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## Cancer & artificial sweeteners

### Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study

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#### BACKGROUND

The food industry uses artificial sweeteners in a wide range of foods and beverages as alternatives to added sugars, for which deleterious effects on several chronic diseases are now well established. The safety of these food additives is debated, with conflicting findings regarding their role in the aetiology of various diseases. In particular, their carcinogenicity has been suggested by several experimental studies, but robust epidemiological evidence is lacking. Thus, our objective was to investigate the associations between artificial sweetener intakes (total from all dietary sources, and most frequently consumed ones: aspartame [E951], acesulfame-K [E950], and sucralose [E955]) and cancer risk (overall and by site).

#### METHODS AND FINDINGS

Overall, 102,865 adults from the French population-based cohort NutriNet-Santé (2009-2021) were included (median follow-up time = 7.8 years). Dietary intakes and consumption of sweeteners were obtained by repeated 24-hour dietary records including brand names of industrial products. Associations between sweeteners and cancer incidence were assessed by Cox proportional hazards models, adjusted for age, sex, education, physical activity, smoking, body mass index, height, weight gain during follow-up, diabetes, family history of cancer, number of 24-hour dietary records, and baseline intakes of energy, alcohol, sodium, saturated fatty acids, fibre, sugar, fruit and vegetables, whole-grain foods, and dairy products. Compared to non-consumers, higher consumers of total artificial sweeteners (i.e., above the median exposure in consumers) had higher risk of overall cancer (n = 3,358 cases, hazard ratio [HR] = 1.13 [95% CI 1.03 to 1.25], P-trend = 0.002). In particular, aspartame (HR = 1.15 [95% CI 1.03 to 1.28], P = 0.002) and acesulfame-K (HR = 1.13 [95% CI 1.01 to 1.26], P = 0.007) were associated with increased cancer risk. Higher risks were also observed for breast cancer (n = 979 cases, HR = 1.22 [95% CI 1.01 to 1.48], P = 0.036, for aspartame) and obesity-related cancers (n = 2,023 cases, HR = 1.13 [95% CI 1.00 to 1.28], P = 0.036, for total artificial sweeteners, and HR = 1.15 [95% CI 1.01 to 1.32], P = 0.026, for aspartame). Limitations of this study include potential selection bias, residual confounding, and reverse causality, though sensitivity analyses were performed to address these concerns.

#### CONCLUSIONS

In this large cohort study, artificial sweeteners (especially aspartame and acesulfame-K), which are used in many food and beverage brands worldwide, were associated with increased cancer risk. These findings provide important and novel insights for the ongoing re-evaluation of food additive sweeteners by the European Food Safety Authority and other health agencies globally.