

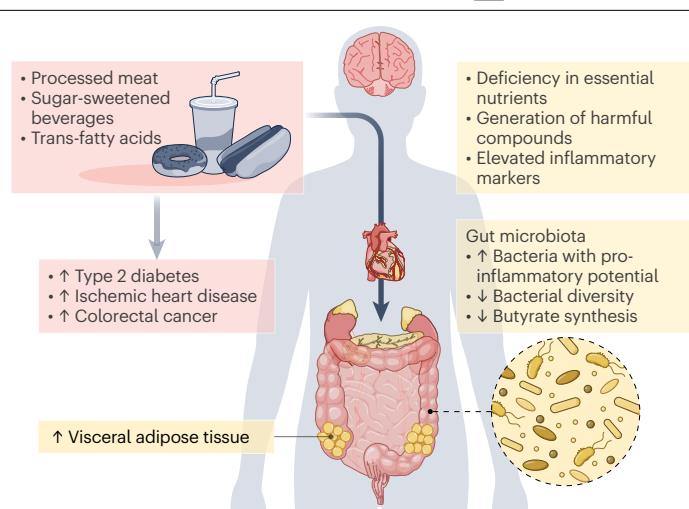
# Updating the evidence on ultra-processed foods and health

Wanglong Gou & Ju-Sheng Zheng

A new analysis supports dietary guidelines to reduce the consumption of processed meat, sugar-sweetened beverages and trans-fatty acids – highlighting the need for a collaborative, meticulous health assessment framework for ultra-processed foods.

In modern society, almost all foods undergo some degree of processing, but characterizing the health effects of food processing has proven a challenging and complex task. According to the most widely used assessment, the NOVA food classification system, foods are categorized into four groups by their level of processing, with the highest level designated as ultra-processed foods (UPFs)<sup>1</sup>. UPFs are characterized as formulation ingredients, primarily of exclusive industrial use, that are typically created through a series of industrial techniques and processes—including a broad range of ready-to-eat products. In recent decades, there has been a substantial expansion in the types, quantities and widespread availability of UPFs globally<sup>2</sup>. Given the transition to a more processed global diet, the health consequences of UPF consumption are attracting enormous interest from the public and the scientific community. In this issue of *Nature Medicine*, Haile et al.<sup>3</sup> performed an updated assessment of the health effects of three major components of UPFs: processed meat, sugar-sweetened beverages (SSBs) and trans-fatty acids (TFAs).

Nutritional research in diverse human populations has faced challenges related to dietary measurement error and residual confounding, leading to between-study heterogeneity and inconsistent findings. Robust analytical approaches and large sample sizes are needed to address these challenges: for example, to assess the association between processed meat and type 2 diabetes, Haile et al.<sup>3</sup> included 15 global cohorts covering participants from the USA, Europe and several Asian countries. Moreover, quantification of the nonlinear relationship between diet and disease is important for making dietary recommendations, even for well-established risk factors, such as SSB and TFA consumption. The recently developed Burden of Proof meta-regression framework<sup>4</sup>, as applied by Haile et al.<sup>3</sup> and in several previous studies, could help provide a more accurate summary of the (nonlinear) relationship between diet and diseases, and provides a star rating system for cross-study comparison and interpretation<sup>4–6</sup>. Haile et al.<sup>3</sup> applied this method to assess the health effect of three important UPF components, providing cutting-edge evidence of the health impacts of these dietary factors. Their results show that higher consumption of processed meat and SSBs is associated with a higher risk of type 2 diabetes, and higher consumption of SSBs and TFAs is associated with higher risk of ischemic heart disease. Moreover, the authors found a positive association between processed meat intake and colorectal cancer risk.



**Fig. 1 | Potential mechanisms linking UPFs with adverse health outcomes.**

Key components of UPFs, such as processed meat, sugar-sweetened products and TFAs, are associated with increased risks of type 2 diabetes, ischemic heart disease and colorectal cancer. The underlying mechanisms include the generation of harmful compounds, increased levels of inflammatory markers, visceral adipose tissue accumulation and disruptions of the gut microbiome.

