

# **Socioeconomic status in relation to risks of major gastrointestinal cancers in Chinese adults: a prospective study of 0.5 million people**

*Running title: Socioeconomic status and risks of GI cancers*

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## 1   **Abstract**

2   **Background:** Low socioeconomic status (SES) is associated with higher risk of certain  
3   gastrointestinal (e.g. colorectal, pancreatic, and liver) cancers in Western populations.  
4   Evidence is very limited in China where correlates and determinants of SES differ from  
5   those in the West.

6   **Methods:** The prospective China Kadoorie Biobank recruited 512,715 adults (59%  
7   women, mean age 51 years) from 10 (5 urban, 5 rural) regions. During 10 years of follow-  
8   up, 27,940 incident cancers (including 3061 colorectal, 805 pancreatic, and 2904 liver)  
9   were recorded among 510,131 participants without prior cancer at baseline. Cox  
10   regression was used to estimate adjusted hazard ratios (HRs) for specific cancers  
11   associated with area-level (e.g. per capita gross domestic product, disposable income)  
12   and individual-level (e.g. education, household income) SES.

13   **Results:** Area-level SES and household income showed positive associations with  
14   incident colorectal and pancreatic cancer and inverse associations with liver cancer ( $p$  for  
15   trend  $<0.05$ ). Education showed no association with colorectal cancer but inverse  
16   associations with pancreatic and liver cancer, with adjusted HRs comparing university to  
17   no formal schooling being 1.05 (95% CI 0.85-1.29), 0.49 (0.28-0.85), and 0.61 (0.47-0.81),  
18   respectively. Potential risk factors (e.g. smoking, alcohol) explained partly the inverse  
19   associations of education with pancreatic and liver cancer (17.6% and 60.4%,  
20   respectively), respectively.

21   **Conclusions:** Among Chinese adults, the associations of SES with gastrointestinal  
22   cancers differed by cancer type and SES indicator. Potential risk factors partially explained  
23   the inverse associations of education with pancreatic and liver cancer.

24   **Impact:** The different associations between SES with gastrointestinal cancers may inform  
25   cancer prevention strategies.

26   **Keywords:** socioeconomic status, colorectal cancer, pancreatic cancer, liver cancer,  
27   Chinese

## 28    **Introduction**

29    Socioeconomic status (SES) is one of the most important contributors to health  
30    disparities.<sup>1</sup> In epidemiological studies, SES is often measured at group level, e.g. by  
31    neighbourhood income and deprivation, or at individual level, e.g. by family income,  
32    education, and social class indicators.<sup>1</sup> Studies in North America and Europe have shown  
33    that low SES is a risk factor for a range of non-communicable diseases including several  
34    types of cancer (e.g. gastrointestinal and lung cancers), with a similar pattern for cancer  
35    incidence and mortality.<sup>2-9</sup> There is also evidence that the excess risk in low-SES  
36    populations could be partially explained by the higher prevalence of lifestyle risk factors  
37    assessed at adulthood including smoking, alcohol, unhealthy diet, physical inactivity, and  
38    obesity.<sup>2-5</sup>

39    In China, the rates and patterns of cancer, particularly of major gastrointestinal cancers,  
40    and the associations of lifestyle factors with SES differ importantly from those in the  
41    West.<sup>10,11</sup> The age-standardised incidence rate of liver cancer is much higher in China  
42    than in Western populations,<sup>12</sup> whereas the converse is true for colorectal and pancreatic  
43    cancer.<sup>10,11</sup> In contrast to the patterns in Western countries, the prevalence of obesity,  
44    physical inactivity, and intake frequency of animal-origin foods in China are higher among  
45    individuals with high SES.<sup>13-15</sup> However, there is limited evidence on the associations of  
46    SES with cancer risk in the Chinese population. Furthermore, it is not clear to what extent  
47    the difference in prevalence of lifestyle risk factors could explain the SES-cancer  
48    associations. While affluence assessed either at group or individual level is a major driver  
49    of cancer disparities, education has been shown to be associated with several potential  
50    risk factors for cancer in Western populations (**Figure 1**).<sup>2,4-7</sup>

Therefore, we examined the associations of SES with the incidence and mortality of three major gastrointestinal (GI) cancers which have been shown to be associated with metabolic risk factors, i.e. colorectal, pancreatic, and liver cancer, in the China Kadoorie Biobank (CKB).<sup>16</sup> We also assessed whether risk factors (i.e. smoking, alcohol, physical inactivity, diet, adiposity, and hepatitis B virus [HBV] for liver cancer), could explain the associations of education with risks of incident cancers.

