Supplementary Materials

Premature Mortality Attributable to Ultra-Processed Foods in the Eight Countries

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Text A. Data sources and modelling steps

Baseline food consumption

The food recall data for the adults from, each country were collected from the most recent national dietary surveys: POF, 2017-18 (Brazil), NHANES, 2017-18 (United States), NDNS, 2018-19 (United Kingdom), CCHS-Nutrition, 2015 (Canada), ENSANUT, 2016 (Mexico), ENSIN, 2015 (Colombia), ENCA, 2010 (Chile) and NNPAS, 2011-12 (Australia).

The data on the foodstuffs were divided into different groups in each survey. Based on this division and after being converted into energy, the records were reunited in the food groups according to the NOVA food classification: *in natura* and minimally processed foods, processed culinary ingredients, processed foods and ultra-processed foods.

Text B

Comparative risk assessment analysis

The comparative risk assessment model was developed and validated for estimating the impact of ultra-processed food consumption on all-cause mortality. The model can be adapted to different countries using similar inputs to specific realities (population, mortality and food consumption). By addressing all-cause mortality, the model is intended to estimate the total burden of ultra-processed foods and support research on food policies intended to reduce ultra-processed food consumption and compare different scenarios of changes in diet.

The first step of the modeling is to estimate the estimated relative risks for all-cause mortality within each sex-and-age-stratum assuming that the equivalent to the theoretical minimum risk exposure level for ultra-processed foods consumption would be zero and considering discrete intervals of 0.1% of contribution of ultra-processed foods to total energy intake from 0.0% (RR=1.00) to 100% (RR=1.27), based on the summary relative risk from our new meta-analysis.

Then, similarly to other validated macrosimulation models that address dietary risk factors [4], we modelled the distribution of UPF consumption using a log-linear function for the mean contribution of ultra-processed foods to total energy intake of the diet and its standard deviation and the national population (Table F).

Based on these intermediate outputs of the model, we calculated the estimated population attributable fraction (PAF) for mortality outcome (o) in each age group (a) and sex (s) stratum for each counterfactual scenario through the following formula:

$$PAF_{oas} = \frac{\int_{x=0}^{m} RR_{oa}(x)P_{as}(x)dx - \int_{x=0}^{m} RR_{oa}(x)P'_{as}(x)dx}{\int_{x=0}^{m} RR_{oa}(x)P_{as}(x)dx}$$

Where: Pas(x) and P'as(x) are the UPF intake distributions at the baseline and in the counterfactual scenario, respectively. RRoa(x) is the relative risk for all-cause mortality (outcome o) as a function of UPF participation in the energy of the diet, according to age group.

We utilized estimates of the total number of deaths in each country based on national official records. The averted deaths in each counterfactual scenario were computed by multiplying an age- and sex specific PAF by the baseline total number of deaths for the same stratum. For each scenario, the model generated the total numbers of deaths prevented or postponed as outputs.

As modeled estimations of the impact of ultra-processed food consumption, the results were presented for adults aged 30 to 79 years for 2019, rounded to 2 significant digits (uncertainty intervals, UI 95%, were not rounded). The outcomes for individuals with less than 30 years of age were excluded from the analysis because of the possible lag-time between changing dietary risk factors, such as UPF intake, and disease outcomes and excluded the individuals over 70 years of age to account only for the premature deaths attributable to UPF intake.

Considering the uncertainty of outcomes in the model, probabilistic sensitivity analysis is recommended to explore the potential effects of reducing ultra-processed food consumption on all-cause mortality. Probabilistic sensitivity analysis requires a stochastic (random) variation of parameters based on the sizes of the effects obtained from the literature, as using Monte Carlo simulations. By using this methodology, the model results are recalculated iteratively and uncertainty intervals of 95% (UI 95%) are generated for the median using the bootstrap percentile method.

The parameter uncertainty in all modelled estimates was quantified using Monte Carlo iterations with the Ersatz program (n = 5,000). For each simulation, the simulation works thorough producing a draw from the distributions of a) baseline contribution of ultra-processed foods to total energy intake of the diet, b) the relative risks of UPF intake and all-cause mortality, c) the current number of deaths. Each set of draws were used to calculate PIF and averted events of each outcome for each age-sex stratum and results were reported for the 50th, 2.5th and 97.5th percentiles of estimates across all simulations as the central estimate and 95% uncertainty intervals (UI), respectively.

