

## Null Results in Brief

# Ginseng Intake and Gastric Cancer Risk in the Shanghai Women's Health Study Cohort

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## Introduction

Ginseng is a deciduous perennial plant that is cultivated in East Asia and North America, and is commonly used as a herbal medicine in East Asian countries (1). The most commonly used types of ginseng are American ginseng (*Panax quinquefolius*), and white and red ginseng, which are prepared from Chinese/Korean ginseng (*Panax ginseng*).

Several studies have suggested that ginseng root may prevent the formation of carcinogen-induced tumors in animals (2, 3). A large case-control study (4, 5) and a small cohort study (6) have suggested that ginseng use is associated with a 60% to 70% reduction in gastric cancer risk in Korean populations. No data are available from other populations. Therefore, we used data from a large population-based Chinese cohort study to examine whether ginseng intake is associated with a reduced risk of gastric cancer.

## Materials and Methods

**Study Participants.** Details of the study design have been previously published (7). The study population included 74,942 women who participated in the population-based Shanghai Women's Health Study, which was conducted in seven urban communities in Shanghai, China. Participants were 40 to 70 years old at baseline between 1997 and 2000.

**Data Collection.** At study baseline, after obtaining informed consent, information on demographic characteristics, education and income, life-style and habits, diet, and several other factors were obtained via a combination of self-administered questionnaires and in-person interviews, yielding a response rate of 93%. Participants were asked whether they had regularly taken ginseng (more than five times a year) within the past 3 years. For those who reported using ginseng, the age started and stopped using ginseng products, the type of ginseng (i.e., white, red ginseng, or American), and quantity of use were ascertained.

**Outcome Assessment.** Outcome ascertainment was conducted by in-person interviews, and by linking the Shanghai Cancer Registry and the Shanghai Vital Statistics Unit records to the cohort database. Participants were paid an in-home

visit every 2 years to record details of their interim health history, including any cancer diagnosis. For cancer patients, information on date of diagnosis was collected and medical charts and diagnostic slides were reviewed to verify diagnosis. Cases in this report were those who were diagnosed until June 30, 2004.

**Statistical Analysis.** Subjects with a history of cancer prior to study enrollment ( $n = 1,490$ ) were excluded from the analysis. We used Cox proportional hazards models to calculate hazard ratios (HR) and 95% confidence intervals (95% CI) for the association between ginseng use and gastric cancer. The last day of follow-up was defined as the date of gastric cancer diagnosis, date of death, or date of last follow-up (June 30, 2004), whichever came first. The associations between subtypes of ginseng (i.e., white, red, American, and other types) with gastric cancer were also examined. Adjustment was conducted for potential confounding factors, including age, intake of fruits and vegetables, smoking history, education, and income. Finally, a lag-time analysis was done, excluding participants who had <2 years of follow-up.

**Power Calculation.** After excluding subjects with a prior history of cancer, data from 73,452 study subjects (153 gastric cancer cases and 73,299 non-cancer subjects) were used for this analysis. Ginseng was used by ~29% of cohort members. For a two-sided  $\alpha = 0.05$ , these numbers provided 80% power to detect a HR of >1.6 or <0.6.

## Results

Of the 73,452 study participants, the 21,318 (29%) subjects who had used ginseng at least five times a year in the past 3 years were classified as ginseng users. Mean follow-up time for ginseng users and nonusers was 5.68 and 5.65 years, respectively. The incidence of gastric cancer (number of cases/10<sup>5</sup> person-years) among ginseng users and nonusers were 46.2 and 33.0, respectively (Table 1). The unadjusted HR (95% CI) associated with ginseng use was 1.39 (1.00-1.94). However, when adjusted for age, this risk estimate was reduced to 1.04 (0.74-1.45). Further adjustment for fruit and vegetable intake, smoking, education, and income made no material difference (Table 1). There was no statistically significant association between years of ginseng intake and gastric cancer risk, with age-adjusted HR (95% CI) of 0.95 (0.81-1.11) for 5-year increments in duration of ginseng use. Excluding subjects with <2 years of follow-up from the analyses did not make a notable difference in the results.

Table 1 also summarizes the associations between each type of ginseng and gastric cancer. American ginseng was the most common type used. As displayed in this table, all associations were statistically nonsignificant.

