



Title	Association of dietary intakes of vitamin B12, vitamin B6, folate, and methionine with the risk of esophageal cancer: the Japan Public Health Center-based (JPHC) prospective study
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# 論文内容の要旨

## Synopsis of Thesis

氏 名 N a m e	Paramita Khairan
論文題名 Title	Association of dietary intakes of vitamin B12, vitamin B6, folate, and methionine with the risk of esophageal cancer: the Japan Public Health Center-based (JPHC) prospective study (ビタミンB12、ビタミンB6、葉酸およびメチオニンの食事摂取と食道がんのリスクとの関連について)
<p>論文内容の要旨</p> <p>〔目 的(Purpose)〕</p> <p>Esophageal cancer (EC) is the sixth most common cause of cancer-related mortality around the world. Esophageal squamous cell carcinomas account for 88% of EC cases, with an increasing trend of incidence among women in several countries, including Japan.</p> <p>B vitamins and methionine are essential substrates in the one-carbon metabolism pathway involved in DNA synthesis and methylation. They may have essential roles in cancer development. We aimed to evaluate the associations of dietary intakes of vitamin B12, vitamin B6, folate, and methionine with the risk of esophageal cancer (EC) using data from the Japan Public Health Center-based Prospective Study.</p> <p>〔方法ならびに成績(Methods/Results)〕</p> <p><u>Methods</u> : The Japan Public Health Center-based Prospective Study (JPHC Study) is a large population-based cohort study that began in 1990–1994 to investigate the risk factors for cancer, metabolic diseases, and other lifestyle-related diseases. The participants eligible for this study were those who participated in the JPHC study who gave feedback in the 5-year follow-up self-administered questionnaire surveys. The 5-year follow-up self-administered questionnaire surveys was including more comprehensive information of food intake's frequency. The surveys were distributed to residents of 11 public health center areas in 1995–1999 who were aged 45–74 years. The 5-year follow-up questionnaire survey included a food frequency questionnaire (FFQ) to estimate the dietary intake of food items. Ascertainment of EC cases EC data were collected from the cancer registries, medical records from hospitals in the study areas, reviews of the death certificate, or both medical records and death certificates. Statistical analyses were based on EC incidence values during 15.8 median years of follow-up until December 31, 2013 for Kochi and Nagasaki area, and December 31, 2015 for the other PHC areas. For each individual, person- years of follow-up were calculated from the day of submitting the 5-year follow-up survey to whichever of these endpoints occurred first: diagnosis of EC, death, emigration, or December 31, 2013. The hazard ratios (HRs) with 95% confidence intervals (CIs) of the incidence of EC were calculated using time-dependent Cox proportional hazard models.</p> <p><u>Results</u>: We included 87,053 Japanese individuals who completed a food frequency questionnaire and were followed up from 1995–1998 to 2013 and 2015. After 1,456,678 person-years of follow-up, 427 EC cases were documented. The multivariable HR (95% CI) of incident EC in the highest versus lowest quintile of dietary intake of vitamin B12 was 1.75 (1.13–2.71; p-trend=0.01). Stratification analysis based on alcohol consumption showed that higher dietary intakes of vitamin B12 and methionine were associated with an increased risk of EC among never-drinkers; HRs (95% CIs) were 2.82 (1.18–6.74; p-trend=0.009; p-interaction=0.18) and 3.45 (1.32–9.06; p-trend=0.003; p-interaction 0.02) for vitamin B12 and methionine, respectively. Meanwhile, there was no association between vitamin B12 and methionine intake with the risk of EC among drinkers. There were no associations between dietary intake of folate or vitamin B6 and the risk of EC.</p> <p>〔総 括(Conclusion)〕</p> <p>Dietary intake of vitamin B12 was positively associated with the risk of EC in the Japanese population.</p>	

## 論文審査の結果の要旨及び担当者

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**論文審査の結果の要旨**

Esophageal cancer is one of the leading cause of cancer related mortality around the world. It is important to investigate the risk factor and protective factor of this cancer in order to prevent the incidence. B vitamins and methionine are essential substrates in the one-carbon metabolism pathway involved in DNA synthesis and methylation. They may have essential roles in cancer development. Our research evaluated the associations of dietary intakes of vitamin B12, vitamin B6, folate, and methionine with the risk of esophageal cancer (EC) using data from the Japan Public Health Center-based Prospective Study. We included 87,053 Japanese individuals who completed a food frequency questionnaire and were followed up from 1995-1998 to 2013 and 2015 from the JPHC study. After 1,456,678 person-years of follow-up, 427 EC cases were documented. The multivariable HR (95% CI) of incident EC in the highest versus lowest quintile of dietary intake of vitamin B12 was 1.75 (1.13-2.71; p-trend= 0.01). Stratification analysis based on alcohol consumption showed that higher dietary intakes of vitamin B12 and methionine were associated with an increased risk of EC among never-drinkers; HRs (95% CIs) were 2.82 (1.18-6.74; p-trend=0.009; p-interaction=0.18) and 3.45 (1.32-9.06; p-trend=0.003; p-interaction 0.02) for vitamin B12 and methionine, respectively. Meanwhile, there was no association between vitamin B12 and methionine intake with the risk of EC among drinkers. There were no associations between dietary intake of folate or vitamin B6 and the risk of EC.

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