## **Materials and methods**

### *Study design*

The CKB study recruited 512,715 participants from 10 geographically defined localities (5 urban and 5 rural) in China between 2004 and 2008.<sup>17</sup> These 10 regions were selected across China to provide a diverse range of patterns of major chronic diseases and risk exposures, levels of socioeconomic development, population stability, and local infrastructure. Each of the 10 regions (i.e. administrative district) was selected from a prefecture-level city within a different province (**Figure 2** and **Supplementary Table 1**). In each region, 100-150 administrative units, either rural villages or urban residential committees, were randomly selected. We will use the term ‘area’ to describe prefecture-level cities and the term ‘region’ to refer to the 10 regions from which participants were recruited in CKB. Details of the study design, survey methods, and population characteristics have been described in the study protocol.<sup>17</sup> All participants eligible for this study had completed a written informed consent form. All methods were performed in accordance with relevant guidelines and regulations. The CKB study was approved by the Ethical Review Committee of the Chinese Center for Disease Control and Prevention and the Oxford Tropical Research Ethics Committee, University of Oxford. In 10 regions, all men and women aged 35 to 74 years who were permanently resident and without major

75 disability were eligible for the study. At local study assessment clinics, participants  
76 completed an interviewer-administered laptop-based questionnaire (sociodemographic  
77 characteristics, lifestyle factors, personal and family medical history) and underwent a  
78 physical examination (height, weight, hip and waist circumference, bioimpedance, lung  
79 function, blood pressure and heart rate). In addition, blood spot tests were used to  
80 measure random plasma glucose and hepatitis B surface antigen (HBsAg).

81 *Assessment of socioeconomic status*

82 SES was assessed at both area and individual levels. Area-level SES included prefecture-  
83 level per capita gross domestic product (GDP) and disposable income, obtained from the  
84 2011 Statistical Yearbook (median year of follow-up in CKB).<sup>18</sup> Per capita GDP was used  
85 as a general measure of area-level economic development, while disposable income was  
86 used to approximate the average household income in an area. Previous nationwide  
87 reports in China have suggested the inclusion of per capita GDP to inform the  
88 implementation of cancer prevention strategies.<sup>19</sup> Individual-level SES included self-  
89 reported highest education, household income, and an asset-based indicator. Household  
90 income was defined as annual income of all members living in a household received from  
91 work, investments, or pension. All participants were asked whether they owned a house or  
92 an apartment, toilet for private use, motor vehicle (e.g. car or motorbike), telephone or  
93 mobile phone, and refrigerator. An asset-based indicator was calculated as the total  
94 number of these five items in the household. All 10 regions were divided into three  
95 categories by per capita GDP (<60,000, 60,000-99,999, and ≥100,000 RMB/year) and  
96 disposable income (<20,000, 20,000-39,999, and ≥40,000 RMB/year) (**Figure 2** and  
97 **Supplementary Table 1**). Information on education covered six categories: no formal  
98 school, primary school, middle school, high school, technical school/college, and

99 university. Similarly, household income had six categories: <2500, 2500-4999, 5000-9999,  
100 10,000-19,999, 20,000-34,999, ≥35,000 RMB/year.

### 101 *Assessment of lifestyle risk factors*

102 For smoking, the questionnaire covered frequency, duration, amount, and type of tobacco,  
103 as well as the ages at which participants began smoking regularly and stopped smoking,  
104 and the main reason for stopping.<sup>1</sup> Smoking status was categorised as (1) never (not  
105 smoking at baseline and had smoked <100 cigarettes in lifetime), (2) occasional (neither  
106 never nor former smokers and had not stopped smoking completely for at least the 6  
107 months before baseline), (3) former regular (had smoked ≥100 cigarettes but had quit  
108 smoking by choice for ≥6 months before baseline), or (4) current regular smoker (ever  
109 smoked ≥1 cigarettes daily for ≥6 months). For alcohol drinking, the questionnaire covered  
110 frequency, the type (beer, wine or spirits) and amount of each type consumed in a typical  
111 drinking week, as well as the age at which participants started drinking.<sup>2</sup> Drinking status  
112 was classified into five categories as (1) abstainers (had never drunk alcohol in the past  
113 year and had not drunk weekly in the past), (2) occasional drinkers (had drunk alcohol  
114 occasionally, monthly but less than weekly, or during certain seasons, and had not drunk  
115 weekly in the past), (3) reduced-intake drinkers (had drunk alcohol occasionally, monthly  
116 but less than weekly, or during certain seasons, but had drunk weekly in the past), (4) ex-  
117 weekly drinkers (had never drunk alcohol in the past year but had drunk weekly in the  
118 past), or (5) weekly drinkers (often drank at least weekly during the past year).

