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ORIGINAL PAPER

Relationship between cancer mortality/incidence and ambient ultraviolet B irradiance in China

Wanqing Chen · Mark Clements · Bayzidur Rahman · Siwei Zhang · Youlin Qiao · Bruce K. Armstrong

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Abstract
Background Studies finding an inverse correlation of ambient solar irradiance with cancer mortality were the first to suggest that sun exposure and probably, therefore, vitamin D might protect against some cancers. Such correlation has been shown in Asian populations in some studies. We analyzed the correlation between mortality and incidence from a number of cancers and ambient solar ultraviolet (UV) B irradiance in China.
Methods Cancer mortality data were obtained from the Second National Death Survey conducted in a sample of 263 counties in China from 1990 to 1992. National cancer registration data 1998–2002 in China were used for estimation of cancer incidence. Satellite measurements of cloud-adjusted ambient UVB intensity at 305 nm were obtained from a NASA database and GIS methods used to estimate the average daily irradiance for the 263 counties in 1990. We estimated cancer mortality rate ratios per 10 mW/(nm m^2) change in UVB by fitting a negative binomial regression model with mortality as the response variable and UVB as the independent variable, adjusted for sex, age, and urban or rural area.
Results Mortality rates for all cancers and cancers of the esophagus, stomach, colon and rectum, liver, lung, breast, and bladder were inversely correlated with ambient UVB. This correlation was present in men and women and rural residents for all these cancers but not urban residents for cancers of the esophagus, colon and rectum and liver. Lung cancer mortality showed the strongest inverse correlation with an estimated 12% fall per 10 mW/(nm m^2) increase in UVB irradiance even if adjusted for smoking. Only incidence rates for cancers of the esophagus, stomach, colon and rectum and cervix were inversely correlated with ambient UVB. Mortality and incidence from nasopharyngeal cancer increased with increasing UVB [respectively 27 and 12% per mW/(nm m^2)]. Mortality from cancer of the cervix also increased, but to a lesser extent and mortality from leukemia was not consistently correlated with UVB irradiance.
Conclusion Mortality from all cancers together and most major cancers in China was inversely associated with solar UVB. These associations were similar to those observed in a number of populations of European origin. Incidence of some cancer types had the same correlation with UVB. They suggest the possibility that vitamin D may reduce the incidence or improve the outcome of cancer in Chinese people.

Keywords Cancer · Mortality · Incidence · UVB · Negative binomial regression

W. Chen (✉) · S. Zhang
National Office for Cancer Prevention and Control, Cancer Institute, Chinese Academy of Medical Sciences, No.17 Pan-Jia-Yuan South Lane, 100021 Chaoyang District, Beijing, China
e-mail: chenwq@cicams.ac.cn

M. Clements
National Centre for Epidemiology and Population Health, Australian National University, East Road, Acton, ACT 2601, Australia

W. Chen · M. Clements · B. Rahman · B. K. Armstrong
School of Public Health, The University of Sydney, City Road, Camperdown NSW2006, Australia

Y. Qiao
Department of Cancer Epidemiology, Cancer Institute, Chinese Academy of Medical Sciences, No.17 Pan-Jia-Yuan South Lane, 100021 Chaoyang District, Beijing, China

Introduction

Sun exposure is the main cause of skin cancer [1]. However, recent research suggests that sun exposure may protect against some other types of cancer, including prostate cancer, breast cancer and non-Hodgkin lymphoma [2–4]. The first indications that such protective effects were possible came from ecological studies that showed an inverse association between mortality from a number of different cancers and estimated ambient solar or solar ultraviolet B (UVB) irradiance across geographical units of the USA, as exemplified by Garland et al. [5] early paper on colorectal cancer and summarized in a recent, comprehensive review [6]. Experiments with human and animal cells also suggest that vitamin D, which is synthesized in the skin through exposure to UVB from the sun, might protect against cancer, and there are analytical epidemiological studies that support this suggestion [7–12].

While most of the early reports of an inverse association between solar UVB and cancer mortality came from the USA, this association has been reported for prostate and breast cancer across multiple other countries with European origin populations and for breast cancer across a mixture of European and Asian origin populations [6, 11]. Several studies have been done solely in Asian region populations. A positive association of mortality from pancreatic cancer with latitude across the 47 prefectures of Japan (from which an inverse association with solar radiation can be inferred) was reported in both men and women in 1985 [13]. This association was demonstrated again recently in the same population (using average annual solar radiation levels rather than just latitude) and also reported for mortality from cancers of the esophagus, stomach, colon, rectum, and gallbladder and bile ducts [14, 15]. Another recent Japanese study found direct rather than inverse associations between ambient solar UVB radiation and mortality from lymphoid neoplasms [16]. A study reported in 1989 found that gastric, liver and rectal cancer mortality increased with increasing latitude in women in 65 counties in China in 1973–1975 while mortality from cancers of the esophagus and colon did not [17]. A more recent report also correlated mortality rates from the 1973–1975 death survey in China with latitude and found significant positive associations with all cancers (females), esophageal, gastric, colorectal (females), lung (males), and cervical cancers and significant negative associations with liver cancer (males) and nasopharyngeal cancer [18]. These studies suggest that the generally inverse ecological correlation between cancer mortality and ambient solar radiation observed in populations of European origin is also seen in the populations of Japan and China and may suggest protective effects of vitamin D against death from cancer in these populations.

