

Vital Surveillances

Trends in Incidence Rates, Mortality Rates, and Age-Period-Cohort Effects of Cervical Cancer — China, 2003–2017

Kexin Sun¹; Rongshou Zheng¹; Lin Lei²; Siwei Zhang¹; Hongmei Zeng¹; Shaoming Wang¹; Li Li¹; Ru Chen¹; Bingfeng Han^{1,2,3}; Ji Peng²; Wenqiang Wei^{1,#}; Jie He^{3,#}

ABSTRACT

Introduction: This study reported the trends and analyzed the age-period-cohort effects on the incidence and mortality rates of cervical cancer in China.

Methods: The age-standardized incidence rate (ASIR) and mortality rate (ASMR) by Segi's world standard population were calculated using qualified consecutive data from 22 cancer registries from 2003 to 2017 in China. We performed joinpoint analysis to describe the trends and age-period-cohort analysis to estimate the independent effects of age, period and cohort on trends in incidence and mortality rates of cervical cancer.

Results: The ASIR and ASMR for cervical cancer in females over 20 years old increased during 2003–2017. For females <50 years, a decreasing trend in ASIR and a stable trend in ASMR were observed in urban areas after 2009. But the ASIR and ASMR kept increasing in rural areas during the whole period. For females >50 years, the ASIR and ASMR increased both in urban and rural areas. Age-period-cohort analysis showed increasing period effects on cervical cancer incidence and mortality during the whole period. The cohort effects exhibited a downward-upward-downward pattern for the incidence (1918–1938, 1938–1963, 1963–1993) and mortality rates (1918–1943, 1943–1963, 1963–1993) in urban areas, a fluctuating pattern for incidence rate and a continuing downward pattern for mortality rate (1918–1993) in rural areas.

Conclusions: The increases in cervical cancer incidence and mortality rates can be mostly explained by period effects. We observed decreases in risk for cervical cancer incidence and mortality in young female generations, which were more obvious in urban areas.

Cervical cancer is a major public health problem

among women in China. China is one of the few countries experiencing an increase in cervical cancer incidence (1). Middle-aged females with large social and family responsibilities are at high risk of cervical cancer incidence, which results in poor health outcomes and an increased financial burden. Therefore, there has been much concern about the changing trend in age distribution of cervical cancer.

In recent years, the Chinese government has devoted resources to preventing and treating cervical cancer in rural areas (2). Currently, there is a gap in the literature examining incidence and mortality of cervical cancer in China (3). Hence, we aimed to describe the trends in incidence and mortality rates of cervical cancer from 2003 to 2017 and to identify risk factors for cervical cancer by geography. Our study can provide references for effectiveness evaluation of existing anticancer strategies and for future policy planning in China.

METHODS

Cancer Registry Data

We extracted and pooled cervical cancer datasets (codes: C53, International Statistical Classification of Diseases and Related Health Problems 10th Revision) of 22 population-based cancer registries (11 in urban areas and 11 in rural areas) from 2003 to 2017 in China. A total of 41,326 cervical cancer cases and 10,863 cancer deaths from a population of 329,750,392 person-years (35,420 cases and 8,899 deaths from 274,073,539 person-years in urban areas and 5,906 cases and 1,964 deaths from 55,676,853 person-years in rural areas).

We excluded data from females over 20 years old since the number of cases and deaths of females in this population was less than 5 in each age group ($n < 5$). We classified districts as urban areas and counties/county-level cities as rural areas. The incidence and mortality rates were calculated using 5-year age grouping (20–24, 25–29, ..., 80–, ≥ 85), by 5-

year period (2003–2007, 2008–2012, 2013–2017) and by geography (urban and rural areas).

Statistical Analysis

The age-standardized incidence rate (ASIR) and mortality rate (ASMR) were calculated using Segi's world standard population (4). We used Joinpoint regression analyses for trend analysis and reported the annual percent changes (APC), and average annual percent change (AAPC). Age-period-cohort effects were analyzed using the intrinsic estimator method and risk ratios were reported (5). Statistical analyses were performed using Stata (version 13.0, Stata Corporation, College Station, Texas, USA) and Joinpoint software (version 4.6.0.0 Applications Branch, National Cancer Institute, Bethesda, USA).