Finally, we analyzed the model development and its inputs using the STREAMS-P tool, that provides guidelines on a standardized approach for assessing and reporting how methodological decisions that might affect the validity of the estimates. The information of the analysis is summarized in Supplementary Table J.

Table A. Modelling input parameters

Model inputs	**Relative risk**	**Source**
Baseline characteristics		
Demographics		National oficial records
Deaths		Global Burden of Disease Study
Consumption of ultra-processed foods		National Dietary Surveys
Relative risks of all-cause mortality for each 10% increase in the % of UPF intake	1.027 (1.017-1.037)	New meta-analysis

Table B. Key assumptions and restrictions of the model that estimates the impact of ultra-processed food consumption on all-cause mortality.

Category	Assumption/Restriction	Motivation
Ultra-processed food consumption	Log-linear distribution of UPFconsumption by age and sex groups.	Prior literature for dietary risk factor models [46].
Comparative risk assessment	The analysis of all-cause mortality encompasses the overall burden of this risk factor but does not disentangle the causes of death.	Consistent with previous studies on attributable all-cause mortality [10111213]
	The theoretical minimum risk exposure level for ultra-processed foods consumption is zero	Prior literature have not reported an association of ultra-processed foods and beneficial health outcomes [14]
	All beneficial effects on health (all-cause mortality) are related to reducing the consumption of ultra-processed foods.	Conservatively, we did not consider potential benefits on all-cause mortality of replacing ultra-processed foods with fresh and minimally processed foods, increasing fibre, fruit, and vegetable intake, for example.
	The risk of all-cause mortality follows a log-linear dose-response to the contribution of ultra-processed foods to total energy intake.	Consistent with previous validated risk assessment models with other dietary risk factors [46].
	The reduction in ultra-processed food consumption and benefits on health and all-cause mortality are assumed to be concurrent.	Consistent with previous macrosimulation studies for other dietary risk factors [159].

Table C. Application of the STREAMS-P tool[17] for assessing and reporting how methodological decisions were made in the development and validation of the model.

Section	Item should be present	
Title and abstract	Risk/s factor/s under study	Page 1-2
	Country or area under study	Page 1-2
	Age range under study	Yes
	Information about the methodology	Page 1-2
Introduction/ Objectives	Risk(s) factor(s) under study	Page 3-4
	Key aspects of the population: location and year of study	Page 3-4
Methods		
Methodology	Main characteristics of applied method	Page 4-5
Observed mortality	Cause(s) and the International Classification of Diseases (ICD) Code	Yes
	Causal, causal/suggested, all-causes approach	Page 4-5
	Underlying/contributory causes of death	No
	Age range studied	Yes
	Year/s of mortality data	Yes
	Data sources (whether registry-based or not)	Page 4-5
	Include the proportion of deaths in the category known as "garbage codes"	No
Prevalence	Data source (representativeness, response rate and year of study)	Page 5
	Definition of the categories of exposure	No
	Self-reported vs. objective measures	Page 5
	Describes choice of groupings by category of exposure	No
	Age-dependent categories of exposure	Page 5
	Considers intensity of exposure	Yes
	Considers duration of exposure	No
	Uses a correction factor (if necessary)	NA
Risks	Data source, including sample size, place and date of study	Page 5
	Age-group specific risks (if necessary)	No
	The impact of the adjustment for potential confounders	No
Results	Observed mortality figures	Page 5
	Attributed mortality figures taking into consideration selected groupings	Page 5
	Population attributable fractions in selected groupings	Page 5
	Prevalence and their precision (eg, 95% confidence intervals) as handled in the analyses.	Yes
	Risk values and their precision (eg, 95% confidence intervals) as handled in the analyses.	Yes
	Attributed mortality precision (eg, 95% confidence intervals)	Yes (Table 2)
	Sensitivity analysis	No (provided in previous paper on the model)

Discussion	Statement on prevalence employed	Yes
	Prevalence correction (if applied)	NA
	Statement on the risks employed	Yes
	Statement on the observed mortality employed and its validity	Yes
	Statement on the strength of evidence regarding the exposure-risk association	Page 7-8