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The Association of Dietary Vitamin D and Zinc Intake with Cancer Prevalence: Analysis of NHANES 2017-2018

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Abstract

Background: *Cancer remains a leading cause of mortality globally, emphasizing the need for preventive strategies. Dietary intake of zinc and vitamin D has been studied for their potential cancer-preventing effects, given their roles in the immune response and essential cellular functions, including cell differentiation, repair, and gene regulation. However, evidence linking these micronutrients and vitamins to the reduction of cancer prevalence remains inconclusive. Considering lifestyle modifications, this study evaluated whether recent dietary intake of zinc and vitamin D is associated with lower cancer prevalence.*

Methods: *This analysis utilized data from the 2017-2018 National Health and Nutrition Examination Survey (NHANES). The final sample included 5,569 participants after excluding those with missing data. Descriptive statistics were applied to assess demographic characteristics, and logistic regression models were used to evaluate associations between recent dietary intake($\leq$30 days of consumption) of zinc and vitamin D and cancer prevalence, adjusting for covariates. Analyses were conducted using StataNow/BE, version 18.5.*

Results: *No significant association was found between recent zinc or vitamin D intake and the prevalence of cancer after adjustment. The significant predictors of cancer prevalence included age and smoking status.*

Conclusions: *These findings suggest that recent dietary intakes of zinc and vitamin D may not significantly reduce cancer prevalence in the general population. Cancer prevalence was more strongly associated with demographic factors, such as age and sex. As recent intake of these nutrients may not reflect long-term use, future research should investigate the long-term effects of these nutrients in specific subgroups or through randomized controlled trials.*

Introduction

The number of new cancer cases is expected to exceed 2 million and cause more than 600,000 deaths by 2024 in the United States (Siegel et al., 2024). The primary causes of cancer include population growth and ageing. At the same time, lifestyle factors, such as unhealthy diets, sedentary habits, and exposure to many toxins, such as alcohol consumption and

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smoking, are expected to further contribute to the increasing cancer burden (Marino et al., 2024).

Extensive research has been conducted on the role of nutritional supplementation and dietary factors in cancer prevention (Martínez et al., 2012), mainly focusing on the intake of zinc and vitamin D, which are considered crucial immune response modulators and inhibitors of carcinogenesis (Skrajnowska & Bobrowska-Korczak, 2019; Garland et al., 2006). Vitamin D is thought to influence cellular differentiation and apoptosis, potentially reducing the risk of cancer (Brenner et al., 2016; Chandler et al., 2020; Giammanco, 2015; Jeon & Shin, 2018; Zhang et al., 2019), while zinc is included in maintaining DNA repair and immune function (Ayatollahi et al., 2022; Bikle, 2016; Li & Gai, 2017). For instance, a pooled analysis combining data from randomized trials and prospective cohort studies on vitamin D concentrations and malignancy reported that women with higher serum vitamin D levels (/*geq*40 ng/ml) had a 67% lower risk of cancer than those with lower levels (McDonnell et al., 2016). Similarly, a randomized clinical trial on the role of zinc in DNA repair was associated with a lower risk of developing prostate and esophageal cancer (Ayatollahi et al., 2022).

However, while some studies have suggested that vitamin D and zinc protect against certain types of cancers (Jahan et al., 2024), others have not established a consistent relationship (O'Connor et al., 2022), leading to conflicting findings, and further analysis focusing on broader populations is still needed.

Therefore, we conducted an observational cross-sectional study using data from the NHANES 2017–2018 survey to examine recent dietary zinc and vitamin D intake in relation to cancer prevalence in a diverse U.S. population. Our primary objective was to determine whether a higher recent intake of these nutrients is associated with lower cancer prevalence, with the aim of providing nutritional guidelines and public health interventions. We hypothesized that participants with higher zinc and vitamin D intakes would show lower prevalence rates than those with minimal or no intake.

Materials and Methods

Study Design

Observational cross-sectional study based on the NHANES 2017-2018 survey.

Data Description

The NHANES 2017-2018 dataset provides nationally representative health and nutritional data for the civilian population in the US. Of the 16,211 individuals, 9,254 completed the interview, and 8,704 completed the health examination. The response rates were 52% and 49% for the interviewed and examined samples, respectively. Data collection included interviews, physical examinations, and laboratory investigations to assess the health and nutritional status (Chen et al., 2020).

The survey adhered to ethical standards and was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (McQuillan et al., 2021). Informed consent was obtained from all participants.