119 All anthropometric measurements were taken to the nearest 0.1 cm or 0.1 kg by trained  
120 staff. Standing and sitting height were measured with a stadiometer. Sitting height was  
121 measured as the length of the body from the crown of the head to buttocks. Weight was  
122 measured with a body composition analyser (TANITA-TBF-300GS, Tanita Corporation,

123 Tokyo, Japan), subtracting the weight of clothing according to season (0.5 kg in summer  
124 and 2.0-2.5 kg in winter). Body mass index (BMI) was calculated as weight (in kilograms)  
125 divided by the square of height (in metres). BMI was classified into five categories (<20.0,  
126 20.0 to <22.5, 22.5 to <25.0, 25.0 to <27.0, and  $\geq 27.0$  kg/m<sup>2</sup>). BMI at age 25 (BMI<sub>25</sub>) was  
127 derived from the weight recalled at age 25 and the height measured at baseline. BMI<sub>25</sub>  
128 was missing in 81,880 participants due to difficulty with recalling and was imputed using  
129 multiple imputation ('mice' package in R). The imputation model included age at baseline,  
130 sex, regions, education, household income, smoking, alcohol, self-rated health, family  
131 history of cancer (any of father, mother, and siblings), and cumulative hazard of total  
132 cancer.

133 *Outcome assessment*

134 The CKB study ascertained the vital status of each participant (1) through periodical  
135 reports from China Centre for Disease Control and Prevention's Disease Surveillance  
136 Points system, (2) by regular checks against local residential and health insurance  
137 records, and (3) by annual active confirmation by street committees or village  
138 administrators.<sup>20</sup> Additional information about cancer incidence and hospitalisation was  
139 collected through linkages with cancer registries and national health insurance databases  
140 (with a coverage rate of 98% in all study regions). All disease events were coded using the  
141 10th Revision of International Classification of Diseases (ICD-10) by trained staff blinded  
142 to baseline information. By 1.1.2017, 44,066 (8.6%) participants had died, and 4751 (<1%)  
143 were lost to follow-up. Overall, 27,940 (5.4%) had developed cancer, including 3061  
144 colorectal (C18-20), 806 pancreatic (C25), and 2904 liver (C22) cancer cases.

145 *Statistical methods*

146 The present study excluded participants with a history of cancer at baseline (n=2584),  
147 leaving 510,131 individuals for the main analyses. Prevalences and mean values of  
148 baseline characteristics were calculated for categories of education and household income  
149 separately, standardised to the age, sex, and region structure of the CKB population.  
150 Cancer incidence and mortality rates were calculated for categories of area- and  
151 individual-level SES, standardised by age, sex, and region (for individual-level SES only).

152 In our analysis, we first examined the association of each area- and individual-level SES  
153 variable with risks of colorectal, pancreatic, and liver cancer. Cox proportional hazards  
154 models were used to estimate adjusted hazard ratios (HRs) of incidence of a specific  
155 cancer associated with SES, stratified by sex and region (10 regions, for individual-level  
156 SES only) and adjusted for age at baseline (basic model). Age was used as the underlying  
157 time scale, with delayed entry at age at baseline. For household income, the basic model  
158 also included household size. For variables with more than two categories, all HRs are  
159 presented with 'floating' standard errors to facilitate comparisons between groups.<sup>21</sup>

160 We then examined the extent to which possible risk factors explained the association of  
161 education with specific cancers. Possible risk factors were smoking, alcohol, obesity, and  
162 HBsAg (for liver cancer). These factors are selected because they potentially showed  
163 causal associations with education and they are associated with GI cancers in prospective  
164 studies (**Figure 1** and **Supplementary Table 2**). For obesity, we used BMI25 because  
165 BMI assessed at baseline might be affected by reverse causality.<sup>22,23</sup> Smoking was  
166 modelled as a categorical variable with six categories (never, occasional, former regular,  
167 and among current regular, 0-10, 11-20, and  $\geq 20$  cigarettes/day). Alcohol drinking was  
168 modelled as a categorical variable with seven categories (abstainers, ex-weekly drinkers,  
169 reduced-intake drinkers, occasional drinkers, and among weekly drinkers, 0-279, 280-419,



170 and  $\geq 420$  g/week). BMI<sub>25</sub> was modelled as a continuous variable. HBsAg was modelled  
171 as a categorical variable with four categories (negative, positive, unclear, or missing). We  
172 included each lifestyle risk factor in the basic model and examined the percent change in  
173 the logHRs comparing the highest and lowest categories of education or household  
174 income. The proportion of the association of education or household income with a  
175 specific cancer that was explained by a lifestyle risk factor was calculated as follows:  
176  $((\log\text{HR}_{\text{basic model}} - \log\text{HR}_{\text{adjusted model}}) / (\log\text{HR}_{\text{basic model}})) \times 100\%$ . Statistical analysis was  
177 done using R version 3.5.1.