As a prelude to more direct study of associations of vitamin D with cancer risk in China, we have refined the previous studies from China by using mortality data from 263 counties in the second national death survey in 1990–1992, adding incidence data from 30 cancer registries in 1998–2002, and using estimates of ambient UVB irradiance relevant to vitamin D synthesis from NASA satellites rather than just latitude.

Materials and methods

Estimation of cancer mortality

The Chinese Second National Death Survey was carried out in 1993 and covered deaths occurring in the 3 years from 1990 to 1992 in one tenth of the country's population [19]. A stratified random sample of 263 counties was selected so as to be representative of province and country level mortality. Deaths were ascertained in a similar way to the First National Death Survey (1973–1975) [20, 21]. When a county was selected, all deaths in 1990–1992 were identified from death registries, hospitals and the Civil Administration Bureau. Population information was also retrieved from official registration records. Cause of death was obtained from the death certificate when provided by hospitals. If a death certificate was unavailable, households were visited and information on cause of death collected by interviews with relatives. Data on sex, age at death and date of death were also obtained from each of the selected counties and entered, together with cause of death, into a single computer database. Cause of death was coded using ICD-9. Cause-, sex- and age-specific cancer mortality rates were calculated in all sampled counties and analysis limited to the most frequent cancer causes of death: cancers of the nasopharynx, esophagus, stomach, colon and rectum, liver, lung, breast, cervix, and bladder and leukemia, and all cancers together. Counties were classified as either urban or rural as a rough indicator of socioeconomic status.

Estimation of cancer incidence rate

The National Central Cancer Registries (NCCR) of China collects cancer incidence and mortality data from population-based cancer registries in China for evaluation and reporting. Cancer registration is voluntary in China; thus, most of the registries are in bigger cities with better economies and generally, therefore, in the east of the country. Some rural cancer registries were established to support research into particularly high risks for cancers of the nasopharynx, stomach, liver and cervix identified in some areas in the first national death survey conducted in 1973–1975. A few other rural cancer registries have also been established. Thus, the Chinese cancer registries do not necessarily cover a representative sample of the whole Chinese population.

During the period 1998–2002, there were 30 county-based cancer registries reporting cancer registration data. The registries identified new cancer cases from all hospitals, community health centers, death registries and the Civil Administration Bureau, which holds cremation records. Population information was obtained from official registration records. For this study, the data on cancer site (coded using ICD-10), sex and age at diagnosis were retrieved from each cancer registry's database. Site-, sex- and age-specific cancer incidence rates were calculated for all cancer registries and the analysis was limited to the cancer types used in the analysis of the National Death Survey. Cancer registries' locations were also classified as either urban or rural.

Ultraviolet B measurements

The estimated daily cloud-adjusted ambient solar UVB irradiance at 305 nm, expressed in milliwatts per meter squared per nanometer [mW/(nm m^2)], was obtained on a 1° of latitude by 1° of longitude grid for the whole of China from a NASA Goddard Space Flight Center Data Archive Center database of readings from the total ozone mapping spectrometer (TOMS) mounted on the Nimbus-7 satellite [22]. We estimated the UV measure by averaging daily estimates from 1996 through to 2003, which made the assumption that the relative distribution of annual UV irradiance for counties in China was stable over time. ArcGIS 9.1 (http://www.esri.com/software/arcgis/index.html) software was used for spatial modeling of the UVB data and the Kriging method of interpolation was used to obtain county level average daily irradiance over the whole year. UVB at 305 nm was chosen because it is the available wavelength that corresponded most closely to the peak in the action spectrum for UVB caused vitamin D production in skin [23].

Statistical analysis

SAS version 9.1 (SAS Institute, Cary, NC) and R version 2.5.0 (www.r-project.org) were used for the statistical analysis. Pearson's product moment correlation was used to assess the association between UVB irradiance and longitude and latitude; confidence intervals were calculated using Fisher's Z transform. Negative binomial regression modeling was used to evaluate the relationship between cancer death and UVB irradiance [24]. Counts of cancer deaths for each county, specific to cancer type, sex, age group (0–14, 15–29, 30–44, 45–64, 65+) and location (urban or rural), were modeled and the log of the specific populations used as an offset term. Separate analyses were undertaken by cancer type, with sex, age and location used as explanatory factors; analyses were also undertaken for each sex and for each location. The results were expressed as rate ratios for a ten mW/(nm m^2) increase in UVB irradiance with their 95% confidence intervals. Interactions in the association with UVB exposure by sex and by location were formally assessed using likelihood ratio tests comparing models with main effects only with models with an interaction term between either UVB exposure and sex or UVB exposure and location.

