

It's definitely time to consider diet in its ultra-processing form as a major risk factor for thrombotic vascular disorders

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Shuai Yuan *et al.* recently examined whether ultra-processed food (UPF) intake is associated with an increased risk of venous thromboembolism (VTE).¹ To accomplish this, they longitudinally analysed data on 186,323 participants free of VTE at baseline from the larger UK Biobank cohort, with a total of 4235 incident VTE cases recorded after a 10.5-year follow-up. After adjusting for known risk factors, results showed that a higher UPF intake was associated with 10% to 21% increased risk of VTE.

In most countries, VTE is one of the most common vascular diseases, and its incidence is estimated to be ~1-2 per 1000 per-

son-years in Europe and the USA, respectively, varying widely by age, sex, race and medical conditions.²

Unprovoked VTE, which occurs in the absence of triggering factors such as immobilization, trauma, surgery, cancer or hospitalization,² could be theoretically avoided through lifestyle choices, such as absence of smoking and having a healthy body weight.³

A number of studies have also examined the potential role of diet quality on VTE risk, but failed to provide robust evidence;⁴ some randomized controlled trials and cohort studies indicated that diets rich in fruits and vegetables, moderate alcohol, vitamin E, vitamin B6, and fibre are possibly associated with a reduced VTE risk.² Lack of convincing evidence on the impact of diet on VTE could be possibly due to the fact that traditional approaches to the diet-disease relationship have been mainly targeted to the nutritional quality assessment, regardless of food processing. However, it is largely acknowledged that the nutritional composition alone does not exhaustively explain the overall food health potential, and that other non-nutritional factors could be equally relevant to human health.⁵

In order to adequately capture all dimensions of food, Brazilian researchers conceptualized and developed the Nova classification.⁶ This classification was originally proposed as a novel way to look at foods based on the degree of processing of foods rather than on their nutritional composition, postulating that processing may be as relevant to health as food composition, possibly through mechanisms that are triggered by non-nutritional components of these foods, such as degradation and artificialization of the food matrix, cosmetic additives, food contact materials, or neo-formed compounds (Figure 1).⁵⁻⁸

The term *ultra-processed foods* indicates industrially manufactured ready-to-eat or ready-to-heat formulations made mostly or entirely from substances extracted from foods or derived from food constituents often containing added flavours, colours, emulsifiers and other cosmetic additives,^{6,8} most importantly, UPFs are intentionally produced to be hyper-palatable and attractive, with long shelf-life, and able to be consumed anywhere at any time, and their formulation, presentation and marketing often promote overconsumption.⁹

Examples of typical UPFs are carbonated drinks, fruit yogurt, fruit drinks, sweet or savoury packaged snacks, ice-cream, chocolate, candies (confectionery), mass-produced packaged breads and buns, and many others.⁶

In the last decade, the number of studies examining the relationship of UPF and health has dramatically increased, due to the fact that consumption of highly processed food is on the rise globally. Actually, UPFs have progressively displaced unprocessed or minimally processed foods and traditional cooking

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NOVA Food classification





Unprocessed or minimally processed foods	Processed culinary ingredients	Processed foods	Ultra-processed foods
<p>Foods which did not undergo processing or underwent minimal processing techniques, such as fractioning, grinding, pasteurization and others.</p> 	<p>These are obtained from minimally processed foods and used to season, cook and create culinary dishes.</p> 	<p>These are unprocessed or minimally processed foods or culinary dishes which have been added processed culinary ingredients. They are necessarily industrialized.</p> 	<p>These are food products derived from foods or parts of foods, being added cosmetic food additives not used in culinary.</p> 
<p>Legumes, vegetables, fruits, starchy roots and tubers, grains, nuts, beef, eggs, chicken, milk</p>	<p>Salt, sugar, vegetable oils, butter and other fats.</p>	<p>Bottled vegetables or meat in salt solution, fruits in syrup or candied, bread, cheeses, purees or pastes.</p>	<p>Breast milk substitutes, infant formulas, cookies, ice cream, shakes, ready-to-eat meals, soft drinks and other sugary drinks, hamburgers, nuggets.</p>

Figure 1. The Nova food classification. Reprinted from de Oliveira PG *et al.*²⁷

in the diet worldwide, and now constitute more than half of the total calories eaten daily in many high-income Countries.¹⁰

In Mediterranean Countries such as Spain and Italy, the proportion of food that is ultra-processed among adults is about 24% and 17%, respectively,^{11,12} probably because home cooking is still part of a traditional Mediterranean diet.

Robust and well-conducted cohort studies worldwide found that a larger dietary share of UPF is associated with shorter survival and an increased risk of non-communicable diseases,¹³ including cardiovascular disease (CVD),¹⁴ type 2 diabetes,¹⁵ and cancer.¹⁶

Analyses from the Moli-sani Study in Italy have shown that UPF intake is an independent risk factor for mortality not only in the general population, but also among participants with pre-existing CVD.¹⁷

Potential mechanisms linking UPFs to cardiovascular health include, among others, altered low-grade inflammation - possibly triggered by contaminants (*e.g.*, phthalates, bisphenols that migrate from contact packaging to foods),^{10,18,19} altered food matrix, and food additives - that is a major risk factor for cardiovascular disease,²⁰ and VTE.²¹

Also, higher intake of UPF has been associated with impaired renal function and obesity,^{17,22,23} which have been reportedly linked to increased VTE risk in prior cohort studies.²⁴⁻²⁶

Interestingly, most of the reported associations between UPF intake and adverse health outcomes were independent of the overall diet quality; this means that the poor diet quality of this foods (*e.g.* high in sugar, salt, cholesterol, and low in fibre, minerals and vitamins) only partially accounts for the excess of death or disease associated with UPF consumption,¹⁷ and this may explain the weak associations between diet quality and VTE observed so far.

In light of this, the relationship between dietary habits and VTE, as well as other blood clotting-related diseases, will likely benefit from a paradigm shift aimed to examine the overall food health potential rather than the nutritional composition alone. This would possibly help clarifying the role of diet (as a broader concept) to the pathogenesis of these diseases and also contribute to the reduction of their burden globally.

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