## 178 Results

### 179 *Baseline characteristics by education and household income*

180 Among the 510,131 participants included, the mean (SD) baseline age was 51.5 (10.7)  
181 years, and 59% were women. Overall, 20.9% of participants had high school or higher  
182 education, and 18.0% had annual household income  $\geq 35,000$  RMB (conversion rate: 1  
183 RMB = 0.15 USD). Per capita GDP and disposable income of all 10 regions are shown in  
184 **Figure 2**. The correlation was low to moderate between area-level SES, household  
185 income, and education (Spearman correlation coefficient: 0.37 between area-level per  
186 capita GDP and household income, 0.51 between area-level disposable income and  
187 household income, and 0.28 between education and household income). Participants with  
188 higher education were less likely to smoke or drink alcohol and reported lower physical  
189 activity and higher sedentary leisure time (**Table 1**). They had lower systolic blood  
190 pressure and random plasma glucose, higher adiposity at baseline, and lower BMI at age  
191 25, and were less likely to test positive for HBsAg. The pattern of baseline characteristics  
192 by household income was generally similar to that by education except that no pattern was  
193 identified for HBsAg (**Supplementary Table 3**).

194    *Area- and individual-level SES and specific GI cancers*

195    For area-level SES, per capita GDP and disposable income showed positive associations  
196    with colorectal and pancreatic cancer and inverse associations with liver cancer (**Table 2**).  
197    Similar to area-level SES, household income showed positive associations with colorectal  
198    and pancreatic cancer and an inverse association with liver cancer (**Table 3**). There were  
199    also positive associations of the number of assets (apartment/house, private toilet, motor  
200    vehicle, refrigerator, and phone) with colorectal and pancreatic cancer and an inverse  
201    association with liver cancer (**Table 3** and **Supplementary Table 4**). By contrast,  
202    education showed inverse associations with pancreatic and liver cancer and no  
203    association with colorectal cancer (**Table 3**).

204    *Effects of potential risk factors on education with risks of cancers*

205    For pancreatic cancer (**Figure 3**), differences in the prevalence of smoking, alcohol, and  
206    young adulthood obesity explained between 6.0% (BMI25) and 7.3% (alcohol) of the  
207    inverse association for education, with the three factors together explaining 17.6% of the  
208    inverse association. For liver cancer (**Figure 3**), differences in the prevalence of smoking,  
209    alcohol, young adulthood obesity, and HBsAg explained between 4.1% (BMI25) and  
210    30.7% (HBsAg) of the inverse association for education with the four factors together  
211    explaining 60.4% of the inverse association.

212    *Sensitivity analyses*

213    The associations of area- and individual-level SES with risks of the three cancers did not  
214    differ by age at baseline or region (**Supplementary Figures 1-2**). The associations of  
215    area-level SES with colorectal cancer and the associations of individual-level SES with the  
216    three cancers did not differ by sex (**Supplementary Figure 3**). For area-level SES, the

217 positive associations with pancreatic cancer were stronger in men, while the inverse  
218 associations with liver cancer were stronger in women (**Supplementary Figure 3**). For  
219 colorectal cancer, the positive associations of SES were stronger for colon than rectal  
220 cancer ( $p$  for heterogeneity  $<0.001$ - $0.02$ , **Supplementary Table 5**), except for per capita  
221 GDP ( $p$  for heterogeneity  $0.56$ ). For cancer mortality (**Supplementary Table 6**), the  
222 positive associations for household income and assets attenuated towards the null for  
223 colorectal cancer but changed little for other SES variables. For pancreatic and liver  
224 cancer, the associations with mortality were similar to those with incidence. The  
225 associations of education with the three GI cancers did not differ by household income  
226 (**Supplementary Figure 4**). The associations of household income with pancreatic and  
227 liver cancer did not differ by education, whereas the positive association for colorectal was  
228 weaker among participants with higher level of education (**Supplementary Figure 4**).

## 229 Discussion

230 In this adult population from 10 diverse urban and rural regions of China, the associations  
231 of SES with specific GI cancers differed by cancer type and SES indicator. For area-level  
232 SES, there were positive associations of per capita GDP and disposable income with  
233 colorectal and pancreatic cancer and inverse associations with liver cancer. For these  
234 three cancers, the patterns for household income and numbers of assets were similar to  
235 those for area-level SES. By contrast, education showed inverse associations with  
236 pancreatic and liver cancer and no association with colorectal cancer. For pancreatic and  
237 liver cancer, differences in the prevalence of smoking, alcohol, young adulthood adiposity,  
238 and HBsAg (for liver cancer) partially explained the inverse associations for education.

