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## Original Research

# Different trends in colorectal cancer mortality between age groups in China: an age-period-cohort and joinpoint analysis



X. Liu <sup>a</sup>, Y. Bi <sup>b</sup>, H. Wang <sup>b</sup>, R. Meng <sup>a</sup>, W. Zhou <sup>a</sup>, G. Zhang <sup>a</sup>, C. Yu <sup>a</sup>,  
Z.-J. Zhang <sup>a,\*</sup>

<sup>a</sup> Department of Epidemiology and Biostatistics, School of Health Sciences, Wuhan University, Wuhan 430071, China

<sup>b</sup> Department of Occupational and Environmental Health, School of Health Sciences, Wuhan University, Wuhan 430071, China

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## ABSTRACT

**Objectives:** China is undergoing a rapid aging transition. The trends in age-specific mortality rates from colorectal cancer remain unknown, and a number of studies have not distinguished the age, period, and cohort effects simultaneously.

**Study design:** A descriptive study was implemented with a joinpoint regression analysis and age–period–cohort (APC) model based on the intrinsic estimator (IE).

**Methods:** Age-specific mortality rates of colorectal cancer (1987–2016) were collected by gender (men/women) and region (urban/rural). The average annual percentage change (AAPC) and relative risks in the trend were identified using joinpoint Poisson regression and APC model (IE), respectively.

**Results:** Joinpoint regression analysis revealed that the rates decreased in the younger (men aged <45 years and women aged <75 years) but increased in the older (men aged >75 years and women aged >80 years) age groups. The APC model (IE) showed that the rates increased with age and time period but decreased with birth cohorts. But from 2000 to 2005, the period effects showed a substantial decline among urban residents. From the 1910–1914 to the 1915–1919 birth cohort, mortality increased among men, and from the 1925–1929 to the 1930–1934 birth cohort, mortality increased among rural residents.

**Conclusions:** The trends in colorectal cancer mortality are different between age groups. The younger age groups show a decreasing trend, whereas the older age groups an increasing trend. Cost-effective prevention and control should be implemented more in the elderly and for older cohorts at high risk.

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\* Corresponding author. Department of Epidemiology and Biostatistics, School of Health Sciences, Wuhan University, No. 185 Donghu Road, Wuhan 430071, China.

E-mail address: [zhang22968@163.com](mailto:zhang22968@163.com) (Z.-J. Zhang).

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## Introduction

Colorectal cancer is the third most commonly diagnosed cancer in men and the second in women, with an estimated 1.4 million cases and 693,900 deaths occurring worldwide in 2012.<sup>1</sup> Nearly three-fifths of all colorectal cancer deaths occur in developing countries, and colorectal cancer was ranked fifth for all cancer deaths in 2013 in China.<sup>2</sup> It is of public health significance to control the burden of colorectal cancer.

There has also been significant improvement in screening, diagnosis,<sup>3</sup> treatment,<sup>4</sup> and even chemoprevention<sup>5–7</sup> for colorectal cancer, but the temporal trend of colorectal cancer mortality in China remains unclear. Most previous studies assessed the trends in colorectal cancer mortality using age-standardized rates and reported an increasing trend in China.<sup>8,9</sup> Yang et al.<sup>9</sup> found an increase in colorectal cancer mortality in the older age groups (65+ years) from 1987 to 1999, and Center et al.<sup>8</sup> found a 0.78% increase per year in men from 1985 to 2005. However, China has undergone a rapid aging transmission, as well as changes in lifestyle, dietary, physical activity, and medical care. In addition, national screening programs for colorectal cancer have been implemented since 1987 in China. All these changes may impact the mortality rates differently for different age groups. However, few studies have examined the trends in age-specific mortality rates from colorectal cancer. We, thus, examined the trends in mortality rates from colorectal cancer in each 5-year age group in China from 1987 to 2016.