RESULTS

Trends in Incidence Rate

Supplementary Table S1 (available in <http://weekly.chinacdc.cn>) presents the incidence rates of cervical cancer. Overall, the ASIR for cervical cancer in females over 20 years old increased from 6.66/100,000 in 2003 to 16.30/100,000 in 2017. A clear upward trend was observed during 2003–2007, but this trend dampened during 2007–2017. In urban areas, the ASIR increased from 6.91/100,000 in 2003 to 16.15/100,000 in 2017. ASIR increased significantly during 2003–2009, and then leveled off. In rural areas, the ASIR increased from 5.72/100,000 in 2003 to 17.07/100,000 in 2017. The ASIR increased during 2003–2007, however, this upward trend slowed down during 2007–2017 (Figures 1A, 1B, 1C). The corresponding APCs and AAPCs for incidence rates were provided in Supplementary Table S2 (available in <http://weekly.chinacdc.cn>).

In urban areas, the ASIR in females aged 20–34 years decreased significantly from 2003–2017. The ASIR in females aged 35–49 years varied, increasing from 2003–2009, then decreasing from 2009–2017. The ASIR in females aged 50–64 years increased significantly during 2003–2006, however, this upward trend slowed down afterwards. The ASIR in females over 65 years increased during 2003–2017 (Figure 1B).

In rural areas, the ASIR in females aged 20–34 years and 50–64 years increased significantly during 2003–2017. The ASIR in females aged 35–49 years increased during 2003–2017. The ASIR in females over 65 years was stable during 2003–2010 but

increased rapidly afterward (Figure 1C).

Trends in Mortality Rate

Supplementary Table S3 (available in <http://weekly.chinacdc.cn>) presents the mortality rates of cervical cancer. In all areas, the ASMR increased from 2.07/100,000 in 2003 to 4.16/100,000 in 2017. In urban areas, it increased from 1.86/100,000 in 2003 to 3.91/100,000 in 2017. In rural areas, it increased from 3.12/100,000 in 2003 to 5.56/100,000 in 2017. The ASMRs all followed continuously increasing trends (Figures 1D, 1E, and 1F). The corresponding APCs and AAPCs for mortality rates were provided in Supplementary Table S4 (available in <http://weekly.chinacdc.cn>).

In urban areas, the ASMR in females aged 20–34 years stayed stable. The ASMR in females aged 35–49 years increased during 2003–2007 and then leveled off. The ASMR in females aged 50–64 years and over 65 years increased during the whole period of 2003–2017 (Figure 1E).

In rural areas, the increasing trend of ASMR in females aged 20–34 years was not significant. The ASMR in females aged 35–49 years increased during 2003–2017. The ASMR in females aged 50–64 years stayed stable. The ASMR in females over 65 years fluctuated during 2003–2009 and then increased during 2009–2017 (Figure 1F).

Trends in Age Distribution of Cervical Cancer Incidence

In urban areas, the peak age group for the incidence rate rose by one age group each 5-year period, from 40–44 years during 2003–2007 to 45–49 years during 2008–2012, and to 50–54 years during 2013–2017. Compared to period 2008–2012, the age-specific rates were lower in age groups <45 in period 2013–2017. The trends in all areas were similar to those in urban areas (Figure 2B).

In rural areas, the age group with the highest incidence rate was 55–59 years during 2003–2007. It decreased to 45–49 age group during 2008–2012, and then rose to 50–54 age group during 2013–2017. The age-specific incidences in most age groups increased with period (Figure 2C).

The incidence rates increased for cohorts between 1928 and 1978 (25–79 years) in urban areas and cohorts between 1918 and 1978 (>25 years) in rural areas (Figures 3A, 3B).