To graphically represent the trends, we plotted the age-standardized mortality rates, using Segi's world population as the standard [25], against UVB irradiance. For each plot, we fitted the trend line and its 95% confidence interval from a generalized linear regression model with a Gaussian distribution and a log-link, weighted by the inverse of the variance for the age-standardized rate [26]. We also used this model to investigate whether any particular county was influential, with influence measured by Cook's statistic [27].

Finally, any association between lung cancer mortality and UVB exposure might be confounded by smoking exposure. We propose an adjustment for this potential confounding in the "Appendix". To provide tentative estimates of the change in smoking prevalence by UVB, we extracted data on smoking prevalence among controls from Fig. 3 of Liu et al. [28], calculated UVB exposure estimates for each city, and fitted a log-binomial model to estimate the change in smoking prevalence with changing UVB.

Results

The Second National Death Survey included 2,022,433 cancer deaths and 334,213,493 person-years, with a crude annual cancer mortality rate of 108.3 per 100,000. Standardized to the Segi's world population, the cancer mortality rate was 124.5 per 100,000, ranging from 30.5 to 373.2 across the 263 surveyed counties (the counties are shown in Fig. 1). For individual cancer types, the ranges in age-standardized mortality rates per 100,000 were: nasopharynx 0.1–13.9, esophagus 0.4–155.2, stomach 3.3–204.3, colon and rectum 1.2–19.8, liver 4.5–61.1, lung 2.2–67.0, breast 0.0–12.4, cervix 0.0–42.0, bladder 0.1–3.8, and leukemia 1.4–8.2.

Cancer registrations in the 30 counties (see Fig. 1) covered 424,088 cancer cases and 189,974,837 person-years, with a crude annual cancer incidence rate of 223.2 per 100,000. The age-standardized incidence was 177.7 per 100,000 and the age-standardized mortality 121.7 in these 30 counties. For individual cancer types, ranges in age-standardized cancer incidence rates were: all registered cancers 78.4–623.8, nasopharynx 0.2–25.8, esophagus 0.3–132.7, stomach 4.7–157.2, colon and rectum 2.4–74.7, liver