## Methods

### Data source

Colorectal cancer mortality, as tabulated in the year of death, sex, 5-year age groups, and area (rural and urban) were extracted from the World Health Organization (WHO) mortality database for the period 1987–2000 and from the China Statistical Yearbook for 2002–2016. Colorectal cancer refers to cancers in the colon, rectum, or anus. Both the data sets were obtained from the cancer reporting system operated by the Center for Health Information and Statistics, which is considered to be nationally representative as it is based on a 10% sample of the national population (between 100 and 120 million persons).<sup>10–12</sup>

Colorectal cancer was coded by the International Classification of Disease (ICD)-9 (153–154) during 1987–2000 and the ICD-10 (C18–C21) during 2002–2016. The mortality data for 2001 were missing from the two databases; the mortality data in 2002 from the data set were deemed to be unreliable because of the transition from ICD-9 to ICD-10 in that year. Therefore, age-specific rates in 2001 and 2002 were imputed by using an interpolation method.<sup>13</sup>

### Joinpoint regression analysis

A joinpoint regression analysis was used to estimate the average annual percent change (AAPC) of mortality rates in each 5-year age group.<sup>14</sup> To compare, we also calculated age-

standardized mortality rates (ASMRs) for all ages (from 20 years and above) and truncated rates (TRs) (20–64 years, 65–85+ years), using the direct method based on the new WHO World Standard Population.<sup>15</sup>

The joinpoint analysis was performed using 'Joinpoint' software from the Surveillance Research Program of the US National Cancer Institute.<sup>16</sup>

### Age–period–cohort analysis

Mortality reflects death risks experienced by the population in the current year and the accumulation of health risks since birth. Age–period–cohort (APC) analysis could estimate age, period, and cohort effects simultaneously,<sup>17,18</sup> which can be used to decompose trends in colorectal cancer mortality rates and to give hypotheses regarding effective measures to address colorectal cancer in China. But collinearity problems were the general issues of the APC model application because there has a linear relationship among the age, period, and cohort (birth cohort = period – age). The APC model based on the intrinsic estimator (IE) not only solves the issue of model identification but also provides unbiased and relatively efficient estimation results.<sup>19,20</sup>

In the APC model (IE), age-specific mortality rates were recoded into consecutive 5-year periods from 1990 to 2015 and successive 5-year age groups (20–24, 25–29, ..., 80–84 years) to estimate age, period, and cohort effects of colorectal cancer mortality. The group above 85 years and groups under 20 years were excluded, which did not conform to the requirement of the APC model. The APC model could be expressed as:

$$Y_j = \mu + \alpha \text{ age}_j + \beta \text{ period}_j + \gamma \text{ cohort}_j + \varepsilon_i \quad (1)$$

where  $Y_j$  denoted the response variable—the net effect on colorectal cancer mortality for group  $j$ ,  $\alpha$ ,  $\beta$ , and  $\gamma$  denoted the coefficient of age, period, and cohort of the APC model, respectively, and  $\mu$  denoted the intercept of the model.  $\varepsilon_i$  denoted the residual of the APC model.

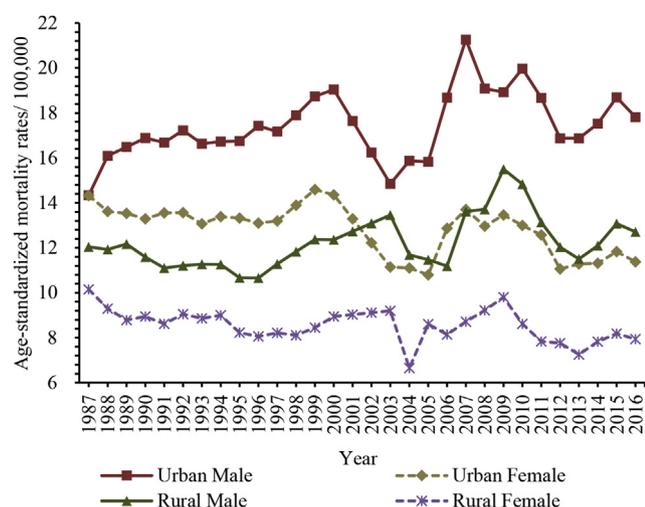
APC analysis was implemented using Stata 12.0 software (StataCorp, College Station, TX, USA). Deviance, Akaike information criterion, and Bayesian information criterion were used to check the degree of model fitting.