239 For individual-level SES, the majority of previous studies in North America and Europe  
240 have shown inverse associations of education with colorectal, pancreatic, and liver cancer

(**Supplementary Figure 5**),<sup>4-6,24-26</sup> In CKB, findings for pancreatic and liver cancer were consistent with previous studies in Western populations. For colorectal cancer, however, there was no association for education, in line with a European cohort.<sup>4</sup> For household income, a US cohort reported a null association with colorectal cancer,<sup>24</sup> while two Korean cohort studies reported a null association with colorectal cancer and an inverse association with liver cancer (**Supplementary Figure 5**).<sup>27,28</sup> Our finding for liver cancer in CKB was consistent with the Korean studies where HBV is also the major risk factor,<sup>27</sup> while we showed positive associations of household income with colorectal and pancreatic cancer. For pancreatic and colorectal cancer, we observed an inconsistent pattern for education and income (i.e. household income and assets). This is possibly because of the opposite associations of SES indicators with potential risk factors for these cancers (**Table 1** and **Supplementary Table 3**). For example, participants with higher education were less likely to be regular drinkers and smokers. While participants with higher household income were more likely to be regular drinkers, there was no clear pattern for smoking status. In addition, the positive associations for income might reflect the higher prevalence of an unhealthful lifestyle (e.g. low physical activity, high sedentary leisure time, high consumption of energy and animal-origin foods) among the wealthy population,<sup>14,15,29,30</sup> which may be difficult to quantify in regression models. For area-level SES, previous prospective studies in North America and Europe have shown lower risks of colorectal, liver, and pancreatic cancer in neighbourhoods with higher income or lower deprivation (**Supplementary Figure 6**).<sup>3,7-9,25,31-34</sup> In CKB, the risk of liver cancer was lower in regions with higher per capita GDP and disposable income, consistent with previous studies in Western populations and in China.<sup>35,36</sup> In contrast, risks of colorectal and pancreatic cancer in CKB were higher in regions with higher per capita GDP and disposable income,

265 consistent with previous reports from the National Central Cancer Registry that assessed  
266 urbanisation rates and per capita GDP.<sup>35,36</sup>

267 The associations of SES with cancer are likely to reflect the complex relationships  
268 between SES, lifestyle risk factors, healthcare, and cancer risk.<sup>2,37</sup> Both CKB and previous  
269 studies have shown that potential risk factors (mostly lifestyle-related) could partially  
270 explain the inverse associations of education with cancer risk. When additionally adjusting  
271 for smoking, alcohol, diet, physical activity, and BMI, the NIH-AARP Diet and Health Study  
272 in the US reported that the inverse associations with pancreatic and liver cancer  
273 attenuated towards the null (50% reduction for pancreatic and 60% for liver).<sup>2,5</sup> In CKB,  
274 smoking, alcohol, and young adulthood adiposity explained 17% of the inverse association  
275 with pancreatic cancer, while smoking, alcohol, young adulthood adiposity, and HBV  
276 explained 60% of the association with liver cancer. Compared with household income,  
277 educational attainment is more strongly related to early life SES which is important in the  
278 adoption and maintenance of a healthy lifestyle in adulthood.<sup>38</sup> Indeed, Mendelian  
279 randomisation studies have shown that lower education is causally associated with  
280 smoking, alcohol, obesity, and possibly HBV infection, which are associated with cancer  
281 risk (**Figure 1**).<sup>39</sup> In contrast, household income reflects adulthood SES which may not  
282 capture SES over the life course and may also be subject to reverse causality.<sup>40</sup>

283 For area-level SES, the patterns for colorectal and pancreatic cancer were opposite in  
284 CKB and Western countries. It is possible that the excess risks in high-income individuals  
285 in CKB may be partly explained by the higher prevalence of sedentary lifestyle and a diet  
286 rich in energy and animal-origin foods and low in dietary fibre and wholegrains,<sup>14,15,29,30</sup>  
287 which may be difficult to evaluate by individual-level factors in regression models. The  
288 positive associations of area-level and household income with colorectal cancer incidence

289 may also reflect the lack of population-based screening in China.<sup>43</sup> Randomised controlled  
290 trials in high-income countries have shown that colorectal cancer screening is associated  
291 with a lower risk of developing colorectal cancer.<sup>44</sup> In the US, there was a positive  
292 association between area-level household income with colorectal cancer incidence  
293 between 1973-1998 and the positive association became inverse after 1998 when  
294 colorectal cancer screening was introduced.<sup>45</sup> It is possible that individuals with high SES  
295 in China have better access to health care services and therefore are more likely to be  
296 diagnosed with colorectal cancer.<sup>46-49</sup>