Trends in Age Distribution of Cervical

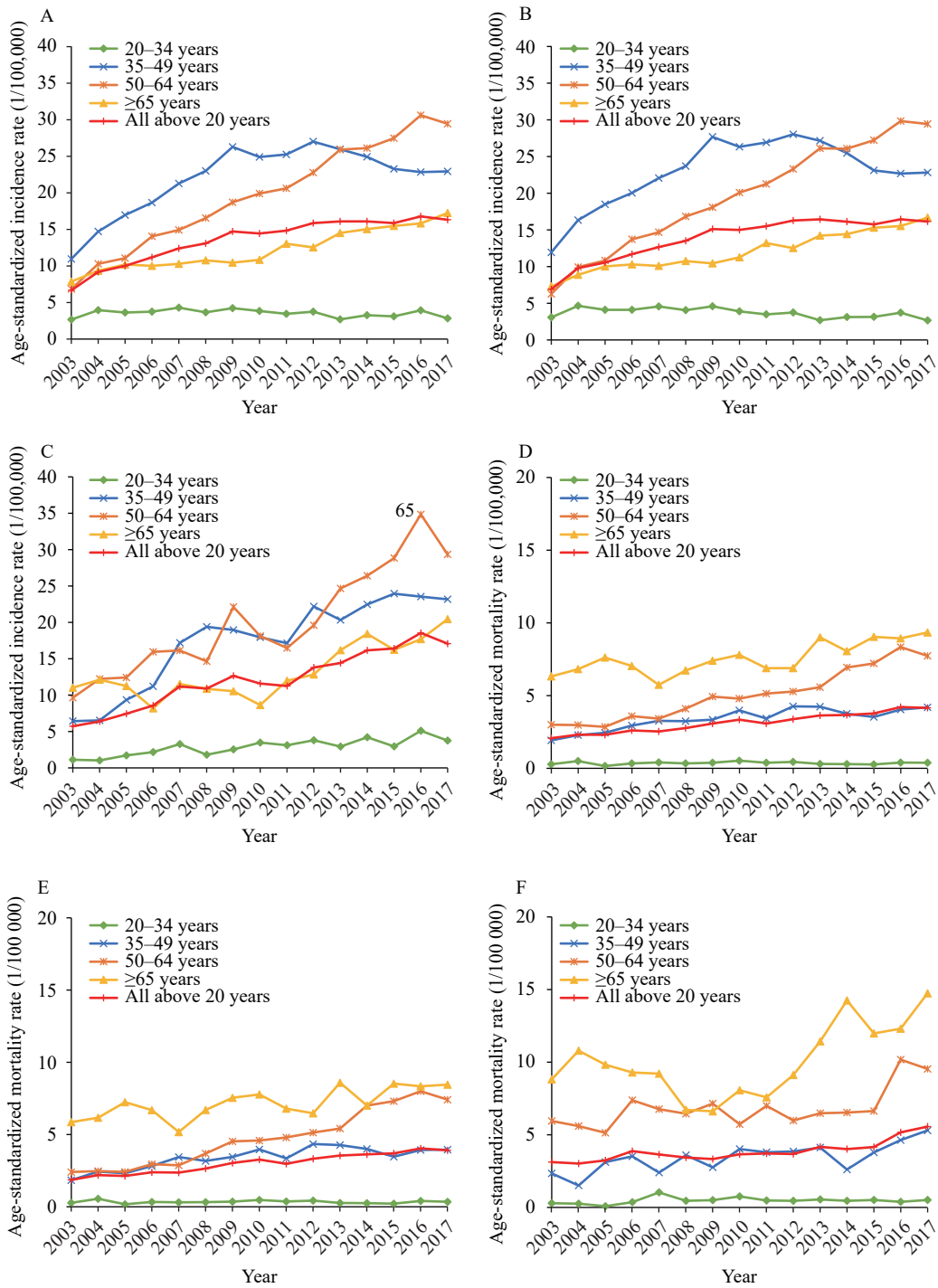


FIGURE 1. The trends of incidence and mortality rates of cervical cancer by age group and area, from 2003 to 2017. (A) Incidence rates in all areas, (B) Incidence rates in urban areas, (C) Incidence rates in rural areas, (D) Mortality rates in all areas, (E) Mortality rates in urban areas, (F) Mortality rates in rural areas.

Cancer Mortality

In urban areas, the age-specific mortality rate peaked at 45–49 years during 2003–2012 and at 50–54 years during 2013–2017. From the 60–64 year age group, mortality rates increased continuously with age. The trends in all areas were similar to those in urban areas

(Figure 2E).

In rural areas, the mortality rate increased with age all along, and no peaks were found in young age groups (Figure 2F).

The mortality rates of cervical cancer increased for younger cohorts between 1943 and 1978 but