## Results

### Trend of ASMRs

Fig. 1 presents the ASMRs between 1987 and 2016. The rates did not change materially in urban or rural areas over the past 30 years.

Table 1 shows the joinpoint regression analysis for colorectal cancer mortality in men and women (aged more than 20 years) from 1987 to 2016. For ASMRs, the rates significantly decreased in women (AAPC: –0.61% in urban, –0.45% in rural) but slightly increased in men (0.47% in urban, 0.55% in rural); for TRs, the rates significantly decreased in the populations aged 20–64 years (–0.23% in urban men, –1.93% in urban women, –0.63% in rural men, –1.37% in rural women), but the rates increased over 65 years (0.79% in urban men, 0.10% in



**Fig. 1 – Age-standardized (world population) mortality rates of colorectal cancer between 1987 and 2016, according to gender and area.**

urban women, 1.32% in rural men, 0.20% in rural women) but there was no statistical significance in females.

#### Trends of age-specific mortality rates using joinpoint regression analyses

For the younger age groups (from the age group of 20–24 to 40–44 years), substantial declines were observed in the four populations. For the age group 45–49 years, the rates significantly declined in women (–1.80% in urban, –2.13% in rural), but there was no statistical significance in men (–0.56% in urban, –0.95% in rural). For the age group 50–54 years, the rates significantly declined in women (–0.98% in urban, –0.78% in rural) but not in men (0.90% in urban,  $P < 0.05$ ; –0.36% in rural,  $P > 0.05$ ). For the age group 55–59 years, the rates also significantly declined in women (–1.67% in urban, –0.78% in rural), while no statistically significant changes were observed in men (0.41% in urban, –0.12% in rural,  $P > 0.05$ ). For the older age groups (from the age group of 60–64 to 70–74 years), the rates significantly declined in women, while the rates increased in men in both areas. For the oldest age groups (80–84, 85+ years), the rates markedly increased in both areas for both sexes. Summarily, substantial declines were observed in the younger groups (men aged <45 years and women aged <75 years), including the age groups of 20–24, 25–29, 30–34, 35–39, and 40–44 years among men and from the age groups of 20–24 to 70–74 years among women, while more marked increases were observed in the older groups (men aged >75 years and women aged >80 years), including the age groups 80–84 and 85+ years among women and urban men and the age groups 75–79, 80–84, and 85+ years among rural men.

#### APC analysis

The APC model (IE) provided estimated coefficients for the age, period, and cohort effects (Supplementary Table A), which were calculated to the exponential value ( $\exp(\text{coef.}) = \text{ecoef.}$ ) (Table 2). The exponential value denotes

the mortality relative risk (RR) of a particular age, period, or birth cohort relative to average levels. We also plotted Fig. 2 based on the exponential value for reflecting the age, period, and cohort effect trends.

#### Age effects

Colorectal cancer mortality risk significantly increased with age, which indicated that colorectal cancer mortality might increase with advancing age. The RR of colorectal cancer mortality increased exponentially in the four populations from ages 20–24 to 80–84 years, and the RR of urban populations increased more quickly than that of rural populations. However, from ages 75–79 to 80–84 years, the mortality risks stopped increasing sharply and only exhibited a slight increase in rural females. From ages 20–24 to 80–84 years, the colorectal cancer mortality risks increased by 131.97, 112.48, 41.68, and 48.31 times in urban men, urban women, rural men, and rural women, respectively. These four values were calculated by the exact values of the coefficients.

#### Period effects

The period effects that provided substantial increases of mortality risks were observed among the four populations. For urban populations, the changes could be divided into one decelerating decrease and four accelerating increases. The RR stopped increasing and exhibited declining intervals from 2000 to 2005. For rural populations, there was one decelerating decrease in men but two decreases in women. The RR stopped declining and exhibited increasing intervals from 1995 to 2010

**Table 1 – The average annual percent changes in ASMRs, TRs, and age-specific mortality rates of colorectal cancer, 1987–2016.**

