

# Food Processing and Incident Hypertension: Causal Relationship, Confounding, or Both?

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Diet has a prominent, if not predominant, role in the pathogenesis of elevated blood pressure (BP).<sup>1</sup> Dietary factors that raise BP include suboptimal dietary pattern, excess sodium intake, insufficient potassium intake, excess weight, and high alcohol consumption.<sup>2,3</sup> While diet studies have examined individual nutrients, foods, and overall dietary patterns (e.g., DASH, Mediterranean, and vegetarian patterns), other aspects of diet might be relevant to health, including type of preparation (e.g., fried, barbecued) and level of processing.<sup>4</sup>

Food processing reflects both formulation (i.e., ingredients) and manufacturing steps (i.e., unit operations).<sup>5</sup> Foods can range anywhere from simple formulations with minimal unit operations (e.g., a food like butter) to complex formulations with multiple unit operations (e.g., granola bars). Concerns about the formulation of processed foods arise from their current tendency to contain excess amounts of certain nutrients (particularly, sodium, sugar, and saturated fat) and nonnutritive ingredients (e.g., noncaloric sweeteners, dyes for color), as well as inadequate amounts of other nutrients (e.g., vitamins, potassium, fiber). Some unit operations further reduce desirable nutrients (e.g., folate) or concentrate undesirable ones (e.g., arsenic in brown rice syrup). The purpose of food processing is also relevant to health consequences. Specifically, food processing allows foods to be inexpensive and readily available for immediate consumption in a wide variety of locations and settings, thereby increasing the potential for excess calorie intake.

Classification of foods by level of processing is complex and imprecise. One system used to classify foods by level of processing is called NOVA, which divides all foods into 1 of 4 groups: unprocessed or minimally processed food, processed ingredients, processed food, and ultra-processed food.<sup>4,6</sup> The groups are based on the “extent and purpose” of processing used in their manufacture.<sup>6</sup> Ultra-processed food (UPF) is not defined by the nutritional impact of the formulation or unit operations, but rather whether the ingredients

and processes used in their manufacture are in “common culinary use”.<sup>6</sup>

In this issue of the *American Journal of Hypertension*, Mendonça *et al.* examined the association between self-reported dietary exposure to NOVA-defined UPF and self-reported incident hypertension in the Seguimiento Universidad de Navarra (SUN) project, an ongoing prospective cohort of college graduates in Spain.<sup>7</sup> They analyzed 14,790 participants, followed for an average of 9.1 years, and observed 1,702 incident cases of hypertension. Overall, they reported a higher risk of developing hypertension among those in the highest tertile of UPF consumption (mean 5.0 servings/day) compared to those in the lowest tertile (mean 2.1 servings/day) with an adjusted hazard ratio of 1.21 (95% confidence interval 1.06–1.37).

Dietary exposure was measured at baseline using a self-administered 136-item semi-quantitative food frequency questionnaire (FFQ), of which 33 items were later classified as UPF. Tertiles of baseline UPF consumption were derived after excluding participants with prevalent hypertension ( $n = 2,378$ ); very high or low energy intake at baseline ( $n = 1,826$ ); cancer, diabetes, or cardiovascular disease ( $n = 1,310$ ); and those lost to follow up ( $n = 1,374$ ). There were multiple, substantial, and statistically significant differences in baseline dietary and nondietary characteristics of participants by tertile of UPF consumption. On average, those in the highest tertile of UPF consumption were 7.1 years younger, were more likely to be male, reported less exercise, and watched more television compared to those in the lowest tertile. Interestingly, while those in the highest tertile of UPF were more likely to report weight gain greater than 3 kg of body weight in the 5 years prior to study enrollment ( $P < 0.001$ ), they did not, on average, have higher baseline body mass indices ( $P = 0.31$ ).

Strengths of this study include the use of a fairly large cohort with almost a decade of follow-up. This allowed them

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to observe a large number of events. However, this study also has important limitations. Of greatest concern is confounding due to the nutrient content of UPF. For example, although the authors controlled for sodium intake using estimates of the 136 foods on the FFQ, the FFQ is a notoriously poor instrument to estimate usual sodium intake. Hence, the persistent and unchanged association of UPF consumption and blood pressure, even after controlling for sodium intake, does not rule out the possibility that sodium intake mediates the observed association. Secondly, the lack of specificity in the FFQ and NOVA makes misclassification of UPF unavoidable. For example, only some hamburgers are considered UPF in the NOVA, while the FFQ used in this study groups all types of hamburgers together. In this case, misclassification might lead to either attenuation or overestimation of the true association.

In addition, the commonness of ingredients (key to the NOVA definition of UPF) varies greatly by time and culture, blurring the lines of classification as a UPF. Finally, a large number of participants were excluded for prevalent conditions. If those in the lowest tertile of UPF consumption were significantly more likely to be excluded for prevalent hypertension than those in the highest tertile, the reported association would be stronger than the true association. If, however, those in the lowest tertile of UPF consumption were significantly less likely to be excluded for prevalent hypertension than those in the highest tertile, the reported association would be weaker than the true association.

In conclusion, the study by Mendonça *et al.* has identified an association of UPF with incident HTN. Critical issues are whether the relation is real (or merely an artifact as a result of inclusion criteria) and, if the association is real, whether known nutrients, foods, food patterns, and nondietary factors account for the observed relationship. We expect that high consumption of UPF is heavily confounded with multiple dietary factors—excess sodium, insufficient potassium, excess calories, and other factors. Still, even if confounding

accounts for much of the relationship, the association observed by Mendonça *et al.* highlights important concerns with currently available processed foods. Given that processed foods are commonly used throughout the world (and will most likely continue to be so in the future), it will be critical to identify modifiable aspects of food processing (formulation and unit operations) that can improve the nutritional quality of our food supply.

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