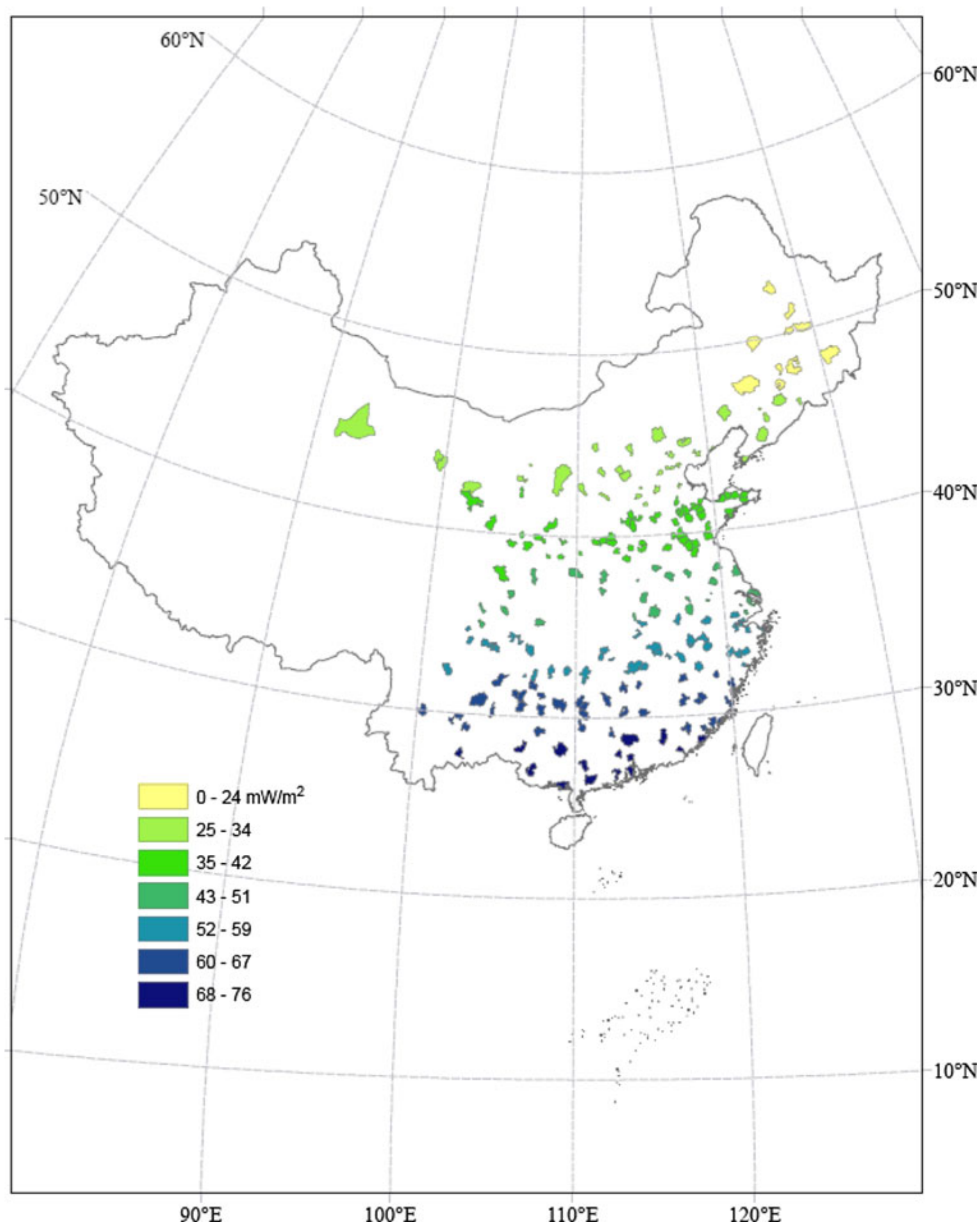

Fig. 1 Average daily ambient UVB irradiance (mW/m^2) at 305 nm in 1990 in 263 counties included in the Chinese Second National Death Survey

5.2–74.2, lung 9.9–116.9, breast 1.6–39.5, cervix 0.0–39.3, bladder 0.4–15.2, and leukemia 0.2–20.0.

The annual cloud-adjusted ambient solar UVB irradiance at 305 nm ranged from 16.8 to 76.0 mW/(nm m^2) across the 263 counties (Fig. 1). Oddly, UVB irradiance was more strongly correlated with longitude (Pearson's correlation: $r = -0.73$, 95% CI: −0.78, −0.67) than latitude ($r = -0.41$, 95% CI: −0.51, −0.31). This strong correlation with longitude may be due to less cloud cover in the east of the country and the fact that the geographical bulk of China shifts to the north east as latitude increases (Fig. 1). The lowest UVB was recorded in Tongxian County, Beijing (longitude 116.70° and latitude 39.85°) and the highest in Jingyuan County, Ningxia Province (longitude 106.33° and latitude 35.50°).

Mortality rates for all cancers and most individual cancer types, adjusted for sex, age and urban or rural residence, fell with increasing UVB irradiance (Table 1; Fig. 2). This pattern was also observed in both males and females and both urban and rural areas for all cancers and cancers of the stomach, lung, breast, and bladder; a similar pattern was observed for most combinations of sex and location for cancers of the esophagus, colon and rectum and liver, except in urban areas where mortality rates tended to be flat or rise a little with increasing UVB (Table 1). There was little evidence for a consistent association between leukemia and ambient UVB and mortality from cancers of the nasopharynx and cervix increased with increasing UVB in both urban and rural areas (Table 1).

Table 1 Modeled mortality rate ratios per 10 mW/m^2 change in 305 nm average daily ambient solar UVB radiation, across 263 counties in China during 1990–1992 by cancer site, sex, and urban or rural location

Cancer type or site	Mortality rate ratios (95% confidence intervals)			*p* value for interaction by sex	Mortality rate ratios (95% confidence intervals)		*p* value for interaction by location
	Both sexes and both locations[a]	Males[b]	Females[b]		Urban counties[c]	Rural counties[c]	
All cancers	0.96 (0.95, 0.97)	0.96 (0.95, 0.98)	0.96 (0.95, 0.97)	0.710	0.99 (0.97, 1.00)	0.95 (0.94, 0.96)	0.001
Nasopharynx	1.27 (1.24, 1.31)	1.29 (1.24, 1.34)	1.25 (1.20, 1.31)	0.471	1.23 (1.17, 1.29)	1.29 (1.25, 1.34)	0.161
Esophagus	0.92 (0.90, 0.94)	0.93 (0.91,0.96)	0.91 (0.88, 0.94)	0.218	1.00 (0.96, 1.04)	0.89 (0.87, 0.92)	<0.001
Stomach	0.97 (0.95, 0.99)	0.97 (0.95,0.99)	0.97 (0.95, 0.99)	0.783	0.92 (0.90, 0.94)	0.99 (0.97, 1.01)	<0.001
Colon and rectum	0.97 (0.95, 0.98)	0.98 (0.96, 1.00)	0.96 (0.93, 0.98)	0.103	1.00 (0.98, 1.03)	0.95 (0.93, 0.97)	0.003
Liver	0.96 (0.95, 0.97)	0.97 (0.95, 0.99)	0.95 (0.93, 0.97)	0.080	1.00 (0.98, 1.02)	0.94 (0.93, 0.96)	<0.001
Lung	0.88 (0.87, 0.90)	0.90 (0.89, 0.92)	0.85 (0.84, 0.97)	<0.001	0.93 (0.90, 0.95)	0.86 (0.84, 0.87)	<0.001
Breast	–	–	0.95 (0.93, 0.98)	–	0.97 (0.94, 1.01)	0.94 (0.91, 0.97)	0.204
Cervix	–	–	1.11 (1.07, 1.15)	–	1.20 (1.13, 1.27)	1.08 (1.04, 1.12)	0.022
Bladder	0.94 (0.91, 0.97)	0.95 (0.91, 0.98)	0.93 (0.88, 0.99)	0.763	0.95 (0.90, 1.00)	0.94 (0.90, 0.98)	0.833
Leukemia	1.00 (0.98, 1.01)	0.98 (0.96, 1.00)	1.02 (1.00, 1.04)	0.006	1.03 (1.00, 1.05)	0.98 (0.97, 1.00)	0.015