Age-group (years)	Urban		Rural	
	Male	Female	Male	Female
ASMRs	0.47*	–0.61*	0.55*	–0.45*
TRs (20–64)	–0.23*	–1.93*	–0.63*	–1.37*
TRs (65–85+)	0.79*	0.10	1.32*	0.20
20–24	–2.57*	–4.30*	–4.27*	–4.41*
25–29	–2.93*	–2.84*	–1.90*	–2.93*
30–34	–3.64*	–5.00*	–2.52*	–2.42*
35–39	–3.52*	–4.28*	–2.04*	–2.50*
40–44	–1.48*	–2.61*	–1.14*	–1.26*
45–49	–0.56	–1.80*	–0.95	–2.13*
50–54	0.90*	–0.98*	–0.36	–0.78*
55–59	0.41	–1.67*	–0.12	–0.78*
60–64	0.11	–1.63*	–0.03	–0.98*
65–69	0.31	–1.30*	0.40	–0.55*
70–74	–0.10	–1.00*	0.41	–0.45*
75–79	0.37	–0.22	1.52*	0.48
80–84	1.49*	1.19*	2.21*	1.06*
85+	2.47*	3.02*	3.06*	1.00

ASMRs, age-standardized mortality rates; WHO, World Health Organization; TRs, truncated rates.

ASMRs at all ages directly standardized on the basis of the new WHO World Standard Population. TRs (20–64 years), TRs (65+ years): age-standardized mortality rates were computed in two age groups (20–64 years, 65+ years), on the basis of the new WHO World Standard Population.

\*Significantly different from 0 at  $\alpha = 0.05$  ( $P < 0.05$ ).

