SAFE – Safe Food Advocacy Europe

Food additive mixtures and type 2 diabetes incidence: Results from the NutriNet-Santé prospective cohort.

Would we need a more epidemiologically driven risk analysis approach?

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Who we are

SAFE is an independent non-profit organization that **represents interests of European consumers** all over Europe on issues connected to food safety and agriculture.

Mission

We strives to **protect and advance consumers' rights** in **EU** food policy.

Activities and goals

- Lobbying to improve the EU legislative framework
- Raising public awareness and training consumers
- Leading several EU projects on food safety and agriculture

We have several diets

Mediterranean Diet

Scandivan Diet

….and more…

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But we can have a Mediterranean diet... full of UPFs

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Industrial-type MD

Traditional MD – local, minimally processed

UPF and additives combined exposure

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Mixtures of food additives are commonly found in our daily diet, particularly through the consumption of ultra-processed foods. Until now, the safety of food additives has been assessed individually, due to a lack of data on the effects of combined exposure

UPF and additives combined exposure

A new study conducted by the Eren-Cress team investigated potential associations between exposure to common mixtures of food additives and the development of type 2 diabetes.

Eren-Cress team: *Inserm, INRAE, Université Sorbonne Paris Nord, Université Paris Cité, and Cnam*

UPF and additives combined exposure

In Europe, > 300 food additives are authorized (e.g., emulsifiers, artificial sweeteners, colors, preservatives) and their use in food manufacturing is governed by European regulation EC/1333/2008. Their safety has previously been assessed by the European Food Safety Authority (EFSA), which proposed acceptable daily intake for some of them.

However, these evaluations were constrained by the available scientific evidence at the time, which was limited due to a lack of human data and a predominant focus on specific toxicological targets such as cytotoxicity and genotoxicity.

UPF and additives combined exposure

Diets rich in UPF lead to the consumption of food combinations that result in the ingestion of mixtures of food additives.

These additives may interact through synergistic or antagonistic effects, potentially influencing metabolism and overall health [1,2].

In a recent in vitro study based on four human cell models, it has been observed toxicological effects food additive mixtures, beyond the effect of these substances alone [3].

1-Chazelas E, Druesne-Pecollo N, Esseddik Y, de Edelenyi F, Agaesse C, De Sa A. Exposure to food additive mixtures in 106,000 French adults from the NutriNet-Santé cohort. Sci Rep. 2021;11(1):19680. https://doi.org/10.1038/s41598-021-98880-5

2-Meng X, Yang Y, Zhang J, Su J, Li G, Liu S. Synergistic toxicity of some food additives used in non-alcoholic beverages on renal tubular epithelial cells. Cell Mol Biol Noisy--Gd Fr. 2023;69(10):207–16

3-Recoules C, Touvier M, Pierre F, Audebert M. Evaluation of the toxic effects of food additives, alone or in mixture, in four human cell models. Food Chem Toxicol. 2025;196:115198. https://doi.org/10.1016/j. fct.2024.115198 PMID: 39675459

UPF and additives combined exposure

The NutriNet-Santé cohort study, which collected unique detailed dietary exposure data, including commercial names and brands of industrial products, provided new human data insights, suggesting associations between dietary exposure to widely consumed food additives (e.g., some artificial sweeteners and emulsifiers) and higher incidence of several chronic diseases, in particular type 2 diabetes

UPF and additives combined exposure

A total of **108,643 participants** from the NutriNet-Santé cohort were included in the study among which 79.2% were women. At baseline, the median age of the cohort was 41.2 years (25th–75th percentiles: 29.8–54.5 years). Among the overall cohort, 3.82% (n = 4,150) participants have died since their inclusion (2,411 in the present population study) and 9.5% dropped out because they did not want to receive any more questionnaires. Participants included in this study completed a median of 5 dietary records (25th–75th percentiles: 3–9)

UPF (NOVA 4) accounted for a median of 33.8% (25th–75th percentiles: 25.2%−43.7%) of daily energy intake.

A total of 75 food additives were consumed by at least 5% of the participants and were therefore included in NMF mixture analyses.

