Preservative Food Additives and Breast Cancer Incidence in the NutriNet-Santé Cohort

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Abstract

Background

Experimental studies suggested negative impacts of some preservative food additives via mechanisms involving advanced glycation end products and mutagenic and potentially carcinogenic activities, but human data are lacking. This study aimed to investigate for the first time the associations between exposures to a wide range of preservative food additives and cancer incidence, in particular breast cancer, in a large population-based cohort.

Methods

Participants (n=105,260; 78.7% women; mean age=42.0y SD=14.5) from the French NutriNet-Santé prospective cohort (2009-2023) completed repeated 24h dietary records (mean=21 SD=18), including industrial food brands. Cumulative time-dependent exposure to food additives was evaluated using multiple composition databases and ad hoc laboratory assays in food matrices. Associations between exposure to preservatives (3 categories: sex-specific tertiles or non-exposed/lower/higher exposed participants separated by the sex-specific median) and cancer incidence were characterized using proportional hazards Cox models adjusted for potential confounders.

Results

4226 incident cancer cases were diagnosed (mean follow-up=7.57y; SD=4.56) (incl. 1208 breast, 508 prostate, and 352 colorectal cancers). Regarding breast cancer, higher intakes of the following additives were associated with higher incidence: potassium sorbate with (Hazard Ratio (HR)$_{cat3vs.1}$= 1.26[1.07-1.49]); potassium metabisulfite (1.20[1.04-1.38]); potassium nitrate (1.22[1.05-1.41]); and sodium erythorbate (1.21[1.04-1.41]). Some associations were also observed for overall, prostate and colorectal cancers.

Conclusions

This large prospective cohort revealed multiple positive associations between exposure to widely used preservatives and higher cancer incidence. If confirmed, these new data could lead to a re-evaluation of the safety of these food additives by European and international public health agencies to improve consumer protection.

Introduction

Preservative food additives are often and ubiquitously used (20% items recorded in the Open Food Facts World database contain at least one).
They are added to prolong the shelf life of packaged products, protecting them against deterioration caused by microorganisms and oxidation.
Here, preservative food additives = preservatives *per se* + antioxidant food additives.

Experimental studies suggested preservatives to induce the production of advanced glycation products (AGEs), and exert mutagenic, and potentially carcinogenic activities[1-4]

No previous prospective epidemiological studies on food additive preservatives specifically

→ Our aim was to investigate the associations between time-dependent exposure to preservative food additives and cancer incidence, including prostate and breast cancer incidence in a large prospective cohort of French adults.

Methods and Materials

Participants (n=105,260; 78.7% women; mean age=42.0y SD=14.5) from the French NutriNet-Santé prospective e-cohort (2009-2023).

Detailed evaluation of food & drink intake through sets of 3 validated 24h-dietary records (mean=21, SD=18) including specific brands of industrial products every 6 months.

Health events validated by a committee of MDs & linked to Social Security & mortality medico-administrative databases.

Associations between cumulative time-dependent categorical exposures to food additives and incidence of cancer using multivariable proportional hazards Cox models adjusted for known risk factors.

Only food additives consumed by >10% participants were evaluated (statistical power)
3 categories: sex-specific tertiles if consumed >66% participants or non-exposed/lower/higher exposed participants separated by the sex-specific median

Restricted Cubic Splines linearity test → retained p-value is either the p-trend (p for non-linearity was ≥ 0.05) or the likelihood ratio test (LRT) overall p-value (p for non-linearity was <0.05)

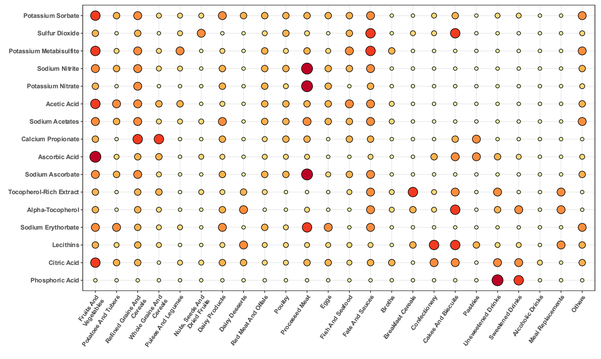


Figure 1. Dietary sources of food additive preservative intakes, NutriNet-Santé, 2009-2023 (n=105,260).
Example of interpretation: ≥ 50% food additive ascorbic acid intake comes from fruits & vegetables

Results

4226 incident cancer cases were diagnosed (mean follow-up=7.57y; SD=4.56) (incl. 1208 breast, 508 prostate, and 352 colorectal cancers).