**Table 2 – Colorectal cancer mortality relative risks due to age, period, and cohort effects.**

Factor	Urban male	Urban female	Rural male	Rural female
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
<b>Age</b>				
20–24	0.07 (0.01–0.33)	0.07 (0.01–0.38)	0.16 (0.06–0.42)	0.11 (0.03–0.43)
25–29	0.13 (0.05–0.34)	0.16 (0.06–0.44)	0.21 (0.10–0.44)	0.21 (0.09–0.51)
30–34	0.27 (0.14–0.55)	0.32 (0.15–0.66)	0.29 (0.16–0.54)	0.39 (0.20–0.76)
35–39	0.34 (0.19–0.62)	0.41 (0.22–0.75)	0.36 (0.21–0.62)	0.43 (0.24–0.80)
40–44	0.49 (0.30–0.80)	0.55 (0.33–0.93)	0.51 (0.33–0.80)	0.55 (0.33–0.92)
45–49	0.73 (0.50–1.09)	0.74 (0.48–1.14)	0.69 (0.48–1.00)	0.70 (0.45–1.09)
50–54	1.01 (0.73–1.39)	1.04 (0.73–1.47)	0.99 (0.73–1.34)	1.01 (0.71–1.44)
55–59	1.43 (1.10–1.86)	1.29 (0.96–1.71)	1.29 (1.00–1.66)	1.33 (0.99–1.80)
60–64	2.38 (1.93–2.94)	2.19 (1.74–2.74)	1.91 (1.56–2.34)	1.92 (1.51–2.44)
65–69	3.43 (2.84–4.15)	3.04 (2.48–3.73)	2.72 (2.27–3.25)	2.46 (1.98–3.05)
70–74	5.05 (4.13–6.17)	4.32 (3.49–5.34)	3.93 (3.29–4.70)	3.52 (2.85–4.35)
75–79	6.75 (5.32–8.56)	6.00 (4.69–7.70)	4.93 (4.03–6.04)	5.23 (4.13–6.62)
80–84	8.86 (6.61–11.87)	7.57 (5.59–10.26)	6.53 (5.12–8.33)	5.49 (4.12–7.30)
<b>Period</b>				
1990	0.79 (0.64–0.97)	0.93 (0.75–1.15)	0.86 (0.71–1.04)	0.91 (0.73–1.13)
1995	0.81 (0.71–0.94)	0.96 (0.83–1.12)	0.78 (0.68–0.90)	0.90 (0.76–1.06)
2000	1.01 (0.92–1.10)	1.08 (0.98–1.20)	0.92 (0.82–1.02)	0.98 (0.86–1.12)
2005	0.94 (0.85–1.03)	0.82 (0.73–0.92)	1.00 (0.90–1.12)	1.04 (0.91–1.18)
2010	1.27 (1.11–1.46)	1.10 (0.95–1.28)	1.27 (1.11–1.45)	1.02 (0.87–1.20)
2015	1.30 (1.07–1.58)	1.15 (0.93–1.42)	1.27 (1.07–1.51)	1.18 (0.97–1.45)
<b>Cohort</b>				
1910–1914	2.31 (1.51–3.55)	1.92 (1.20–3.07)	1.73 (1.15–2.60)	2.31 (1.45–3.66)
1915–1919	2.49 (1.74–3.57)	2.04 (1.37–3.04)	1.92 (1.37–2.70)	1.90 (1.29–2.80)
1920–1924	2.19 (1.60–2.99)	2.12 (1.49–3.01)	1.74 (1.29–2.36)	1.64 (1.16–2.31)
1925–1929	2.19 (1.65–2.89)	2.11 (1.53–2.92)	2.00 (1.52–2.63)	1.63 (1.19–2.23)
1930–1934	2.12 (1.63–2.77)	2.18 (1.60–2.98)	2.22 (1.71–2.88)	2.09 (1.56–2.82)
1935–1939	1.85 (1.41–2.42)	2.08 (1.52–2.85)	1.78 (1.37–2.32)	1.69 (1.25–2.29)
1940–1944	1.42 (1.05–1.92)	1.66 (1.16–2.36)	1.75 (1.31–2.34)	1.63 (1.16–2.28)
1945–1949	1.39 (0.98–1.97)	1.44 (0.96–2.16)	1.47 (1.05–2.06)	1.56 (1.06–2.29)
1950–1954	1.38 (0.92–2.07)	1.41 (0.89–2.23)	1.50 (1.02–2.19)	1.49 (0.96–2.31)
1955–1959	1.30 (0.81–2.09)	1.35 (0.80–2.28)	1.26 (0.81–1.95)	1.21 (0.73–2.01)
1960–1964	1.10 (0.64–1.90)	1.07 (0.59–1.96)	1.06 (0.64–1.76)	0.79 (0.43–1.46)
1965–1969	0.97 (0.52–1.79)	0.81 (0.40–1.61)	0.96 (0.55–1.68)	0.95 (0.50–1.80)
1970–1974	0.58 (0.28–1.23)	0.64 (0.29–1.42)	0.87 (0.47–1.61)	0.73 (0.35–1.54)
1975–1979	0.56 (0.23–1.32)	0.50 (0.19–1.31)	0.56 (0.26–1.24)	0.65 (0.27–1.52)
1980–1984	0.34 (0.10–1.10)	0.40 (0.12–1.34)	0.47 (0.18–1.23)	0.48 (0.16–1.41)
1985–1989	0.37 (0.09–1.47)	0.27 (0.05–1.55)	0.50 (0.17–1.49)	0.39 (0.10–1.57)
1990–1994	0.26 (0.03–2.59)	0.37 (0.04–3.26)	0.29 (0.05–1.60)	0.38 (0.05–2.70)
1995–1999	0.23 (0.00–23.56)	0.25 (0.00–53.28)	0.13 (0.00–8.9)	0.21 (0.00–24.66)
Deviance	10.19	11.25	15.49	17.16
AIC	5.18	4.96	5.13	4.84
BIC	–181.51	–180.44	–176.21	–174.54

RR, relative risk [RR = exp(coefficient)]; CI, confidence interval; AIC, Akaike information criterion; BIC, Bayesian information criterion.

among men, and the increasing intervals among women was from 1995 to 2005 and from 2010 to 2015. However, the mortality risk obviously increased among rural women from 2010 to 2015. From 1990 to 2015, the colorectal cancer mortality risks increased by 1.65, 1.24, 1.48, and 1.30 times for urban men, urban women, rural men, and rural women, respectively. However, Fig. 2b differs from Fig. 1 in that the mortality did not change materially; the bias in Fig. 1 is assumed to be caused by mixed effects of one or both of the other two factors (age and cohort). In this study, the period effects exhibited significant increasing trends, and the cohort effects showed substantial declining trends in these groups. Therefore, the true period effect on colorectal cancer mortality was likely to increase monotonically with advancing period.

