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EFFECTS OF SERUM LEVELS OF VITAMIN A & PRECURSORS ON COLORECTAL CANCER MORTALITY: AN 18-YR FOLLOW-UP STUDY OF A NATIONAL COHORT

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INTRODUCTION

Colorectal cancer is the abnormal growth of cells in the colon and/or rectum. It is the third most common cancer in the world, with nearly 1.4 million new cases diagnosed in 2012 (WHO, 2016)



Figure 1. Colorectal cancer formation

- Vitamin A (i.e., retinoid) and A-carotenoids are essential for normal cell functioning and arrest, and eventually apoptosis which can inhibit tumor cell growth. A-carotenoids, precursors of Vitamin A, are also important for maintenance of optimum physiological levels of this potent antioxidant.
- Vitamin A is naturally found in milk, eggs, cheese, fish, liver, broccoli, sweet potatoes, peppers, and carrots

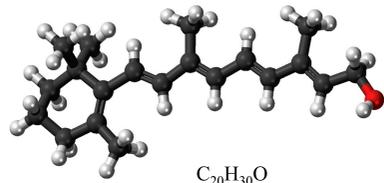


Figure 2. Chemical structure of Vitamin A

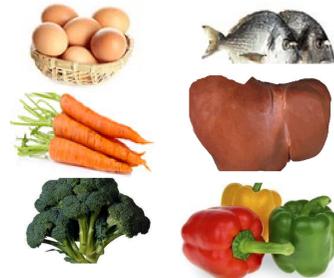


Figure 3. Food sources of Vitamin A

- In its retinol form, vitamin A plays an important role in cell differentiation and has been shown to **inhibit tumor cell growth** (Li et al., 2016)
- Most scientific studies on vitamin A have examined its supplementation and cancer prevention; however, how it influences mortality from colorectal cancer is not clearly defined

OBJECTIVE

- **Objective:** Examine the relationship between serum vitamin A (and its precursors) and colorectal cancer mortality rates
- **Hypothesis:** Serum vitamin A and precursors reduce colorectal cancer mortality

METHODS

- A retrospective cohort study was conducted with 14,358 adults (19 years or older) who participated in phase II of the National Health and Nutrition Examination Survey III (1991-1994) (NHANES III)
- Data were collected via in-home interviews and visits by participants to a mobile examination center for blood sample collection
- Characteristics such as family income, educational attainment, marital status, race and ethnicity, alcohol consumption, cigarette smoking, self-reported health, type of resident, body size, cancer status at baseline, vegetable consumption, and fruit/juice consumption were examined
- Trained technicians collected serum samples from study participants for Vitamin A analysis. This served as baseline and was correlated with the National Death Index database between 1991-2006.
- Hazard ratio (HR) estimates for all-cause and cancer-related deaths among individuals with different serum vitamin A levels were obtained from Cox Proportional Hazards Regression

RESULTS

Table 1. Adjusted Hazard Ratio of Death Caused for A-carotenoid Using 3-Level Categorization

Cause of Death	Serum Level	Adjusted Hazard Ratio ¹	Adjusted Hazard Ratio ²
All Cancer	Low vs. High	1.91 (1.56-2.33)	1.82 (1.48-2.24)
	Medium vs. High	1.36 (1.13-1.63)	1.33 (1.11-1.60)
Colorectal Cancer	Low vs. High	2.86 (1.51-5.41)	2.92 (1.49-5.71)
	Medium vs. High	1.86 (1.03-3.38)	1.89 (1.03-3.45)
Breast Cancer	Low vs. High	2.36 (1.05-5.33)	2.01 (0.88-4.61)
	Medium vs. High	1.28 (0.62-2.63)	1.16 (0.56-2.40)

¹Unadjusted for fruits and vegetables; ²Adjusted for fruits and vegetables
The levels (range) of Vitamin A categorized as high ≥ 66.6 ng/ml, medium $\geq 49.4 - \leq 66.6$ ng/ml and low ≤ 49.4 ng/ml

Table 2. Adjusted versus Unadjusted Hazard Ratios of Deaths Associated with Low Levels of Selected Micronutrients (25% as cutoff) 14358 Adults, NHANES III follow-up study 1988-2006

Causes of Death	Unadjusted Hazard Ratio (25% cutoff)		Adjusted Hazard Ratio (25% cutoff)	
	Vitamin A	A-carotenoid	Vitamin A	A-carotenoid
All Cancer	1.41 (1.16-1.71)	1.93 (1.63-2.30)	1.33 (1.09-1.62)	1.50 (1.25-1.80)
Colorectal Cancer	1.84 (1.02-3.30)	2.34 (1.37-3.99)	1.85 (1.02-3.37)	2.15 (1.22-3.80)
Breast Cancer	1.17 (0.53-2.58)	2.26 (1.18-4.33)	1.08 (0.53-2.18)	1.87 (0.93-3.77)

Note: Adjusted for age, sex, race, family income, education attainment, alcohol drinking, and cigarette smoking
The levels (range) of A-Carotenoids categorized as high ≥ 3.97 ng/ml, medium $\geq 2.0 - \leq 3.97$ ng/ml, and low ≤ 2.0 ng/ml

TOXICOLOGICAL & PUBLIC HEALTH IMPLICATIONS

- Colorectal cancer is a serious public health issue. In 2011, a total of 135,260 individuals were diagnosed with colorectal cancer and 51,783 people died from it (CDC, 2014).
- Optimum physiological levels of vitamin A could substantially reduce cancer mortality without any adverse health outcomes or incurring major financial costs.
- Findings from this study can be utilized to conduct further toxicological studies research on the effect(s) of vitamin A and its precursors on colorectal cancer mortality and determine the safe and effective dose for prevention.
- Study outcomes can be used to design an epidemiologic study that assesses colorectal cancer mortality rates related to use of Vitamin A supplements at varying doses.
- Findings from this research can be utilized to develop intervention strategies for colorectal cancer management, including educational interventions.

STRENGTH AND LIMITATIONS

Strengths:

- To our knowledge, this is the first study performed on a nationally representative U.S. population to examine serum vitamin A and colorectal cancer mortality rates
- Due to the large sample size of this study, we were able to obtain informative risk estimates (Hazard Ratios) even when the data were adjusted for multiple potential confounders
- We selected study participants from the community (extending beyond clinical populations) to achieve a true representation

Limitations:

- Data about past vitamin A use was not included in this study
- Failed to include the elderly in institutionalized facilities
- Look into effect on sensitive population e.g. pregnant women, HIV and other immunocompromised individuals
- Serum vitamin A levels and its precursor A-carotenoids were measured only once during the study
- Look into effect on sensitive population e.g. pregnant women, HIV and other immunocompromised individuals

CONCLUSIONS

- Results indicate that levels of serum Vitamin A and A-carotenoids are significantly associated with the risk of colorectal cancer mortality among adults, even after adjusting for fruits and vegetables
- Results suggest that consumption of foods that are rich in retinol and A-carotenoids are beneficial in reducing the risk of colorectal cancer mortality
- Public health professionals should work to develop intervention strategies for colorectal cancer prevention and management
- Further research is warranted to investigate the toxicological implications of this phenomenon and determine the most effective Vitamin A dosage for colorectal cancer patients

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