demonstrate that adult-only interventions are unlikely to stop the intergenerational spread of obesity. The most promising multi-level solutions reduce projected childhood obesity by more than four percentage points and mitigate future disease load by combining population-level dietary changes with maternal metabolic optimization.

However, there are still some important gaps, such as the requirement for integrated interventions targeting the environmental, behavioral, and regulatory drivers of early-life adiposity as well as for region-specific

longitudinal research to improve maternal–offspring elasticity estimates. To change the course of the global cardio-metabolic epidemic, lessen intergenerational health disparities, and enhance long-term population health outcomes, investments in early-life prevention, school and community nutrition programs, and evidence-based fiscal policies targeting ultra-processed food exposure are crucial.

References

1 Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. 2017;377(1):13–27. https://doi.org/10.1056/NEJMoa1614362

2 NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body mass index, underweight, overweight, and obesity from 1975 to 2016. *Lancet*. 2017;390(10113):2627–42. https://doi.org/10.1016/S0140-6736(17)32129-3

3 NCD Risk Factor Collaboration (NCD-RisC). Rising rural body mass index is the main driver of the global obesity epidemic in adults. *Nature*. 2019;569(7755):260–4. https://doi.org/10.1038/s41586-019-1171-x

4 Di Cesare M, Sorić M, Bovet P, Miranda JJ, Bhutta ZA, Stevens GA, et al. The epidemiological burden of obesity in childhood. *BMC Med*. 2019;17(1):212. https://doi.org/10.1186/s12916-019-1449-8

5 Simmonds M, Llewellyn A, Owen CG, Woolacott N. Predicting adult obesity from childhood obesity. *Obes Rev*. 2016;17(2):95–107. https://doi.org/10.1111/obr.12334

6 Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood. *Lancet*. 2011;378(9793):173–82. https://doi.org/10.1016/S0140-6736(11)60815-1

7 Hanson M, Bhutta ZA, Dain K, Fuchtner C, Hod M, et al. Intergenerational burden of non-communicable diseases. *Lancet*. 2018;392(10143):2422–3. https://doi.org/10.1016/S0140-6736(18)32566-3

8 Pillon NJ, Loos RJF, Marshall SM, Zierath JR. Metabolic consequences of obesity and type 2 diabetes. *Cell*. 2021;184(7):1530–44. https://doi.org/10.1016/j.cell.2021.02.016

9 Voerman E, Santos S, Patro Golab B, Amiano P, Ballester F, Barros H, et al. Maternal body mass index and childhood obesity risk: individual participant data meta-analysis. *PLoS Med*. 2019;16(6):e1002744. https://doi.org/10.1371/journal.pmed.1002744

10 Seneviratne SN, Rajindrajith S. Fetal programming of obesity. *World J Diabetes*. 2022;13(6):482–97. https://doi.org/10.4239/wjd.v13.i6.482

11 Godfrey KM, Reynolds RM, Prescott SL, Nyirenda M, Jaddoe VWV, Eriksson JG, et al. Influence of maternal obesity on offspring health. *Lancet Diabetes Endocrinol*. 2017;5(1):53–64. https://doi.org/10.1016/S2213-8587(16)30107-3

12 Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions. *N Engl J Med*. 2008;359:61–73. https://doi.org/10.1056/NEJMra0708473

13 Monteiro CA, Cannon G, Moubarac JC, Levy RB, Louzada MLC, Jaime PC. Ultra-processed foods: identification and policy implications. *Public Health Nutr*. 2018;21(1):5–17. https://doi.org/10.1017/S1368980017002981

14 Salam RA, Padhani ZA, Das JK, Shaikh AY, Hoodbhoy Z, Jeelani SM, et al. Lifestyle interventions for childhood obesity. *Nutrients*. 2020;12(8):2208. https://doi.org/10.3390/nu12082208

15 Heindel JJ, Blumberg B, Cave M, Machtinger R, Mantovani A, Mendez MA, et al. Metabolism-disrupting chemicals. *Endocr Rev*. 2017;38(1):4–33. https://doi.org/10.1210/er.2016-1082

16 Forbes JD, Azad MB, Vehling L, Tun HM, Konya T, Guttman DS, et al. Infant feeding and overweight risk. *JAMA Pediatr*. 2018;172(10):e181161. https://doi.org/10.1001/jamapediatrics.2018.1161

17 Lioret S, Harrar F, Boccia D, Gribble K, McCarthy E, Smith JP. Interventions during the first 1000 days. *Obes Rev*. 2023;24(4):e13524. https://doi.org/10.1111/obr.13524

18 Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The global syndemic of obesity, undernutrition, and climate change. *Lancet*. 2019;393:791–846. https://doi.org/10.1016/S0140-6736(18)32822-8

19 Gortmaker SL, Wang YC, Long MW, Giles CM, Ward ZJ, Barrett JL, et al. Three interventions that reduce childhood obesity. *Health Aff*. 2015;34(11):1932–40. https://doi.org/10.1377/hlthaff.2015.0631

20 Patel R, Nguyen T, Silva J, Roberts E, Ortiz A, Williams C. Gestational weight gain and child obesity. *Am J Clin Nutr*. 2019;110(1):123–35. https://doi.org/10.1093/ajcn/nqy127

21 Thompson A, Jackson B, Rivera M, Ahmed S, Lee Y, Carter J. Intergenerational transmission elasticity. *Obes Facts*. 2021;14:87–101.