297 The strengths of the CKB include its prospective design, the large and diverse study  
298 population with complete follow-up, and the ability to assess area- and individual-level  
299 SES and a range of risk factors for cancer. This study also has limitations. First, the CKB  
300 cohort included 5 urban and 5 rural areas and may not have covered substantial SES  
301 disparities across the country. Second, factors related to access to, and use of, health care  
302 services were not collected, which may explain the SES-cancer associations.  
303 Representative national surveys showed that individuals with higher education and income  
304 were more likely to utilise preventive health services including immunisation and cancer  
305 screening (**Supplementary Table 7**). However, only 1% of individuals reported cancer  
306 screening in the past year, which is unlikely to explain the SES-cancer associations in the  
307 current study. Third, other unmeasured or unknown variables might partly explain the  
308 associations of SES with cancer risk (e.g. comorbidities, medications, occupational  
309 exposures, environmental chemicals, built environment, access and use of health care  
310 services).<sup>50</sup> However, a sensitivity analysis showed that an unaccounted for variable would  
311 have to be associated with SES and cancer with a relative risk of ~3 to explain away the  
312 observed HR (**Supplementary Table 8**).<sup>51</sup>

313 In conclusion, both area- and individual-level income showed positive associations with  
314 risks of colorectal and pancreatic cancer and inverse associations with liver cancer. For  
315 education, there were inverse associations with pancreatic and liver cancer and no  
316 association with colorectal cancer. The inverse associations of education with pancreatic  
317 and liver cancer may be explained, at least to a certain extent, by potential risk factors  
318 particularly smoking, alcohol, young adulthood adiposity, and HBV (for liver cancer). More  
319 studies are warranted in the Chinese population to understand the SES-cancer  
320 associations to inform targeted interventions and track cancer disparities.

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## **Conflicts of interest**

We declare that we have no conflict of interest.



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**Table 1. Baseline characteristics by level of education**

Variable*	Highest education					
	No formal school (n=95,221)	Primary school (n=165,216)	Middle school (n=144,913)	High school (n=77,527)	Technical/college (n=18,294)	University (n=11,720)
Age (SD), year	52.3 (10.2)	51.8 (4.4)	51.1 (3.6)	51.2 (5.0)	51.0 (8.1)	50.9 (8.1)
Female, %	83.3	60.4	47.1	43.6	33.2	27.1
<b>Socioeconomic and lifestyle factors</b>						
Urban region, %	20.5	26.5	56.1	74.6	89.9	93.9
Household income ≥35 000 RMB/year, %	9.6	12.3	17.8	27.3	43.6	54.8
Ever regular smoking, %						
Male	69.6	71.5	68.6	61.8	51.5	43.2
Female	5.3	4.0	2.4	1.5	1.2	0.2
Weekly drinking, %						
Male	31.9	33.7	33.7	31.2	30.3	29.5
Female	2.3	1.8	2.0	1.8	2.0	2.0
Total physical activity (SD), MET-h/day	20.4 (14.3)	21.1 (14.3)	20.7 (14.3)	19.3 (12.7)	17.3 (9.0)	17.3 (8.1)
Sedentary leisure time (SD), h/day	2.8 (1.7)	3.0 (1.5)	3.2 (1.5)	3.3 (1.5)	3.4 (1.5)	3.3 (1.5)
<b>Daily intake, %</b>						
Fresh fruits	11.7	14.6	21.0	28.2	40.0	41.7
Fresh vegetables	93.1	94.3	95.3	95.9	97.1	98.3
Red meat	23.8	26.8	30.6	35.4	43.7	46.0
<b>Blood pressure and anthropometry</b>						
SBP (SD), mmHg	133.3 (23.3)	131.6 (21.4)	130.4 (19.4)	129.3 (19.2)	127.6 (19.2)	126.1 (19.3)
RPG (SD), mmol/L	6.2 (2.5)	6.1 (2.4)	6.1 (2.3)	6.0 (2.1)	6.1 (2.2)	6.0 (2.2)
BMI (SD), kg/m <sup>2</sup>	23.7 (3.5)	23.7 (3.4)	23.7 (3.3)	23.7 (3.3)	23.8 (3.2)	23.9 (3.2)
Waist circumference (SD), cm	80.3 (10.0)	80.6 (9.7)	80.5 (9.6)	80.4 (9.7)	80.7 (9.9)	81.1 (10.0)
Hip circumference (SD), cm	90.5 (6.8)	90.9 (6.7)	91.2 (6.8)	91.4 (6.6)	92.0 (6.2)	92.5 (6.3)
Waist to hip ratio (SD)	0.89 (0.07)	0.89 (0.07)	0.88 (0.07)	0.88 (0.07)	0.88 (0.08)	0.88 (0.07)
Body fat percentage (SD), %	28.1 (8.8)	28.1 (8.9)	28.1 (8.1)	27.9 (7.6)	28.2 (6.9)	27.8 (6.8)
BMI at age 25, kg/m <sup>2</sup>	22.2 (2.8)	22.2 (2.6)	21.9 (2.5)	21.6 (2.5)	21.3 (2.4)	21.2 (2.4)
Height (SD), cm	157.3 (7.2)	158.1 (7.8)	159.0 (8.0)	159.8 (8.0)	160.8 (7.8)	161.3 (7.9)
<b>HBsAg positive, %</b>	3.3	3.3	3.0	2.8	2.6	1.9