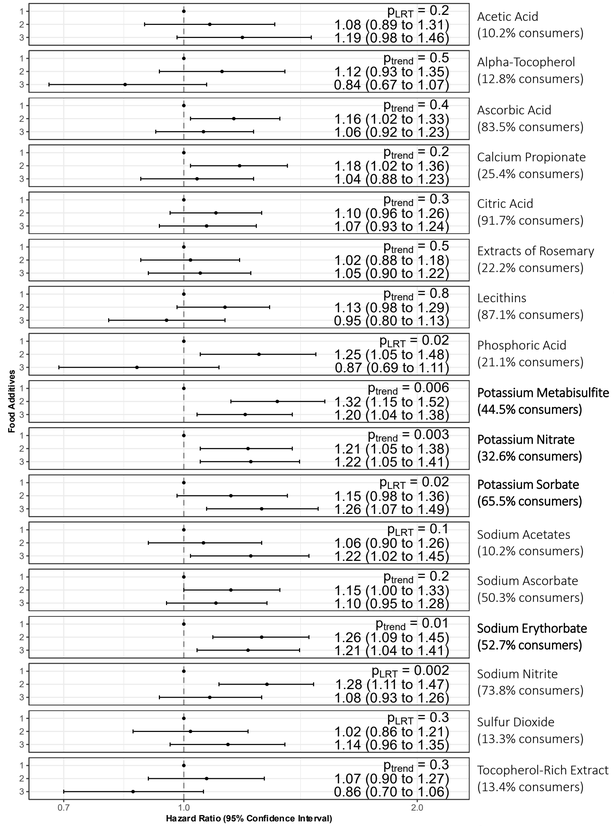


Figure 2. Associations between exposure to individual preservative food additives and breast cancer incidence, NutriNet-Santé cohort, 2009-2023

Discussion

Comparison is not straightforward as, except for the specific case of nitrites/nitrates food additives in processed meat, no other cohort study has investigated preservative food additives specifically so far (See Table 1 and Figure 3)

Table 1. Comparison with other population studies

Nitrites & Nitrates	Sulphites	Vitamins C & E
Consistent with other studies regarding nitrates/breast cancer [5, 6] (prospective studies) Probably carcinogenic [2, 7] (↑colorectal cancer)	Mixed results [8, 9] (workplace exposure, prospective studies)	Inverse associations natural sources/cancer; no evidence on other sources & none investigated food additives specifically[10] (dietary intakes & blood status; systematic review & meta-analysis dose-response)

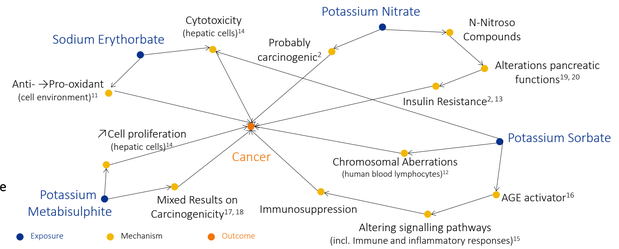


Figure 3. Summary of non-exhaustive existing literature on mechanistic plausibility concerning detect associations

Conclusions

This large prospective cohort revealed multiple positive associations between exposure to widely used preservatives and higher cancer incidence.

Adding to previous experimental data suggesting adverse cancer-related effects of several of these compounds.

Encourage caution regarding benefit/risk balance when evaluating food additives and cancer & supports recommendations to favor minimally processed foods

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