research

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Reasons to avoid ultra-processed foods

ORIGINAL RESEARCH Umbrella review of epidemiological meta-analyses

Ultra-processed food exposure and adverse health outcomes

Lane MM, Gamage E, Du S, et al

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Study question Is higher dietary exposure to ultra-processed foods associated with adverse health outcomes?

Methods This systematic umbrella review analysed 45 pooled analyses (n=9 888 373 participants) that investigated the relation between exposure to ultra-processed food and various health outcomes. Data were sourced from Medline, PsycINFO, Embase, and the Cochrane Database of Systematic Reviews, spanning 2009 to June 2023. The credibility of evidence was evaluated using evidence classification criteria, and the quality of evidence was assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Study answer and limitations Exposure to ultra-processed food was directly associated with 32 (71%) health parameters, including mortality and physical (for example, cancer) and mental health (for example, depression) outcomes. Convincing evidence supported links to incident cardiovascular disease related mortality (risk ratio 1.50, 95% confidence interval 1.37 to 1.63) and type 2 diabetes (dose-response risk ratio 1.12, 1.11 to 1.13), as well as prevalent common mental disorder outcomes (anxiety: odds ratio, 95% confidence interval 1.48,

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Multiple meta-analyses have aimed to consolidate original epidemiological research investigating associations between ultra-processed food and adverse health outcomes
- However, no comprehensive umbrella review has been conducted to provide a broad perspective and evaluate the meta-analytical evidence in this area

WHAT THIS STUDY ADDS

- This umbrella review found consistent evidence of a higher risk of adverse health outcomes associated with greater ultra-processed food exposure
- Convincing and highly suggestive evidence (classes I and II) related to early death and adverse cardiometabolic and mental health outcomes
- These findings support urgent mechanistic research and public health actions that seek to target and minimise ultra-processed food consumption for improved population health

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1.37 to 1.59; combined disorders: 1.53, 1.43 to 1.63). Highly suggestive evidence indicated associations with incident all cause mortality, heart disease related mortality, type 2 diabetes, and depressive outcomes, as well as prevalent adverse sleep related outcomes, wheezing, and obesity. Limitations include the high level of overview of umbrella reviews, such that specific confounder or mediator adjustments and sensitivity analyses were not considered in this study; potential confounding related to overall dietary patterns; and variations in assessment methods for ultra-processed food intake.

What this study adds Higher exposure to ultra-processed foods was associated with higher risks of cardiometabolic, common mental disorder, and mortality outcomes. The study underscores the necessity for population based measures to reduce dietary exposure to enhance human health.

It is now time for United Nations agencies, with member states, to develop and implement a framework convention on ultra-processed foods analogous to the framework on tobacco

COMMENTARY Ultra-processed foods damage health and shorten life

Hundreds of epidemiological studies and meta-analyses have reported associations between ultra-processed food consumption and adverse health outcomes. In their paper, Lane and colleagues have now carefully reviewed the evidence from 45 meta-analyses encompassing almost 10 million participants.[1]

They found direct associations between exposure to ultra-processed foods and 32 health parameters, including mortality, cancer, and mental, respiratory, cardiovascular, gastrointestinal, and metabolic ill health. For instance, a pooled analysis of seven cohorts showed a 10% increase in ultra-processed food consumption to be associated with a 12% (95% confidence interval 1.11 to 1.13) higher incidence of type 2 diabetes.

The quality of the evidence was strong for all cause mortality, obesity, and type 2 diabetes (this evidence was rated as of moderate quality using the GRADE system, which initially considers all observational studies as low quality evidence). Overall, the authors found that diets high in ultra-processed food may be harmful to most—perhaps all—body systems.

What makes these foods harmful?