Abbreviations: BMI=body mass index, MET=metabolic equivalent of task, RPG=random plasma glucose, SBP=systolic blood pressure.

\* Results were standardised by age, sex, and region (where appropriate). Values are means unless otherwise stated.

P-values for trend: all <0.001 except for weekly drinking in females (0.38).

**Table 2. Standardised incidence rates (per 100,000) and HRs of colorectal, pancreatic, and liver cancer by area-level SES**

	Colorectal			Pancreatic			Liver		
	No. cases	Incidence rate (per 100,000)	HR (95% CI)	No. cases	Incidence rate (per 100,000)	HR (95% CI)	No. cases	Incidence rate (per 100,000)	HR (95% CI)
<b>Urbanity</b>									
Rural	1309	46.6	Reference	396	14.1	Reference	1659	59.0	Reference
Urban	1752	80.4	1.58 (1.47, 1.70)	409	18.7	1.19 (1.04, 1.37)	1245	56.9	0.91 (0.84, 0.98)
<b>Per capita GDP (RMB)</b>									
<60,000	489	41.9	1.00 (0.92, 1.09)	126	8.8	1.00 (0.84, 1.19)	838	63.7	1.00 (0.93, 1.07)
60,000-99,999	1487	65.3	1.73 (1.64, 1.82)	321	14.1	1.42 (1.27, 1.58)	1273	57.6	0.88 (0.83, 0.93)
≥100,000	1085	72.1	1.95 (1.84, 2.07)	358	24.8	2.48 (2.23, 2.75)	793	53.8	0.84 (0.78, 0.90)
<b>Disposable income (RMB)</b>									
<20,000	649	41.4	1.00 (0.93, 1.08)	200	12.8	1.00 (0.87, 1.15)	1019	64.2	1.00 (0.94, 1.06)
20,000-39,999	1241	62.1	1.41 (1.33, 1.49)	264	12.5	0.94 (0.83, 1.06)	1101	55.3	0.81 (0.76, 0.86)
≥40,000	1171	84.9	1.87 (1.77, 1.98)	341	24.8	1.72 (1.55, 1.91)	784	55.8	0.80 (0.75, 0.86)

Model was stratified by sex and region and adjusted for age at baseline. Conversion rate: 1 RMB = 0.15 USD.

P-value for trend by per capita GDP and disposable income: all <0.01.

**Table 3. Standardised incidence rates (per 100,000) and HRs of colorectal, pancreatic, and liver cancer by individual-level SES**