#### Birth cohort effects

Later birth cohorts experienced lower colorectal cancer mortality, with the exception of some individual cohorts. For men, the mortality risks significantly increased for the 1915–1919 cohort and subsequently decreased, and the mortality risks slightly increased among the rural residents from the 1925–1929 cohort to the 1930–1934 cohort. For women, the mortality risks significantly increased for the 1930–1934 birth cohort, as well as for the 1915–1919 and the 1920–1924 urban cohorts. However, for women, the mortality risk also increased for the 1990–1994 urban cohort and the 1965–1969 rural cohort. From the 1910–1914 to the 1995–1999 cohort, the colorectal cancer mortality risks decreased by 89.86%, 87.13%, 92.48%, and 91.03% in urban

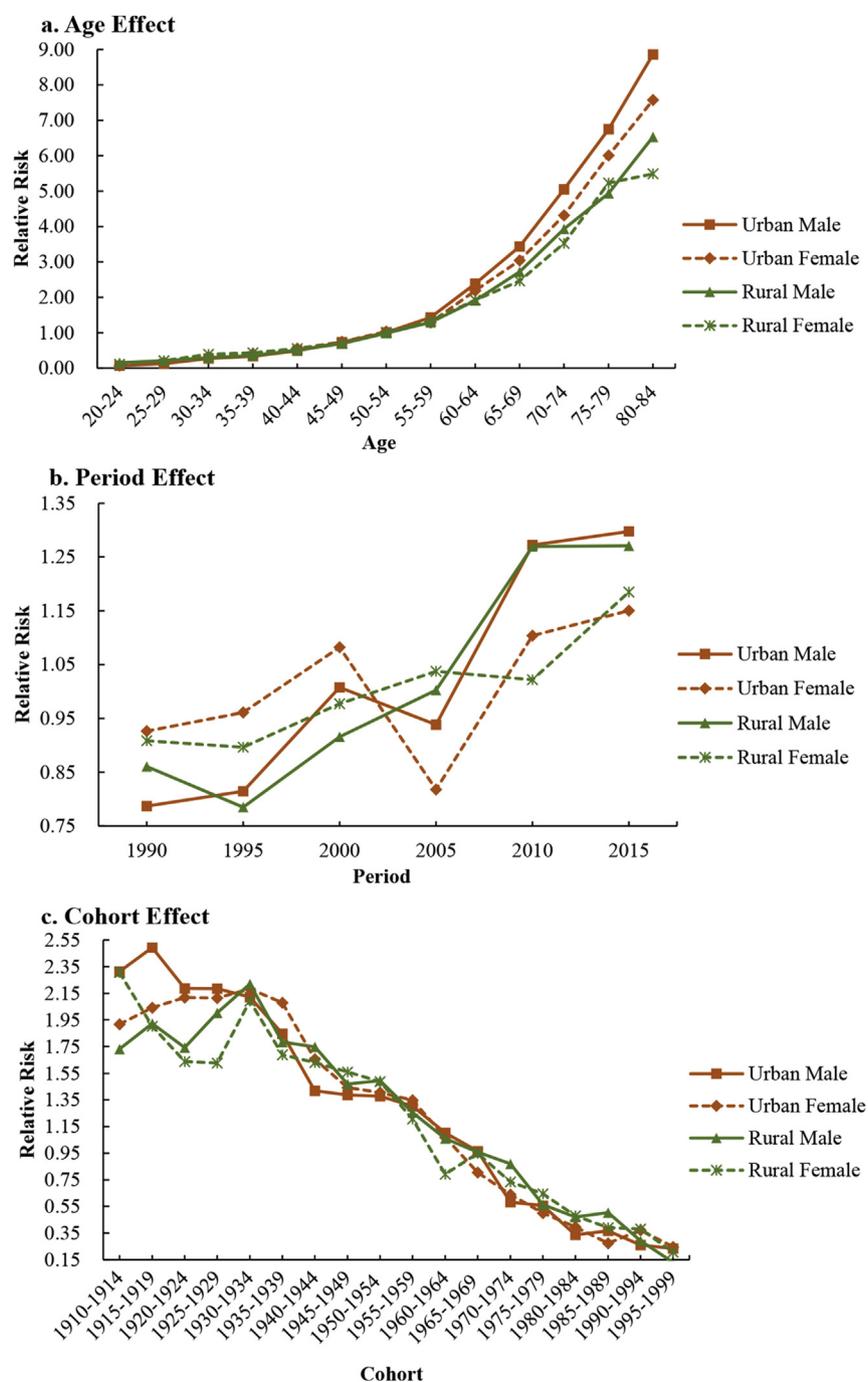


Fig. 2 – Colorectal cancer mortality relative risks due to (a) age; (b) period; and (c) cohort effects.