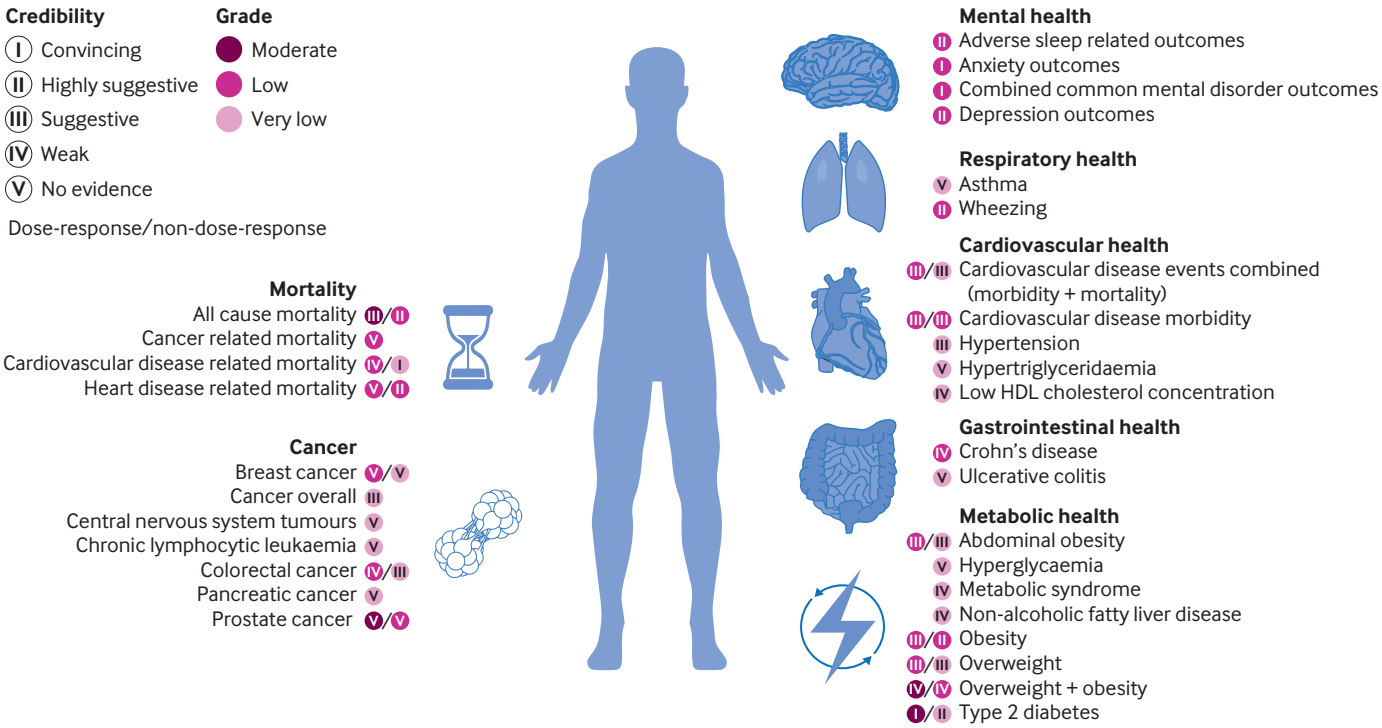
Ultra-processed foods are not merely modified foods. As defined by the Nova classification,[2] they are formulations of often chemically manipulated cheap ingredients such as modified starches, sugars, oils, fats, and protein isolates, with little if any whole food added, made palatable and attractive by using combinations of flavours, colours, emulsifiers, thickeners, and other additives. No reason exists to believe that humans can fully adapt to these products. The body may react to them as useless or harmful, so its systems may become impaired or damaged, depending on their vulnerability and the amount of ultra-processed food consumed.

Lane and colleagues call for more mechanistic research to identify how consumption of ultra-processed food harms health.[1] This does not mean that public policies and actions should be delayed. As these authors acknowledge, multiple mechanisms, likely acting in combination, are plausible.

The grossly imbalanced composition of ultra-processed foods means that their increased intake makes diets energy dense, high in sugar and saturated fat, and low in protein, fibre, micronutrients, and health protective phytochemicals such as flavonoids and phytoestrogens.[3-5] They also contain additives, including colours, emulsifiers, and sweeteners, linked by experimental and epidemiological evidence to imbalances in gut microbiota and systemic inflammation.[1]

Techniques often used, such as extrusion and intense heat, degrade the natural food matrix causing loss of nutrients,[6] disturbances in food digestibility and nutrient bioavailability,[7] and reduction of satiety.[8] They also make ultra-processed food soft, which shortens chewing and

Carlos A Monteiro carlosam@usp.br
Eurídice Martínez-Steele
Geoffrey Cannon
See bmj.com for author details



Credibility and GRADE (Grading of Recommendations Assessment, Development and Evaluation) ratings for associations between greater exposure to ultra-processed foods and risks of each adverse health outcome. HDL=high density lipoprotein

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No funding. For competing interests see full article on bmj.com. Additional data are available on the GitHub repository for the R statistical package metaumbrella at https://github.com/cran/metaumbrella, with raw data on the Open Science Framework at https://osf.io/8j2gt/ and a coding guide provided as a data supplement.

Systematic review registration PROSPERO CRD42023412732.

swallowing time and increases energy intake.[9] Consumption of these foods has also been associated with increased concentrations of acrylamide and phthalates in the blood or urine; these are toxins created during processing or released from packaging materials, respectively.[10 11]

Ultra-processed foods are engineered to be highly desirable, combining sugar, fat, and salt to maximise reward,[12 13] and adding flavours that induce eating when not hungry.[14] Many are addictive, judged by the standards set for tobacco products,[15] and aggressively marketed with meal deals, super sizing, and advertising.

What should be done?

What can be done to control and reduce production and consumption of ultra-processed food, which is rising worldwide?[16] Reformulation does not eliminate harm,[17] and profitability discourages manufacturers from switching to make nutritious foods. Moreover, the investment management companies that increasingly dominate corporate shareholdings would likely resist any such change.[18]

Corporations should be required to explain publicly how products are made and to give evidence

Therefore, public policies and actions are essential. These include national dietary guidelines that recommend varieties of unprocessed or minimally processed foods and freshly prepared meals and avoidance of ultra-processed foods[19]; institutional food procurement that aligns with these guidelines; front-of-pack labels that clearly identify ultra-processed foods; restricting advertising and prohibiting sales in or near schools and hospitals; and fiscal measures that make unprocessed or minimally processed foods and freshly prepared meals as accessible and available as, and cheaper than, ultra-processed foods.