Population

This study analyzed adults from the NHANES 2017–2018 database who reported dietary intake of zinc and vitamin D and responded to the question, 'Have you ever been told you had cancer or malignancy?'. Participants with missing data on cancer status and vitamin D and zinc intake were excluded. Of 9,254 participants, 5,567 met the inclusion criteria. (Figure 1)

Exposure and Outcome

The primary outcome was self-reported cancer prevalence. Cancer type or stage was not assessed owing to database limitations. Exposures were vitamin D and zinc dietary intake. Due to limitations of the dataset, the average daily vitamin D intake was estimated based on consumption over the last 30 days (µg/day) and categorized as 'more' or 'less than the international daily recommended intake' (15 g/day) (Hariri et al., 2023). Average zinc intake was assessed based on consumption within the last 24 hours (mcg/day) and categorized as 'zero intake' or 'above zero.'

Covariates

- **Smoking status:** Defined as *'smoker'* ($\geq$ 100 cigarettes in a lifetime) or *'never smoker'* (Cao et al., 2020).
- **Alcohol consumption:** Categorized as *'none'* (no alcohol), *'occasional'* (1–4 drinks/day), or *'frequent'* ($\geq$ 5 drinks/day) based on the 2020–2025 U.S. Dietary Guidelines (USDA, 2020).
- **BMI:** Categorized using WHO classification (WHO, 2000) as *'underweight'* ($\leq$ 18.5 kg/m^2), *'normal'* (18.5–$<$ 25.0 kg/m^2), *'overweight'* (25.0–$<$ 30.0 kg/m^2), and *'obesity'* grades I–III ($\geq$ 30.0 kg/m^2).
- **Age:** Continuous variables in years.
- **Sex:** Categorical, Female/Male.

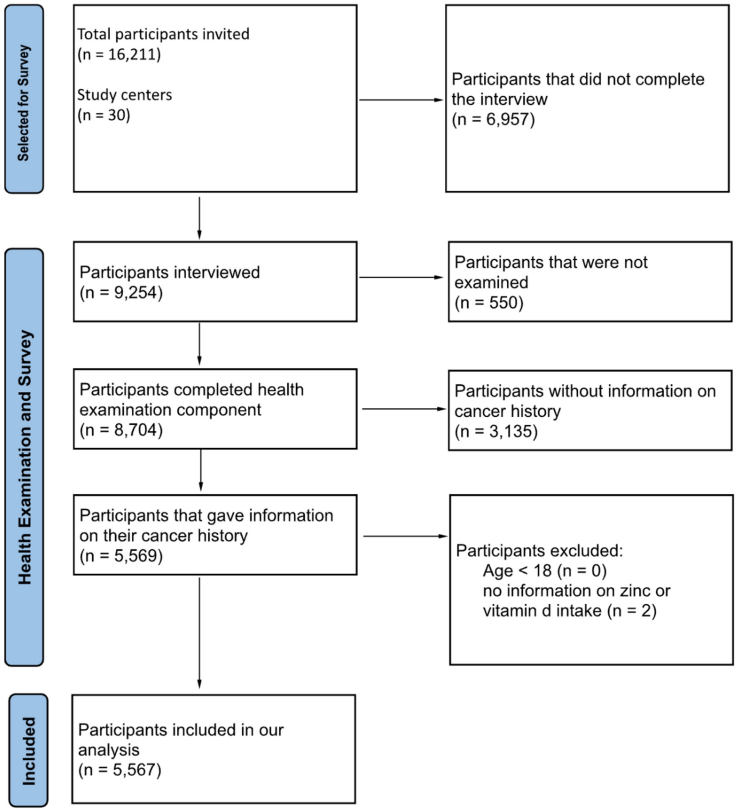

Figure 1: *Assessed study population.*

Statistical Analysis

Missing data were not included for any variable. Categorical variables were reported as frequencies and percentages, whereas continuous variables were reported as means and standard deviations. Normality was then assessed and confirmed. A univariable model was used to assess the association between vitamin D and zinc dietary intake individually and then as a combination. A multivariable logistic regression model was used to assess smoking status, alcohol intake, BMI, and potential effect modification. Statistical significance was set at $p < 0.05$. All analyses were performed using Stata/BE version 18.5.

Multicollinearity among the variables was evaluated. The model's fitness, goodness of fit, and area under the curve (AUC) were evaluated to determine model performance.