men, urban women, rural men, and rural women, respectively.

## Discussion

The findings showed that the colorectal cancer mortality rates markedly increased in the older population, i.e. men aged more than 75 years and women aged more than 80 years, but decreased in the younger population, i.e. men aged <45 years and women aged <75 years. By contrast, the APC model (IE) showed that the rates increased with age and time period but

decreased with birth cohorts. The true age, period, and birth cohort effects on mortality were discussed preliminarily in the following section.

It is noteworthy that Fig. 2a differs from Fig. 1 in that no marked increasing trend is shown in the four populations during 1987–2016, which was mainly related to China's aging progress.<sup>21</sup> As reported, the population aged 60 years and over in 2016 accounts for 16.7% of the total population,<sup>22</sup> and aging in China increased rapidly from 1980 to 2010.<sup>23</sup>

Age effects on colorectal cancer mortality showed an exponential growth trend with advancing age, which was consistent with the study's findings from Yang et al.<sup>9</sup> The

increasing trend in age effects was mainly influenced by biological factors. The elder people might be more exposed to malnutrition, which could cause an increase in colorectal cancer mortality.<sup>24,25</sup> Additionally, elder groups were vulnerable to comorbidity and frailty, which steadily increased among colorectal patients, and these factors were strongly related to the survival in them.<sup>26,27</sup> All these factors related to nutrition might cause the rising age trends in colorectal cancer mortality in China, America, and other East Asian and European countries. Nutrition management is probably one of the urgent issues to be addressed to control and prevent colorectal cancer mortality.

Period effects indicate influential factors that simultaneously affect all populations. Economical, environmental, and national policy factors could explain the increased period trend.<sup>28,29</sup> From 1989 to 2004, owing to the economy transformation and urbanization, the diet rapidly shifted from the traditional pattern (including cereals and vegetables with few animal foods) to the Western pattern (mainly including red meat and processed meat) in China, which might cause the mortality risk increases from 1990 to 2000 in urban residents.<sup>29</sup> From 1989 to 1997, the China Health and Nutrition Survey showed that the prevalence of overweight has tripled in men and doubled in women;<sup>30</sup> unhealthy weight and less physical activity might increase colorectal cancer risk.<sup>31</sup> All these factors might cause the mortality rates increase from 1990 to 2000. But note that the mortality risks rapidly declined among urban populations from 2000 to 2005; the potential reason was that organized screening pilot projects were identified in 2003 and then an effective, nationwide service screening program with a maximum follow-up of 6 years for colorectal cancer mortality was conducted by fecal immunochemical testing in China in 2004.<sup>32,33</sup> But the scale and effectiveness of screening were not satisfactory in China and in Western countries in recent years.<sup>7,33</sup> From 2005 to 2010, a substantial increase was observed, which might be caused by an increase in alcohol consumption.<sup>34,35</sup> Data from the WHO showed that alcohol consumption significantly increased in 2006–2010 and would increase continuously to 2025, mainly in China and India.<sup>36</sup> All these factors might cause the mortality risk increased from 1990 to 2015. Additionally, colorectal cancer was more prevalent in Japan, North America, and parts of Europe,<sup>2</sup> based on the period effects on China, which was likely to be associated with Western diet and lifestyle in Western countries.<sup>31,37</sup> All in all, to decrease colorectal cancer risk, it is required to take measures such as dietary and physical activity improvement and a long-term follow-up of nationwide service screening.