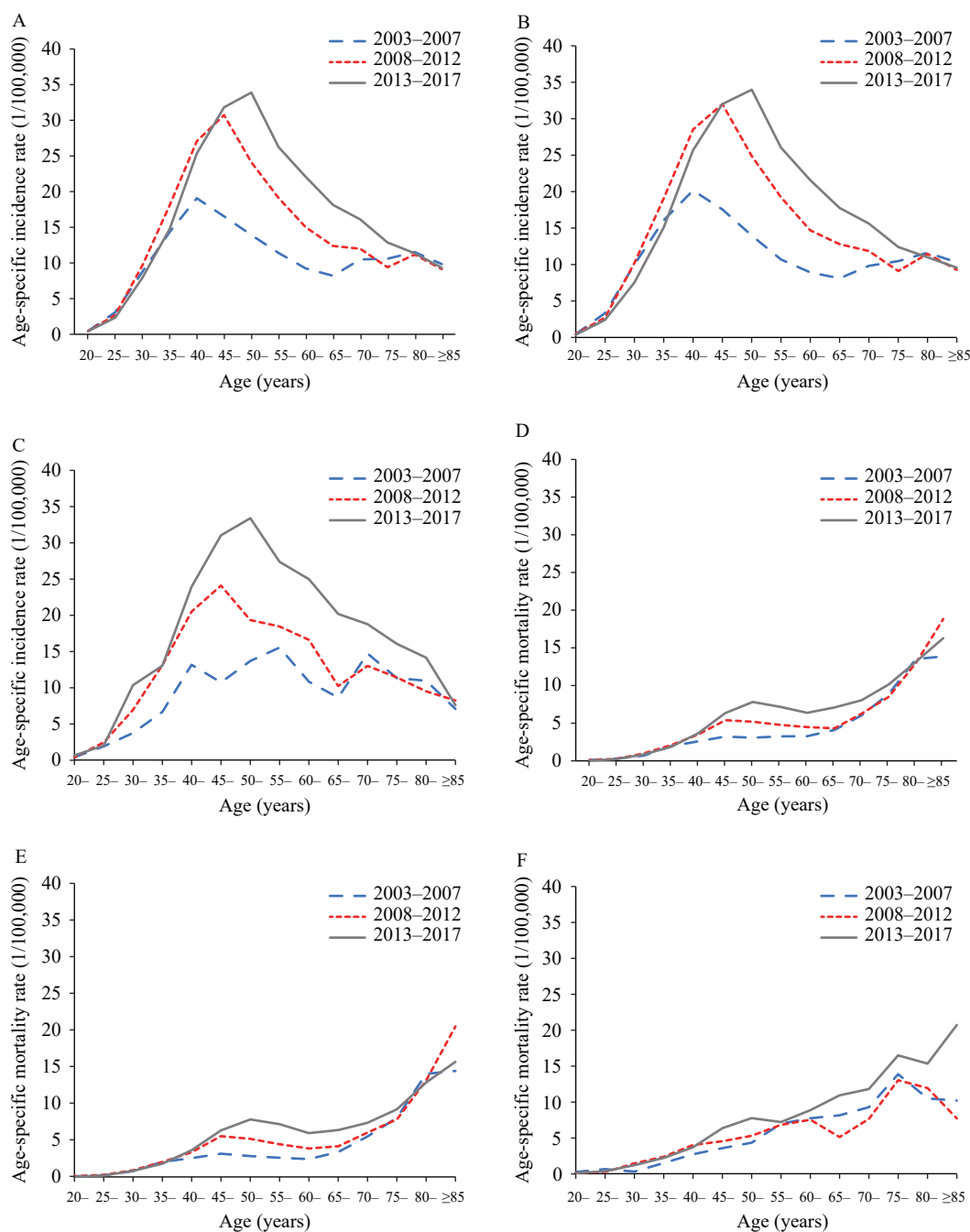


FIGURE 2. The age-specific incidence and mortality rates of cervical cancer, by time period and area. (A) Incident rates in all areas. (B) Incident rates in urban areas. (C) Incident rates in rural areas. (D) Mortality rates in all areas. (E) Mortality rates in urban areas. (F) Mortality rates in rural areas.

Note: Each line represents the connection of age-specific rates for a 5-year period.

fluctuated in elder cohorts between 1918 and 1938 in both urban and rural areas (Figures 3C, 3D).

Results of Age-period-cohort Models

The age effect for cervical cancer incidence rates rose significantly from age groups 20–24 and peaked in the age groups of 45–49 (urban) and 50–54 (rural). It

began to decrease slowly afterward but rose again in the age group of 70–74. The age effect dropped rapidly in subsequent age groups. The age effect on mortality rates increased with age all through in urban areas but fluctuated in elder age groups in rural areas (Figure 4).