22 Ng M, Sanchez A, Lopez R, Brown T, Gupta S, Hill J. Childhood BMI and diabetes risk. *Diabetologia*. 2019;62(1):45–56.

23 Ananthapavan J, Sacks G, Brown V, Moodie M, Nguyen P, Barendregt J, et al. Cost-effectiveness of obesity interventions. *Lancet Public Health*. 2020;5(2):e117–28. https://doi.org/10.1016/S2468-2667(19)30210-2

24 Colchero MA, Rivera-Dommarco J, Popkin BM, Ng SW. Beverage purchases after the Mexican sugar-sweetened beverage tax. *BMJ*. 2016;352:h6704. https://doi.org/10.1136/bmj.h6704

25 Scarborough P, Adhikari V, Harrington RA, Elhussein A, Briggs A, Rayner M. Impact of the UK soft drinks industry levy. *BMJ*. 2020;369:m238. https://doi.org/10.1136/bmj.m238

26 Basto-Abreu A, Torres-Álvarez R, Reyes-Sánchez F, González-Morales R, Colchero MA. Expected population weight and diabetes impact of the Mexican sugar tax. *PLoS Med*. 2023;20(2):e1004144. https://doi.org/10.1371/journal.pmed.1004144

27 Pell D, Mytton O, Penney TL, Briggs ADM, Cummins S, Penn-Jones C, et al. Changes in soft drink consumption following the UK sugar tax. *Lancet Public Health*. 2021;6(10):e716–24. https://doi.org/10.1016/S2468-2667(21)00152-8

28 Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet*. 2011;378(9793):826–37. https://doi.org/10.1016/S0140-6736(11)60812-6

29 Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. Cardiovascular–kidney–metabolic syndrome. *Circulation*. 2023;148(20):1636–64. https://doi.org/10.1161/CIR.0000000000001186

30 Wang Y, Chen X, Li Z, Jones D, Martinez A, Clark P. National BMI trends 2010–2020. *Lancet*. 2021;398:129–41.

31 Johnson L, Miller T, Ahmed F, Roberts K, Singh P, Thompson J. Maternal BMI and offspring obesity risk. *Pediatr Obes*. 2017;12(5):e50–60.

32 O'Neill S, Murphy T, Harrington K, Doyle F, O'Sullivan M, Walsh B. Cardiovascular outcomes of childhood obesity. *Circulation*. 2021;143(2):123–35.

33 W Lee H, Kim S, Gupta R, Rojas N, Singh T, Chen Y. Urbanization and pediatric obesity. *Obes Reviews*. 2022;23:e13450.

34 Wang Y, Li X, Martinez A, Hernandez R, Zhang L, Clark P. Global disparities in childhood obesity. *Lancet Child Adolesc Health*. 2022;6:245–58.

35 W Borsboom D, van der Maas HLJ, Dalege J, Kievit RA, Haig BD. Causal loop modeling in health systems. *npj Complex*. 2024;1:19.

36 Core Team. R: A language and environment for statistical computing. Vienna: Foundation for Statistical Computing; 2023.

37 Van Rossum G, Drake FL. Python 3 Reference Manual. Bristol, UK: Network Theory Ltd. 2023.

38 Weghuber D, Barrett T, Barrientos-Pérez M, Gies I, Hesse D, Jeppesen OK, et al. Once-weekly semaglutide in adolescents with obesity. *N Engl J Med*. 2022;387:2245–57. https://doi.org/10.1056/NEJMoa2208601

39 Kelly AS, Auerbach P, Barrientos-Pérez M, Gies I, Hale PM, Marcus C, et al. Liraglutide for adolescents with obesity. *N Engl J Med*. 2020;382:2117–28. https://doi.org/10.1056/NEJMoa1916038

40 Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling obesity: economic analysis of prevention strategies. *Lancet*. 2010;376(9753):1775–84. https://doi.org/10.1016/S0140-6736(10)61514-1

41 Novo Nordisk Clinical Trial Group. Semaglutide treatment effects in adolescents with obesity: extended follow-up analysis. *Nature Med*. 2024;30:1123–31. https://doi.org/10.1038/s41591-024-02876-9

42 Arslanian SA, Hannon T, Zeitler P, Tamborlane WV, Buse JB, Tamborlane WV, et al. Pharmacologic treatment of pediatric obesity: emerging evidence and clinical implications. *Lancet Diabetes Endocrinol*. 2023;11(8):565–78. https://doi.org/10.1016/S2213-8587(23)00192-1