Importantly, smallholders, family farmers, and independent businesses that grow, make, and sell unprocessed or minimally processed foods should be recognised, supported, and fully represented in all policy making and its monitoring. Conversely, corporations responsible for ultra-processed foods should be required to explain publicly how their products are made and to give evidence to but not be represented on policy making bodies.

It is now time for United Nations agencies, with member states, to develop and implement a framework convention on ultra-processed foods analogous to the framework on tobacco. These agencies also have an important role in publishing, publicising, and promoting examples of best practice.

Finally, multidisciplinary investigations are needed to identify the most effective ways to control and reduce ultra-processing and to quantify and track the cost-benefits and other effects of all such policies and actions on human health and welfare, society, culture, employment, and the environment.

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Added benefit and revenues of oncology drugs approved by the European Medicines Agency between 1995 and 2020

Brinkhuis F, Goettsch WG, Mantel-Teeuwisse AK, Bloem LT

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Study question How does the added benefit compare with the revenues of oncology drugs approved by the European Medicines Agency between 1995 and 2020?

Methods Added benefit was evaluated using ratings published by seven organisations: health technology assessment agencies from the US, France, Germany, and Italy, two medical oncology societies, and a drug bulletin. All retrieved ratings were recategorised using a four point ranking scale to indicate negative or non-quantifiable, minor, substantial, or major added benefit. Revenue data were obtained from publicly available financial reports and compared with published estimates of research and development (R&D) costs. Finally, the association between added benefit and revenue was evaluated. Discrepancies in added benefit and revenues were also analysed across various regulatory pathways of the European Medicines Agency—standard marketing authorisation, conditional marketing authorisation, and authorisation under exceptional circumstances.

Study answer and limitations 131 oncology drugs with 166 indications (oncology drugs can be approved and used for several indications) were evaluated for their added benefit by at least one organisation within the required timeframe, yielding a total of 458 added benefit ratings. Many of these drugs, particularly those approved through expedited regulatory pathways, were reported to offer minimal or no added benefit, with 41% (189 of 458) of the added benefit ratings being negative or non-quantifiable. Drug revenues were in line with added benefit, and most drugs, including those with minimal or no added benefit, recovered estimated R&D costs (£535m, adjusted to 2020 values) in a relatively short timeframe (median time three years); 50 of 55 (91%) drugs recovered these costs within eight years. Drugs with higher added benefit ratings generally had greater revenues. Negative or non-quantifiable added benefit ratings were more frequent for conditional marketing authorisations and authorisations under exceptional circumstances than for standard marketing authorisations (relative risk 1.53, 95% confidence interval 1.23 to 1.89). Conditional marketing authorisations generated lower revenues and took longer to offset R&D costs than standard marketing authorisations (four years compared with three years). The study was limited because patient population sizes were not considered and generalised estimates of R&D costs were used.

What this study adds Oncology drugs approved by the European Medicines Agency between 1995 and 2020 seemed to recover R&D costs effectively, irrespective of their added benefit.

Funding, competing interests, and data sharing
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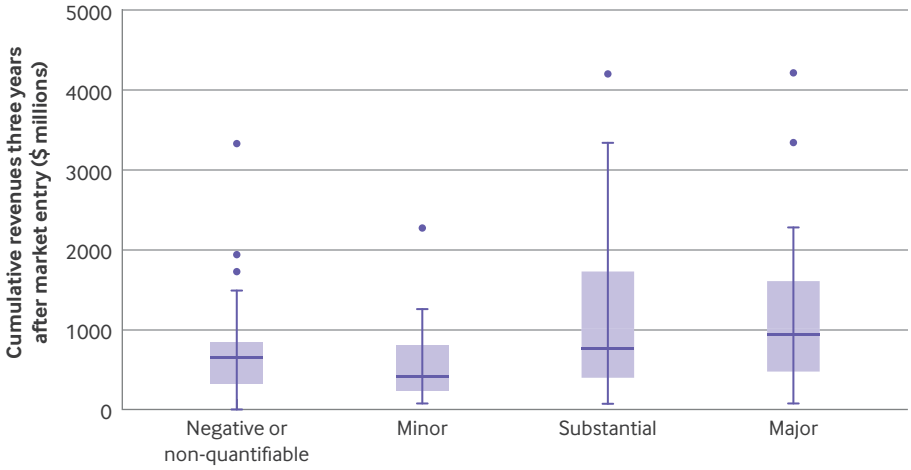

Boxplots (median, maximum, minimum, upper and lower quartile) showing cumulative revenues three years after market entry for oncology drugs that received ratings of negative or non-quantifiable (n=50), minor (n=32), substantial (n=38), or major (n=29) added benefit (149 added benefit ratings for 43 drugs). Dots represent outliers. $1=£0.782, adjusted to 2020 values

Most drugs, including those with minimal or no added benefit, recovered estimated R&D costs