[a] Adjusted for age, sex, and location

[b] Adjusted for age and location

[c] Adjusted for sex (where appropriate) and age

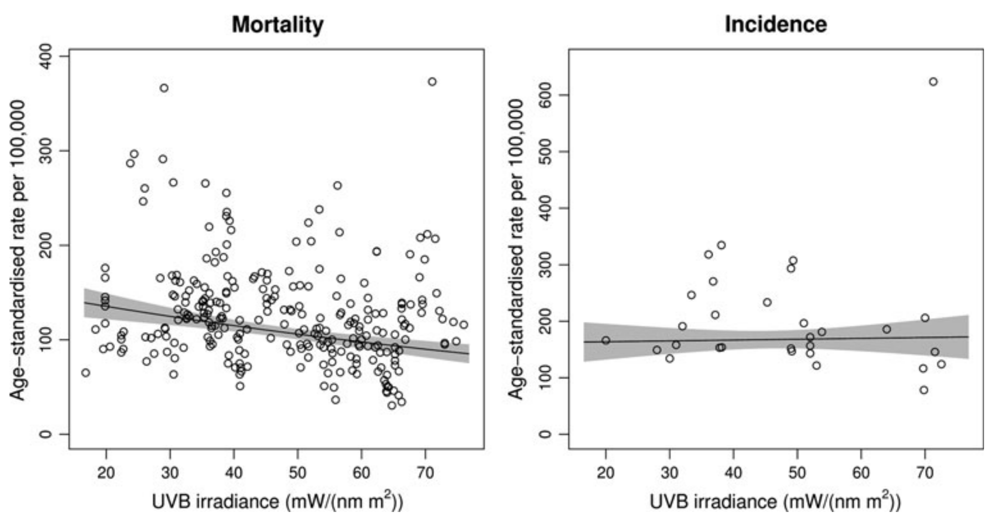

Fig. 2 Scatterplot of mortality and incidence from all cancers in both sexes by average daily ambient UVB irradiance (mW/m^2) at 305 nm in 263 counties included in the Chinese Second National Death Survey and in 30 counties in the Chinese Cancer registration data 1998–2002 (with modeled regression line and 95% confidence intervals)

Somewhat different patterns were seen for incidence rates (Table 2; Fig. 2). Overall, cancer incidence rates rose rather than fell with increasing UVB irradiance but, while they rose in urban areas, they fell in rural areas. For individual cancer types, rates fell with increasing UVB for esophagus, stomach, colorectal, and cervical cancers, but rose for nasopharynx, liver, lung, breast and bladder cancers, and leukemia. No change or a rise with increasing UVB was the pattern for incidence rates of all cancer types in urban areas, while for rural areas, the individual cancer types were equally divided between rising and falling rates.

For all cancers, adjusted mortality fell by 4% per 10 mW/(nm m^2) of UVB (rate ratio 0.96, 95% CI 0.95–0.97, $p < 0.0001$; Fig. 2); for incidence it rose by 7% per 10 mW/(nm m^2) of UVB. The downtrend in mortality rates was significantly stronger in rural areas [5% per 10 unit mW/(nm m^2)] than in urban areas (1%; Fig. 3); for incidence rates, the downtrend in rural areas was 7% per 10 unit of UVB. The strongest mortality downward trend was for lung cancer: 12% per 10 mW/(nm m^2) of UVB overall (rate ratio 0.88, 95% CI 0.87-0.99, $p < 0.0001$) and 14% in rural areas and 7% in urban areas. The downtrend in lung cancer incidence in rural areas was only 2% per 10 mW/(nm m^2) of UVB; it was stronger for some other cancers, for example esophagus cancer 58% (95% CI 54–61%).