The period effect for the incidence and mortality rates of cervical cancer increased during 2003 to 2017

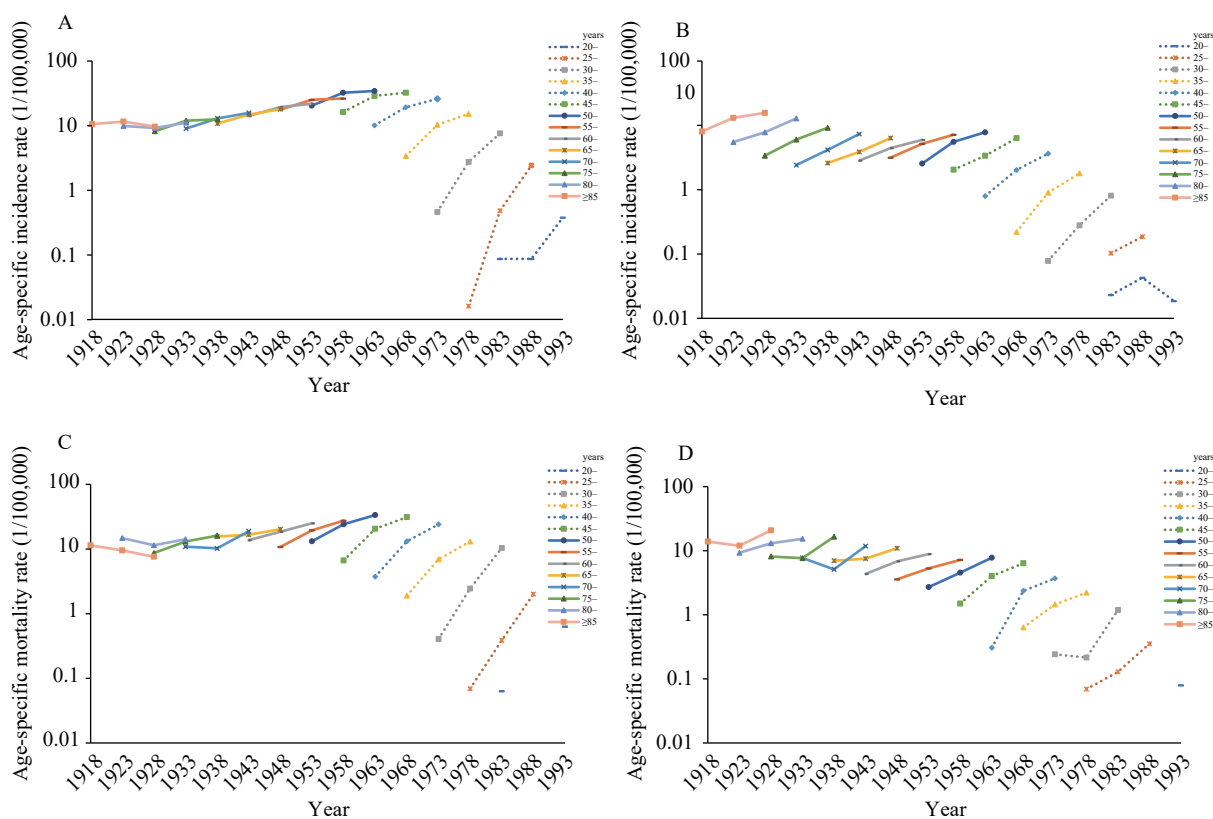


FIGURE 3. The birth cohort-specific incidence and mortality rates of cervical cancer, by area. (A) Incident rates in urban areas. (B) Incident rates in rural areas. (C) Mortality rates in urban areas. (D) Mortality rates in rural areas. Note: Results are not shown in age group 20–24 if the age-specific rate is 0. Each line represents the connection of cohort-specific rates for a 5-year age group.

in urban and rural areas (Figure 4).

For cohort effects in urban areas, the risk ratios of incidence and mortality rates decreased in birth cohorts 1918–1938 and 1918–1943, respectively. Then the risk ratios increased in birth cohorts 1938–1963 and 1943–1963, and decreased after 1963. In rural areas, the risk ratios of incidence rate decreased in birth cohort 1918–1943 and then fluctuated after that. The risk ratios of mortality rate decreased among all cohorts from 1918 to 1993 (Figure 4). The age-period-cohort estimates were provided in Supplementary Table S5–S6 (available in <http://weekly.chinacdc.cn>).