There has been an ongoing debate regarding the health effects of unprocessed and processed meat consumption. A prior burden-of-proof study<sup>6</sup> suggested that there was weak and insufficient evidence to make recommendations of limiting unprocessed meat intake. Nevertheless, the results are more conclusive for processed meat, as indicated in the present study<sup>3</sup>, highlighting the harmful impact of processed meat on the risks of type 2 diabetes and colorectal cancer. Processed meat is characterized by low levels of essential nutrients and high levels of sodium, saturated fat and heme iron. Moreover, processed meat often contains additives and preservatives that may contribute to its adverse health impacts (Fig. 1).

SSBs are the leading sources of added sugars in the diet and have long been recognized for their effect on weight gain and obesity, as evidenced by epidemiological studies<sup>7</sup>. More recently, accumulating evidence shows positive associations of SSBs with type 2 diabetes, cardiovascular diseases and other chronic diseases<sup>7</sup>. The mechanisms underlying these associations involve increased levels of inflammatory markers and accumulation of visceral adipose tissue with high consumption of SSBs (Fig. 1). On top of the prior evidence, the study from Haile et al.<sup>3</sup> shows a monotonic risk curve for higher SSB consumption and higher risk of type 2 diabetes, indicating that even small amounts of SSB consumption would cause a potentially harmful increase in risk. These results further support the promotion of SSB levies by the World Health Organization (WHO) and by many countries in Europe and North America<sup>8</sup>.

TFAs are mainly produced industrially by the partial hydrogenation of liquid oils, but they also occur naturally in some meat and dairy products. TFAs could increase blood levels of 'bad' (LDL) cholesterol, thereby increasing the risk of cardiovascular diseases<sup>9</sup>. Limiting the use of TFAs to a very small proportion of the diet is widely recommended in many countries. The WHO recommends limiting total TFAs to <1% of total energy intake and has provided a detailed recommendation and guideline for the elimination of TFAs in low- and middle-income countries, many of which have high rates of TFA-attributable deaths and limited restrictions on their use<sup>10</sup>. The updated results from the new meta-regression study conducted by Haile et al.<sup>3</sup> reaffirm the strong dose-response link between TFAs and heart disease, supporting the ongoing global efforts to ban or substantially reduce the use of TFAs in food products.

An increasing body of research underscores the direct harmful impacts of UPFs on health outcomes<sup>11</sup>. In regard to underlying mechanisms, recent studies suggest that UPFs can negatively affect gut microbiome health by increasing the abundance of pro-inflammatory bacteria and reducing bacterial diversity<sup>12</sup>. These alterations can, in turn, have an adverse effect on host health (Fig. 1). However, this is not without controversy. Many UPFs and related products are produced with a long shelf life, which may have a positive impact on local food security and accessibility for some countries or regions with limited access to fresh foods. Moreover, these processed foods may have numerous other potential benefits, such as microbial safety and variety. Therefore, it is important to consider both the benefits and the drawbacks of UPFs through integrated, balanced and sustainable strategies.

Despite the complex nature and background of the UPF research field, establishing a meticulous health assessment framework for UPFs and their major components (such as processed meat, SSBs and TFAs) is a high priority. The study by Haile et al.<sup>3</sup> serves as an exemplar in this respect. Moving forward, additional research is essential to fully depict

the evidence landscape regarding the health impacts of UPFs. A more comprehensive understanding and risk assessment of UPFs will not be achieved without collective efforts and collaborations among policy-makers, consumers, the food industry and public health researchers.

**Wanglong Gou<sup>1,2</sup> & Ju-Sheng Zheng<sup>1,2,3</sup>✉**

<sup>1</sup>Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Hangzhou, China. <sup>2</sup>Westlake Laboratory of Life Sciences and Biomedicine, Hangzhou, China. <sup>3</sup>Zhejiang Key Laboratory of Multi-Omics in Infection and Immunity, School of Medicine and School of Life Sciences, Westlake University, Hangzhou, China.

✉e-mail: zhengjusheng@westlake.edu.cn

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## Competing interests

The authors declare no competing interests.