Sensitivity analysis was performed to determine whether recall bias affected the results related to exposure. Further sensitivity analyses were performed by adjusting for BMI, smoking status, and alcohol intake. (Supplementary material)

Results

Data from 9,254 participants in the NHANES dataset were analyzed. After censoring those without any information regarding their cancer diagnosis, 5,569 participants remained. Of these, 51.5% were female and 48.5% were male. As expected, the mean age was higher in patients with cancer because of the higher prevalence in the elderly and longer time of risk exposure. The median doses of vitamin D and dietary zinc intake were similar between the groups (Table 1). 87.8% of the population had vitamin D intake above the daily recommended intake, and 89.2% of the population had zinc intake above zero.

The results were assessed for both crude and adjusted models. The crude data analysis showed that there was no relationship between cancer prevalence and vitamin D dietary intake above the daily recommended intake (DRI) (OR, 1.263; 95%CI, 0.93-1.67; p = 0.104), but it showed a significant association with zinc intake (OR, 1.64; 95%CI, 1.18-2.27; p = 0.003). Testing for both in combination in crude data vitamin D remains not significant (p = 0.074), zinc shows not significant association (p = 0.779) and both combined as "vitamin D more than DRI and zinc intake above zero," the association was diluted and turns not statistically significant (OR 1.51; 95% CI 0.58-3.92; p = 0.387).

After adjusting for covariates, vitamin D intake above the DRI was not significantly associated with cancer risk (OR 1.34; 95% CI, 0.87-2.05; p = 0.174), and zinc intake (OR 1.81; 95% CI, 1.07 - 3.06; p =

	Total	Cancer	No Cancer
Total Population	5,567	588	4,979
Age in years, mean (SD)	51.5 (17.8)	66.7 (13.5)	49.71 (17.40)
Vitamin D - last 30 days dietary intake compared to daily recommended intake *			
Less than DRI	674 (12.1%)	59 (8.8%)	615 (91.2%)
More than DRI	4,893 (87.8%)	529 (10.8%)	4,364 (89.2%)
Zinc - last 30 days dietary intake *			
Zero	600 (10.8%)	42 (7.0%)	558 (93.3%)
Above Zero	4,967 (89.2%)	546 (11.0%)	4,421 (89.0%)
Biological sex *			
Male	2,702 (48.5%)	276 (10.2%)	2,426 (89.8%)
Female	2,865 (51.5%)	312 (10.9%)	2,553 (89.1%)
Smoking status *			
Never smoker	3,234 (58.1%)	287 (8.9%)	2,947 (91.1%)
Smoker	2,333 (49.9%)	301 (12.9%)	2,032 (87.1%)
Alcohol intake profile *			
None	1,276 (22.9%)	156 (12.2%)	1,120 (87.8%)
Occasional	1,674 (30.1%)	132 (7.9%)	1,542 (92.1%)
Frequent	390 (7.0%)	11 (2.8%)	379 (97.2%)
BMI category *			
Underweight	82 (1.5%)	6 (7.3%)	76 (92.7%)
Normal weight	1,255 (22.5%)	120 (9.6%)	1,135 (90.4%)
Overweight	1,667 (29.9%)	185 (11.1%)	1,482 (88.9%)
Obesity - grade I	1,132 (20.3%)	132 (11.7%)	1,000 (88.3%)
Obesity - grade II	568 (10.2%)	56 (9.9%)	512 (90.1%)
Obesity - grade III	469 (8.4%)	36 (7.7%)	433 (92.3%)

* Categorical variables are represented as frequency and percentage. Continuous data is represented as mean and standard deviation. Body mass index (BMI) was categorized according to the OMS obesity classification.

Table 1: *Population characteristics.*

0.025) was significantly associated with cancer risk. Two variables were found to be significant predictors of cancer risk: smoking status (OR, 1.31; 95% CI, 1.00-1.72; p = 0.047) and age (OR, 1.07; 95% CI, 1.06-1.08; p = 0.000), which were the strongest predictors in the model. BMI was not significantly associated with any of the studied categories or biological sex, and did not show an association with cancer prevalence in this adjusted model. Regarding alcohol consumption, only “frequent intake” showed an OR less than 1, suggesting a "protective" effect, which was statistically significant (OR 0.40; 95% CI, 0.20-0.81; p = 0.010).