Table 2 Modeled incidence rate ratios for 10 unit change in 305 nm average daily ambient solar UVB radiation (mW/m^2), across 30 cancer registration counties in China during 1998–2002 by cancer site, sex, and urban or rural location

Cancer type or site	Incidence rate ratios (95% confidence intervals)			p value for interaction by sex	Incidence rate ratios (95% confidence intervals)		p value for interaction by location
	Both sexes and both locations[a]	Males[b]	Females[b]		Urban counties[c]	Rural counties[c]	
All cancers	1.07 (1.045, 1.09)	1.09 (1.06, 1.12)	1.05 (1.02, 1.08)	0.22	1.18 (1.15, 1.21)	0.93 (0.90, 0.96)	<0.001
Nasopharynx	2.12 (2.03, 2.21)	2.17 (2.06, 2.30)	2.04 (1.91, 2.18)	0.27	1.98 (1.89, 2.07)	2.51 (2.31, 2.73)	<0.001
Esophagus	0.73 (0.68, 0.78)	0.76 (0.70, 0.82)	0.68 (0.61, 0.77)	0.13	1.12 (1.02, 1.23)	0.42 (0.39, 0.46)	<0.001
Stomach	0.87 (0.83, 0.91)	0.84 (0.79, 0.89)	0.89 (0.84, 0.95)	0.13	1.08 (1.03, 1.14)	0.62 (0.59, 0.66)	<0.001
Colon and rectum	0.97 (0.95, 0.98)	0.98 (0.96, 1.00)	0.96 (0.93, 0.98)	0.28	1.00 (0.98, 1.03)	0.95 (0.93, 0.97)	<0.001
Liver	1.20 (1.16, 1.23)	1.26 (1.21, 1.32)	1.11 (1.06, 1.16)	<0.001	1.23 (1.19, 1.27)	1.13 (1.06, 1.19)	0.057
Lung	1.04 (1.02, 1.07)	1.07 (1.04, 1.11)	1.01 (0.97, 1.04)	<0.001	1.07 (1.04, 1.11)	0.98 (0.94, 1.02)	<0.001
Breast	–	–	1.12 (1.08, 1.16)	–	1.13 (1.08, 1.19)	1.08 (1.03, 1.14)	0.012
Cervix	–	–	0.87 (0.80, 0.95)	–	1.18 (1.10, 1.25)	0.55 (0.47, 0.64)	<0.001
Bladder	1.09 (1.06, 1.13)	1.13 (1.08, 1.18)	1.02 (0.96, 1.08)	0.003	1.06 (1.02, 1.10)	1.20 (1.12, 1.28)	0.002
Leukemia	1.01 (0.97, 1.06)	0.98 (0.93, 1.04)	1.05 (0.99, 1.12)	0.16	1.11 (1.05, 1.17)	0.85 (0.79, 0.92)	0.027

[a] Adjusted for age, sex, and location

[b] Adjusted for age and location

[c] Adjusted for sex (where appropriate) and age

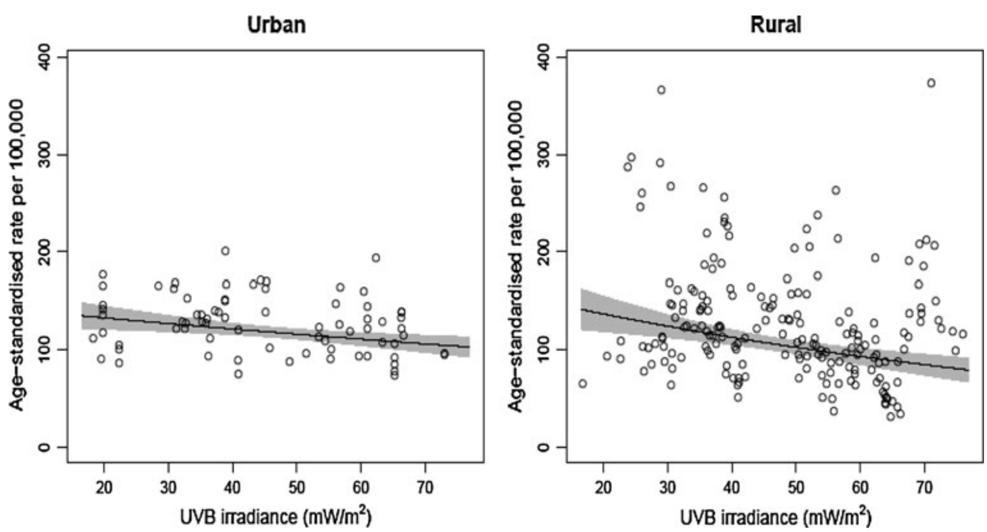

Fig. 3 Scatterplots of mortality from all cancers in both sexes by ambient UVB irradiance (mW/m^2) in 74 urban and 189 rural counties included in the Chinese Second National Death Survey (with modeled regression line and 95% confidence intervals)

