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#### Literature Abstract

#### Folate intake and the risk of oral cavity and pharyngeal cancer: A pooled analysis within the International Head and Neck Cancer Epidemiology Consortium

Folate is necessary in DNA synthesis and repair. Thus, this retrospective study aimed to determine whether there was an association between the amount of folate intake and risk of oral cavity and pharyngeal cancers (OPCs). Individual-level data from 10 case-control studies involving 5,127 cases (13,249 controls) of OPC, were selected from a total of 25,478 cases (37,111 controls) within the International Head and Neck Cancer Epidemiology (INHANCE) Consortium. OPC cases were separated according to three categories of anatomical sites: the oral cavity, the oropharynx, and the oral cavity, pharynx unspecified or overlapping. Cases were more likely cigarette smokers and alcohol drinkers than controls. They were deemed suitable if data regarding folate intake was available for at least 80% of the subjects who had taken the food frequency questionnaire. To obtain an estimate of folate and energy intake, validated study-specific food composition tables were utilized. Folate intake sources include natural sources, folate-fortified food products, and folate supplementation. The association was then obtained by estimating odds ratios (ORs) and the corresponding 95% confidence interval (CI) and using unconditional logistic regression model for each case-control study. There was evidence of an inverse association between OPC risk and folate intake (0.65, 95% CI: 0.43–0.99), which was more evident in oral cavity cancer (OR = 0.57, 95% CI: 0.43–0.75). In heavy alcohol drinkers with low folate intake, versus never/light drinkers with high folate intake, the highest OPC risk was found (OR = 4.05, 95% CI: 3.43–4.79). Researchers found 11.1% of OPC cases could be attributable to biologic interaction amongst heavy drinkers. An OR of 2.73 was also noted for tobacco users with a low folate intake, compared to those with no tobacco intake coupled with an intermediate/high total folate intake. This study then suggests that total folate intake, with inclusion of supplements and fortified food, is inversely related to risk of OPC. A suggestion that high levels of folate intake may then protect against risk of OPC is made. However, this study was unable to distinguish the effect of folate on OPC risk relating to intake of fortified foods or supplements. It was also subjected to recall bias and possible changes in dietary habits postinterview. The association with human papillomavirus, a relevant risk factor for OPC, also was not considered.

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