UPF and additives combined exposure

The study examined five types of additive mixtures that were the most emblematic of each mixture

Table 2. Food additive mixtures identified by nonnegative matrix factorization: loading values of main additive contributors[a], NutriNet-Santé cohort, 2009–2023[b].

Mixture 1 Food additive/Loading value		Mixture 2 Food additive/Loading value		Mixture 3 Food additive/Loading value		Mixture 4 Food additive/Loading value		Mixture 5 Food additive/Loading value	
E500 Sodium carbonates	0.99	Modified starches	0.99	E504 Magnesium carbonates	0.99	E503 Ammonium carbonates	0.99	E330 Citric acid	0.83
E450 Diphosphates	0.78	E440 Pectins	0.31	E101 Riboflavin	0.53	E500 Sodium carbonates	0.35	E331 Sodium citrates	0.63
E422 Glycerol	0.37	E412 Guar gum	0.26	E307 Alpha-tocopherol	0.24	E450 Diphosphates	0.30	E338 Phosphoric acid	0.59
E503 Ammonium carbonates	0.35	E407 Carrageenan	0.24	E503 Ammonium carbonates	0.17	E307 Alpha-tocopherol	0.28	E150d Sulphite ammonia caramel	0.59
E501 Potassium carbonates	0.17	E452 Polyphosphates	0.21			E472e DATEM[c]	0.18	E950 Acesulfame K	0.56
E420 Sorbitols	0.16	E202 Potassium sorbate	0.17			E504 Magnesium carbonates	0.17	E951 Aspartame	0.41
		E100 Curcumin	0.16			E322 Lecithins	0.15	E955 Sucralose	0.25
		E415 Xanthan gum	0.16					E414 Arabic gum	0.23
								E296 Malic acid	0.19
								E903 Carnauba wax	0.18
								E160c Paprika extract, capsanthin, capsorubin	0.17
								E163 Anthocyanins	0.15
								E412 Guar gum	0.15
								E440 Pectins	0.15

UPF and additives combined exposure

Mixture 1 showed moderate correlations with cakes and biscuits (ρ = 0.35) and savory snacks (ρ = 0.18)

Mixture 2 was associated with broth (ρ = 0.40), dairy desserts (ρ = 0.22), and fats and sauces (ρ = 0.21)

Mixture 3 did not correlate with any specific food group, likely due to its additives being dispersed across various products.

Mixture 4, similarly to mixture 1, correlated with savory snacks (ρ = 0.19) and cakes and biscuits (ρ = 0.18).

Mixture 5 was most associated with artificially sweetened soft drinks (ρ = 0.41) and sugary beverages (ρ = 0.37)

UPF and additives combined exposure

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UPF and additives combined exposure

Among the five additive mixtures tested, **mixtures 2 and 5** were significantly associated with an **increased risk of type 2 diabetes**, with hazard ratios per 1 standard deviation increment of 1.08 and 1.13, respectively.

No associations were found for **mixtures 1, 3, or 4**.

Mixture 2 was mainly correlated with intake of broths, dairy desserts, and sauces.

Mixture 5 was linked to consumption of artificially sweetened and sugary beverages.

UPF and additives combined exposure

Mediation analyses suggested that these additive mixtures may partly explain the relationship between certain food groups and diabetes incidence.

Mixture 5 mediated up to 52% of the association between artificially sweetened beverages and type 2 diabetes, and 42% for sugary beverages.

The associations remained robust across multiple sensitivity analyses, including adjustments for dietary patterns, pre-existing metabolic disorders, and regional and behavioral factors. Importantly, **the observed associations were independent of overall diet quality**, as measured by the PNNS-GS2 score.

The findings support a potential synergistic effect of additive combinations on metabolic health outcomes.

UPF and additives combined exposure

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Conclusion

Residual confounding as well as exposure or outcome misclassifications cannot be entirely ruled out and causality cannot be established based on this single observational study.

This study revealed positive associations between exposure to two widely consumed food additive mixtures and higher type 2 diabetes incidence.

Further experimental research is needed to depict underlying mechanisms, including potential synergistic/antagonist effects.

These findings suggest that a combination of food additives may be of interest to consider in safety assessments, and they support public health recommendations to limit nonessential additives

Thank you for your attention!

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