Only for cancer of the nasopharynx did both mortality and incidence rise with increasing UVB, overall, in both sexes and in both urban and rural areas (Tables 1, 2). There was little evidence that outliers influenced these associations; excluding two counties with Cook's statistics greater than 1 did not affect the estimated rate ratios. The patterns of increase, however, were by no means linear and there was a remarkable concentration of high rates of cancer of the nasopharynx at UV irradiances between 55 and 65 mW/(nm m^2; Fig. 4), which suggests a strong impact of some factor other than ambient UVB. For cancer of the cervix, the overall mortality increase was 11% per 10 mW/(nm m^2) of UVB, with moderate evidence that the increase with UVB was higher in urban areas ($p = 0.022$ for interaction) than in rural areas, being 20 and 8% per 10 mW/(nm m^2) of UVB, respectively. Overall, incidence of cancer of the cervix fell by 13% per 10 unit increase in UVB, but rose with increasing UVB in urban areas [18% per 10 mW/(nm m^2)] and fell in rural areas [45% per 10 mW/(nm m^2)].

The mortality rate ratios for females were less than those for males for lung cancer ($p < 0.001$) and for leukemia

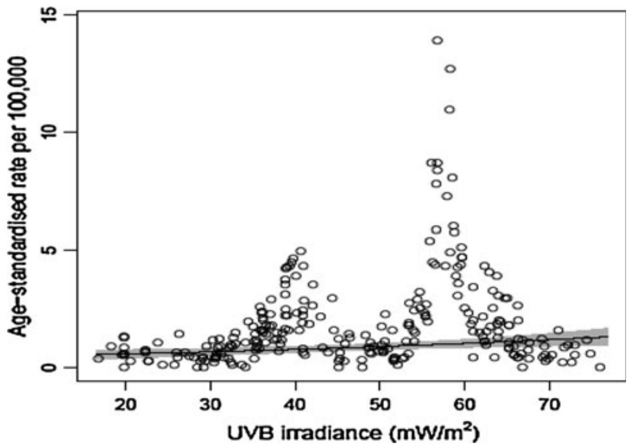

Fig. 4 Scatterplot of mortality from cancer of the nasopharynx in both sexes by average daily ambient UVB irradiance (mW/m^2) in 263 counties included in the Chinese Second National Death Survey (with modeled regression line and 95% confidence intervals)

($p = 0.006$). The incidence rate ratio for lung cancer was also less in females than males. There was consistent evidence for higher mortality rate ratios in urban than rural areas, being present for all cancers and cancers of the esophagus, colon and rectum, liver, lung, cervix and leukemia. The opposite was the case only for cancer of the stomach. This pattern was largely reflected in the incidence rates.

We adjusted the UVB associations with lung cancer to take account of potential confounding by smoking. Smoking prevalence was positively associated with UVB in males [risk ratio per 10 mW/(nm m^2) unit change in UVB of 1.05, 95% CI: 1.04, 1.06] and inversely associated with UVB in females (risk ratio of 0.84, 95% CI: 0.82, 0.86). Using values of the potentially confounded rate ratios from Table 1 and 2, we estimated: an adjusted UVB mortality rate ratio of 0.86 (95% CI: 0.84, 0.88) for males and 1.02 (95% CI: 0.99, 1.05) for females. The adjusted UVB incidence rate ratios were 1.02 (95% CI: 0.98, 1.06) for males and 1.20 (95% CI: 1.15, 1.24) for females. The model for smoking prevalence in females had one highly influential location (Tianjin); when it was excluded, the adjusted UVB mortality rate ratio was 0.91 (95% CI: 0.88, 0.95) and the adjusted UVB incidence rate ratio was 1.07 (95% CI: 1.03, 1.12).

Discussion

Cancer mortality rates in 263 counties in all Provinces of China were inversely associated with ambient UVB exposure for most cancer types, including all cancers and cancers of the stomach, lung, breast, bladder, esophagus, colon and rectum, and liver. Positive associations were found between UVB and cancers of the nasopharynx and cervix, and there was no consistent association found between UVB and leukemia. Cancer incidence rates in 30 counties were inversely associated with ambient UVB for fewer cancer types: cancers of the esophagus, stomach, colon and rectum and cervix. Incidence rates of most other cancer types and all cancers together were positively associated with ambient UVB. Generally, the associations for mortality and for incidence rates were in the same direction in males and females and more consistently inverse in rural counties than in urban counties.