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**Table 1. HRs and 95% CIs for the association between ginseng intake and gastric cancer risk in the Shanghai Women's Health Study**

|                              | Number (%)    | Total person-years of follow-up | Gastric cancer, no. (rate)* | Unadjusted HR (95% CI) | Age-adjusted HR (95% CI) | Adjusted <sup>†</sup> HR (95% CI) |
|------------------------------|---------------|---------------------------------|-----------------------------|------------------------|--------------------------|-----------------------------------|
| No ginseng use               | 52,134 (71.0) | 294,316                         | 97 (33.0)                   | Referent               | Referent                 | Referent                          |
| Any ginseng use <sup>‡</sup> | 21,318 (29.0) | 121,153                         | 56 (46.2)                   | 1.39 (1.00-1.94)       | 1.04 (0.74-1.45)         | 1.03 (0.73-1.44)                  |
| White ginseng                | 3,179 (4.3)   | 18,542                          | 7 (37.8)                    | 1.13 (0.52-2.43)       | 0.79 (0.36-1.70)         | 0.78 (0.36-1.70)                  |
| Red ginseng                  | 369 (0.5)     | 2,145                           | 1 (46.6)                    | 1.42 (0.20-10.1)       | 1.07 (0.15-7.70)         | 1.04 (0.14-7.47)                  |
| American ginseng             | 18,216 (24.8) | 103,520                         | 44 (42.5)                   | 1.28 (0.90-1.83)       | 0.95 (0.66-1.37)         | 0.94 (0.66-1.36)                  |
| Other ginseng                | 1,080 (1.5)   | 6,394                           | 4 (62.6)                    | 1.85 (0.68-5.04)       | 1.31 (0.48-3.60)         | 1.27 (0.47-3.48)                  |

\*Rate per 10<sup>5</sup> person-years of follow-up.

<sup>†</sup> Adjusted for age, smoking history, fruit and vegetable intake, education, and income.

<sup>‡</sup> Defined as taking ginseng at least five times a year in the past 3 y.

## Discussion

Gastric cancer, despite declines in its incidence, is still the second most common cause of cancer death in the world (8, 9). High incidence and low survival rates (10) make prevention a priority for this cancer. Intake of fruits and vegetables may modify gastric cancer risk (11, 12). Our study examined whether intake of ginseng root, previously shown to reduce risk of gastric cancer in Korean populations (5, 6), was also associated with a reduced risk of this cancer in a Chinese cohort.

In contrast with our initial expectation, we found a marginally significant increased risk of gastric cancer risk associated with ginseng intake. However, after adjustment for age, this association became null. In East Asia, ginseng has been used as a medicinal plant since ancient times, mainly to invigorate weak bodies (1). Age was a strong confounder, as it was associated with both cancer risk and ginseng intake.

It is unclear why our results differ from those in the previous case-control (4, 5) and cohort (6) studies. The types of ginseng used by participants in our study were similar to those used in previous studies. The control group in the first Korean case-control study (4) and its extension (5) were selected from among patients with chronic disease referred to the same hospital as the cases. Therefore, the prevalence of ginseng use might have been higher in this control group than the general population, rendering the risk ratios artificially low. It is more difficult to speculate why our results differ from the previous Korean cohort study. Further evaluation in Asian cohort studies may help to clarify ginseng's role in gastric carcinogenesis.

In summary, we found no association between ginseng intake and gastric cancer risk in a large prospective cohort study of Chinese women.

## References

1. Yun TK. *Panax ginseng*—a non-organ-specific cancer preventive? *Lancet Oncol* 2001;2:49–55.
2. Yun TK, Yun YS, Han IW. Anticarcinogenic effect of long-term oral administration of red ginseng on newborn mice exposed to various chemical carcinogens. *Cancer Detect Prev* 1983;6:515–25.
3. Yun YS, Moon HS, Oh YR, Jo SK, Kim YJ, Yun TK. Effect of red ginseng on natural killer cell activity in mice with lung adenoma induced by urethan and benzo(a)pyrene. *Cancer Detect Prev Suppl* 1987;1:301–9.
4. Yun TK, Choi SY. A case-control study of ginseng intake and cancer. *Int J Epidemiol* 1990;19:871–6.
5. Yun TK, Choi SY. Preventive effect of ginseng intake against various human cancers: a case-control study on 1987 pairs. *Cancer Epidemiol Biomarkers Prev* 1995;4:401–8.
6. Yun TK, Choi SY. Non-organ specific cancer prevention of ginseng: a prospective study in Korea. *Int J Epidemiol* 1998;27:359–64.
7. Zheng W, Chow WH, Yang G, et al. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. *Am J Epidemiol* 2005;162:1123–31.
8. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005;55:74–108.
9. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol* 2006;24:2137–50.
10. Cunningham SC, Kamangar F, Kim MP, et al. Survival after gastric adenocarcinoma resection: eighteen-year experience at a single institution. *J Gastrointest Surg* 2005;9:718–25.
11. Riboli E, Norat T. Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk. *Am J Clin Nutr* 2003;78:559–69S.
12. Nouraie M, Pietinen P, Kamangar F, et al. Fruits, vegetables, and antioxidants and risk of gastric cancer among male smokers. *Cancer Epidemiol Biomarkers Prev* 2005;14:2087–92.

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