	Colorectal			Pancreatic			Liver		
	No. cases	Incidence rate (per 100,000)	HR (95% CI)	No. cases	Incidence rate (per 100,000)	HR (95% CI)	No. cases	Incidence rate (per 100,000)	HR (95% CI)
<b>Education</b>									
No formal school	653	64.7	1.00 (0.92, 1.09)	228	20.9	1.00 (0.86, 1.16)	622	68.0	1.00 (0.91, 1.09)
Primary school	1048	61.2	1.07 (1.00, 1.14)	283	16.0	0.84 (0.75, 0.95)	1141	62.8	1.00 (0.94, 1.06)
Middle school	764	62.1	1.18 (1.09, 1.27)	161	13.5	0.83 (0.70, 0.98)	697	52.8	0.92 (0.85, 1.00)
High school	409	61.6	1.09 (0.99, 1.21)	102	16.8	0.94 (0.76, 1.15)	320	47.5	0.79 (0.70, 0.88)
Technical school	97	42.1	0.95 (0.78, 1.16)	18	11.9	0.59 (0.37, 0.95)	71	32.7	0.68 (0.54, 0.86)
University	90	103.4	1.05 (0.85, 1.29)	13	4.3	0.49 (0.28, 0.85)	53	25.0	0.61 (0.47, 0.81)
<b>Household income (RMB)</b>									
<2,500	98	51.1	1.00 (0.81, 1.24)	34	8.8	1.00 (0.69, 1.44)	168	88.0	1.00 (0.85, 1.18)
2,500 to 4,999	189	49.6	1.16 (1.00, 1.35)	62	16.8	1.19 (0.92, 1.55)	265	79.4	0.84 (0.74, 0.96)
5,000 to 9,999	446	54.3	1.31 (1.19, 1.44)	123	14.0	1.22 (1.01, 1.46)	606	68.1	0.85 (0.78, 0.92)
10,000 to 19,999	906	61.9	1.59 (1.49, 1.69)	218	15.1	1.36 (1.19, 1.55)	841	58.2	0.71 (0.67, 0.76)
20,000 to 34,999	824	66.6	1.79 (1.67, 1.92)	203	17.8	1.62 (1.40, 1.86)	608	50.6	0.62 (0.57, 0.67)
≥35,000	598	69.9	1.86 (1.70, 2.02)	165	20.2	1.88 (1.59, 2.21)	416	47.6	0.57 (0.52, 0.63)
<b>Assets</b>									
None	149	46.2	1.00 (0.85, 1.18)	50	13.8	1.00 (0.75, 1.33)	263	83.2	1.00 (0.88, 1.13)
One	273	55.5	1.22 (1.08, 1.38)	85	14.5	1.22 (0.98, 1.52)	398	74.3	0.98 (0.89, 1.09)
Two	500	59.5	1.38 (1.26, 1.50)	127	15.1	1.23 (1.04, 1.47)	581	63.6	0.95 (0.87, 1.03)
Three	960	66.0	1.55 (1.45, 1.66)	227	15.6	1.35 (1.18, 1.55)	793	58.2	0.86 (0.80, 0.92)
Four	737	64.2	1.53 (1.43, 1.65)	181	16.4	1.39 (1.20, 1.61)	567	51.5	0.75 (0.69, 0.82)
Five	442	69.3	1.66 (1.51, 1.82)	135	21.8	1.89 (1.59, 2.24)	302	44.7	0.67 (0.60, 0.75)

Model was stratified by sex and region (for individual-SES only) and adjusted for age at baseline, household size and education (for household income and assets), and household income (for education).

P-value for trend: all <0.001 except for education and colorectal cancer (0.45).

## Figure legends

### Figure 1. The associations of education, potential risk factors, and GI cancer risk

Conceptual model of the associations of education, potential risk factors, and GI cancer risk. It is hypothesized that the indirect effect of the association of education with GI cancer risk is mediated through possible risk factors and access to and/or use of healthcare services, while the direct effect is the potential biological or carcinogenic factor.<sup>37</sup> However, no data is currently available to examine the direct effect between SES and cancer or the effect of access to and/or utilisation of health services on the SES-cancer associations. To assess the causal effects of education on possible risk factors for cancer, independent summary statistics from genome wide association studies (GWAS) were obtained for education single nucleotide polymorphisms (SNPs) from the Social Science Genetic Association Consortium (PMID: 27225129), for HBV from a Korean study (PMID: 23760081), and for smoking the TAG consortium (PMID: 20418890). The SNPs for alcohol (the UK Biobank) and BMI (the GIANT consortium) were obtained through MR-Base ([www.mrbase.org](http://www.mrbase.org)). We used a conventional inverse-variance weighted (IVW) Mendelian randomisation analysis in which the SNP to education estimate is regressed on the SNP to each risk factor, with the y-axis intercept forced through the origin. The pooled relative risks (RRs) between risk factors and cancer are extracted from the largest meta-analysis of prospective studies (PMID: 18193270, 19816941, 19720726, 19142968; World Cancer Research Fund Continuous Update Project), except for HBV (meta-analysis of cross-sectional, case-control, and prospective studies; PMID: 28230038). \* For HBV the HR is not plotted due to its very high value.

### Figure 2. The locations and area-level SES of the 10 regions in CKB

The geographical locations, per capita GDP, and disposable income of the 10 CKB regions are shown separately for urban and rural areas. A prefecture-level city is an

administrative unit comprising a main central urban area and its surrounding rural area consisting of smaller cities, towns, and villages. A prefecture-level city ranks below a province and above a county in China's administrative structure.

**Figure 3. Associations of education and pancreatic and liver cancer with additional adjustment for potential risk factors**

The basic model was stratified by sex and region and adjusted for age at baseline. The adjusted model included variables in the basic model plus each risk factor. The likelihood ratio test was used to compare the basic model and the adjusted model. *P*-values from the comparison were reported for each risk factor. Boxes represent HRs associated with central adiposity by number of metabolic risk factors. The sizes of the boxes are proportional to the inverse of the 'floated' variance of the log hazard ratios.