In this adjusted model, the interaction between vitamin D and zinc was assessed which shows that vitamin D intake over DRI is not associated with cancer (OR 0.67; 95% CI, 0.17-2.53; p = 0.560) as well as zinc (OR 0.94; 95% CI 0.26-3.40; p = 0.934). Combined (vitamin D over DRI and zinc above zero) was not significantly associated with cancer odds (OR 2.12; 95% CI 0.52-8.62; p = 0.291).

Discussion

Vitamin D supplementation has been associated with reduced cancer mortality (Zhang et al., 2019), and populations with low vitamin D levels exhibit higher cancer prevalence (Global Burden of Disease 2019 Cancer Collaboration et al., 2022; Lips et al., 2021). However, the findings remain inconsistent. The VITAL trial, a large placebo-controlled study, found only a weak, non-significant association between vitamin D supplementation and cancer incidence (Manson et al., 2019), which is consistent with our results. Secondary analyses from the VITAL study (Brenner et al., 2021; Chandler et al., 2020) highlighted BMI as a key factor influencing the effects of vitamin D, suggesting that discrepancies may stem from differences in baseline levels, BMI, dosage, or environmental factors such as sunlight exposure and diet.

Zinc has shown potential for cancer prevention, particularly in in vitro studies of prostate, head, and neck cancers (Skrajnowska & Bobrowska-Korczak, 2019; Ressnerova et al., 2016). Observational studies have linked zinc supplementation with reduced risks of pancreatic cancer (Li & Gai, 2017; Shahrokhi Nejad et al., 2024), and zinc deficiency with increased risks of esophageal cancer (Yang et al., 2022). Additionally, randomized trials, such as Ayatollahi et al. (2022), reported the protective effects of zinc against HPV-related carcinogenesis. In our study, zinc intake was significantly associated with cancer prevalence when analyzed independently; however, this effect was not significant when adjusted for vitamin D and other covariates, warranting further investigation. Finally,

	Odds ratio	Confidence Interval	p-value
Vitamin D - last 30 days dietary intake			
More than DR	1.34	0.87 - 2.05	0.174
Zinc - last 24 hrs dietary intake			
Above Zero	1.81	1.07 - 3.06	0.025
Biological sex			
Female	1.18	0.90 - 1.54	0.221
Smoking Status			
Smoker	1.31	1.00 - 1.72	0.047
Alcohol Intake Profile, N=			
Occasional	0.95	0.72 - 1.26	0.756
Frequent	0.4	0.20 - 0.81	0.01
BMI Category N=			
Normal weight	1.44	0.32 - 6.50	0.628
Overweight	1.65	0.37 - 7.32	0.51
Obesity - grade I	1.63	0.36 - 7.30	0.52
Obesity - grade II	1.74	0.38 - 8.00	0.472
Obesity - grade III	1.36	0.28 - 6.46	0.699

Table 2: *Patient and arm characteristics.*

both zinc and vitamin D were assessed as recent dietary intake (30 days or less), so it is possible that this exposure for a number of subjects reflects only recent dietary habits, which may not have had a significant impact on cancer prevalence.

Cancer prevalence was higher among older participants, which is consistent with the role of aging in increasing gene mutations and cancer risk (Campisi, 2013; Laconi et al., 2020). Smoking was significantly associated with higher cancer prevalence, while frequent alcohol consumption was correlated with lower odds of cancer, possibly due to reporting bias, behavioral changes post-diagnosis, or unmeasured confounders.

Strengths and Limitations

This study used the NHANES 2017–2018 dataset, a large, nationally representative sample, to explore the association between dietary intake and cancer prevalence. However, the cross-sectional design precludes causal inferences, and data collection methods may introduce bias. Vitamin D intake was based on a 30-day recall, potentially misrepresenting long-term consumption, while zinc intake reflected only a 24-hour dietary recall, limiting its longitudinal effects. Cancer diagnosis data relies on self-reporting, introducing potential underreporting or misclassification. Furthermore, cancer type and stage were not considered, which could have diluted the observed associations. Despite these limitations, this study highlights the importance of exploring the effects of dietary intake and lifestyle factors on cancer risk.

Conclusions

No significant association was found between vitamin D intake and the prevalence of cancer. Zinc intake showed a significant association in unadjusted analyses, but lost significance in multivariate models, suggesting stronger influences from factors such as age, BMI, and lifestyle. Future research should investigate the long-term effects of vitamin D and zinc supplementation in specific populations to address these gaps and to provide more conclusive evidence.

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