This study has several limitations. First, it is ecological in nature. The UVB exposure measure is based on average annual ambient UVB irradiance in geographical units. As this measure changes gradually across China (Fig. 1), there is potential for confounding with factors that change in a similar manner. Such factors could include lifestyles, such as diet, and occupations that vary with climate and thus might correlate with ambient UVB. If the proposed mediation by vitamin D is correct, then associations might be weakened if consumption of foods high in vitamin D or the taking of supplements were higher, as they might be, in areas of low ambient UVB. We know of no data for China that would allow us to test this possibility. Second, the measurement of ambient UVB exposure may be a poor proxy for individual-level UVB exposure. The error in measurement will include both classical measurement error and Berkson error, which is due to assigning an aggregate level measure to individuals. If the classical measurement error is small relative to the Berkson error and the variance of the Berkson error within counties is small or similar across counties, we would expect little bias in the estimated associations. Strengths of the study design include its very large population base for mortality analysis, over 300 million person-years of observation, and its representative nature, including data from 263 counties in 27 provinces. The incidence database covered all population-based cancer registries in China and included nearly 200 million person-years in 5 years.

Many of the associations we observed have been reported from European origin populations [6, 29]. Some have not: we could find no such studies reporting that mortality rate for liver cancer was inversely associated with UV exposure. The inverse associations we observed for cancers of the esophagus are somewhat inconsistent with positive associations that have been observed between serum vitamin D concentrations and risk of esophageal dysplasia and squamous cell carcinoma in China [30, 31]. The positive association we observed for nasopharyngeal cancer may be due to some factor other than UVB: mortality rates are much higher, and somewhat clustered, in southern China than in northern China

(Fig. 4) and there is at least one risk factor, salted fish consumption, that is particularly important in southern China[32]. Similarly, some other factor probably explains the positive association between UVB and mortality from cancer of the cervix. An effect of UV-induced immune suppression on acquisition of HPV infection [33, 34] is one possibility. Geographical confounding of ambient UVB with infection with human papilloma virus [35] or frequent frying of food [36] are other possibilities, although we do not know that confounding with either exists.

Only a few previous ecological studies of cancer with ambient UVB have included incidence as well as mortality data [37, 38]. It is notable in our data that there was no overall inverse association of cancer incidence with ambient UVB and the incidence rates of fewer individual cancer types were inversely associated with UVB then were mortality rates. A similar difference between mortality and incidence effects was observed in a cohort study of estimated individual serum vitamin D and cancer incidence and mortality [39]. Such differences may suggest that ambient UVB and serum vitamin D affect cancer survival as well as cancer occurrence, as other studies have also suggested [40–42].

While no certain conclusion can be drawn from the ecological associations we have reported, it seems reasonable to suggest they indicate that vitamin D produced by solar UVB radiation protects against death from cancer and, perhaps, occurrence of cancer in the Chinese population. This inference is strengthened by the stronger evidence of inverse relationships between cancer and UVB in rural than in urban counties, which suggests that these relationships are more likely to be present in populations with a traditional agrarian lifestyle than in populations whose lifestyles have been altered by urbanization. Available evidence indicates that vitamin D insufficiency is not uncommon in China and occurs in infants, adolescents and adults [43–48]. There is also no reason to believe that dietary sources would be important to vitamin D nutrition in China [49]. Therefore, there is scope for an important effect of ambient UVB radiation on vitamin D levels in China.

Our data provide ecological support for an inverse relationship between ambient solar UVB radiation and mortality from and, to a lesser extent, incidence of cancer in China. While confounding by unmeasured and uncontrolled factors cannot be excluded as an explanation for these associations, they provide support for the possibility that vitamin D reduces risk of cancer or of death after a diagnosis of cancer in Chinese people. Case–control or cohort studies, with measurement at least of sun exposure, serum vitamin D and cancer occurrence or outcome are needed to test this hypothesis. Its confirmation could have substantial significance for future cancer control in China.

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Appendix

The association between UVB irradiance and lung cancer mortality is potentially confounded by smoking. Assuming that there is no effect modification between UVB and smoking on lung cancer mortality, we can model the lung cancer mortality rate_{LC} by RR_{UVB} $[p_{\text{smoking}}\ \text{RR}_{\text{smoking}} + (1-p_{\text{smoking}})] \cong \text{RR}_{\text{UVB}}\ p_{\text{smoking}}\ \text{RR}_{\text{smoking}}$, where RR_{UVB} is the rate ratio for UVB exposure, p_{smoking} is the prevalence of smoking and $\text{RR}_{\text{smoking}}$ is the rate ratio for smoking. If we model the UVB rate ratio by $\exp(a + b \times \text{UVB})$ and smoking prevalence by $\exp(c + d \times \text{UVB})$ for constants b and d and intercepts a and c, then $\text{rate}_{\text{LC}} = \text{RR}_{\text{smoking}} \exp(a + c + (b + d)\text{UVB})$. We can then estimate an adjusted UVB rate ratio using $\exp(b + d)/\exp(d)$, which requires modeling the change in smoking prevalence by UVB.

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