The cohort effects of influencing factors that arise in gestation and accumulate in old age can be reflected in cohort patterns.<sup>38</sup> In this study, cohort effects showed significant decreasing trends from 1910–1914 to 1995–1999 with the exception of the earlier cohort 1915–1919 and the 1930–1934 cohort. The possible reason was that later cohorts could take adequate nutrition in their childhood, and nutrition is closely related to age; therefore, they have lower risk of malnutrition in their adulthood.<sup>25,39</sup> Additionally, the educational level was high in later stages, and later cohorts had relatively strong

health awareness; thus, they realized the issues around colorectal cancer risk, occurrence, and intervention.<sup>40</sup> Thus, colorectal cancer mortality could not be prevented and controlled among earlier birth cohorts. The change of cohort effects on colorectal cancer mortality significantly increased among men from the 1910–1914 cohort to the 1915–1919 cohort, which was related to the nutrition and air pollution. China and other countries that fought in the First World War experienced too much from 1914 to 1918; the nutritional needs of infants and children are frequently highlighted in the battlefield UK, and nutrition was closely associated with the colorectal cancer mortality; thus, this might explain the high colorectal cancer mortality risk of earlier birth cohorts 1915–1919.<sup>25,39,41</sup> The First World War led to the environmental deterioration during those years; air pollution could increase the risk of colorectal cancer mortality<sup>42,43</sup> and that might cause high risk to the older cohort 1914–1919. The continuous decreases from the 1920–1924 cohort to the 1995–1999 cohort indicated improvements in the situation of colorectal cancer mortality risk attributable to air pollution. Air pollution began to present improvement because of the industrial reform in China in 1920,<sup>44</sup> and the environment change might bring a lasting impact on the disaster risk for the rest of the childhood,<sup>18</sup> which might promote the prevention of colorectal cancer in their childhood. Therefore, the older cohorts at high risk should be emphatically focused and nutrition and environment management should be continued to prevent colorectal cancer.

Air pollution is a major risk factor to health worldwide. Ambient particulate matter pollution was the fourth highest ranked risk factor for death in 2015 in China.<sup>45</sup> In this study, the period trends showed significant increases among rural residents from 1995 to 2015, as well as among urban residents from 1990 to 2000 and 2005 to 2015; the cohort effects showed mortality increase from the 1910–1914 to the 1915–1919 birth cohort. All these increased trends might be related to airborne particulate matter (including PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>), but only a positive association was observed between NO<sub>2</sub> and colorectal cancer mortality and a weak association with PM<sub>2.5</sub> from the 1980s to 2000s.<sup>42,43</sup> From the 1980s to 2000s, environment pollution had gradually increased because of economy development,<sup>28</sup> but there was a huge improvement in air pollution after proposing stricter emission reduction policies in 2006.<sup>46</sup> Although a previous study found that air pollution could concentrate the risk in excess mortality for colorectal cancer,<sup>47</sup> it seemed that the environment improvement over time might not powerfully reduce the increasing mortality risk from 2005 to 2015. The air pollution might still be further improved for prevention of colorectal cancer mortality.

This study has some limitations. First, APC analysis is essentially descriptive, with similar properties as an ecological study, not for causal inference, which likely results in ecological fallacies, and we were, thus, unable to make conclusions regarding the causality of these trends. However, based on the available data and existing literature, we have pointed out scientific hypotheses on analyzing influential factors for colorectal cancer mortality. Second, the effectiveness of screening could not be incorporated in the present study.

## Conclusions

The trends in mortality rates from colorectal cancer are different for different age groups, and the younger age groups show a decreasing trend, whereas the older age groups show an increasing trend. Through APC analysis (IE), colorectal cancer mortality increased exponentially with age, substantially increased with time period and decreased with cohort. Therefore, some effective measures need to be taken to enhance the protection of the elderly and for older cohorts at high risk.

## Author statements

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### Competing interests

None declared.

### Author contributions

Zhi-Jiang Zhang and Xiaoxue Liu substantially contributed to conception and design, acquisition of data, and interpretation of data for the work. Xiaoxue Liu drafted the article. Zhi-Jiang Zhang, Chuanhua Yu, Yongyi Bi, Hong Wang, Runtang Meng, Wei Zhou, and Ganshen Zhang revised the article critically for important intellectual content.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.puhe.2018.08.007>.