DISCUSSION

Shift in trends. Wang et al. (6) showed that the incident rates of cervical cancer were highest in younger populations in Italy and Korea. Similar trends were also observed in China whereby Wei et al. (7) found that the mortality rate of cervical cancer increased in young females aged 25–54 from 1987 to 2015 in urban China, which was different from the

results in our study. Li et al. (3) used cancer registry data and reported that the risk for younger females was rising in China. In this study, we updated the same cancer registry data for 3 years and found contrasting trends in incidence/mortality rates in younger females (<50) in recent 8 years, which were more significant in urban areas than in rural areas. This evidence indicated that the increasing trend in cervical cancer disease burden in younger females was being arrested in urban areas.

Age effect. We observed that the risk for cervical cancer incidence plateaued at age 40–74 in China, which was also observed in India (8) and Russia (9), indicating that the age span of targeted population for cervical cancer screening programs can be larger.

Period effect. The increased trends in cervical cancer incidence and mortality rates can be explained by period effects, which are caused by factors that can influence all age groups during a particular period of time. Considering that the National Cervical Cancer Screening Program in Rural Areas (NCCSPRA) was launched in 2009 for females aged 35–59, the effect of

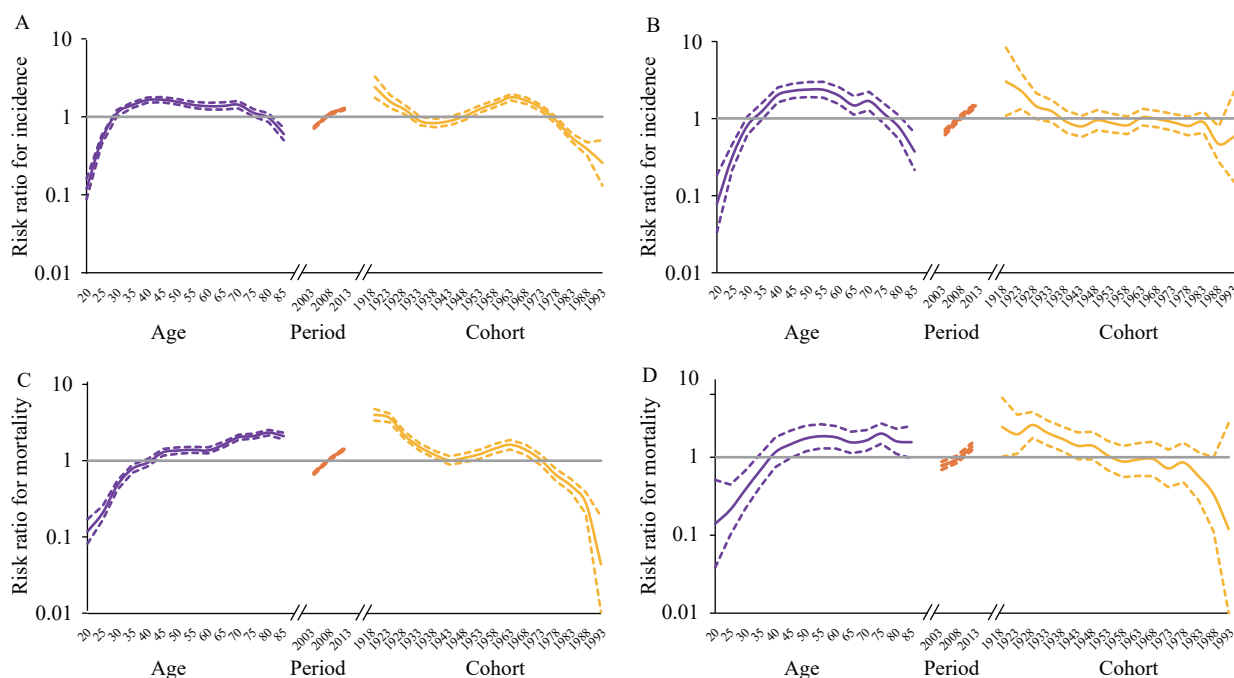


FIGURE 4. The result of age-period-cohort analysis of incidence and mortality rates of cervical cancer, by area. (A) Incident rates in urban areas; (B) Incident rates in rural areas; (C) Mortality rates in urban areas; (D) Mortality rates in rural areas. Notes: Purple solid and dash lines represent the age effect and 95% confidence interval. Orange solid and dash lines represent the period effect and 95% confidence interval. Yellow solid and dash lines represent the cohort effect and 95% confidence interval.

this screening program may have resulted in the cohorts rather than the periods in China. Guo et al. (10) also reported similar period effects on cervical cancer mortality. The possible explanation might also be the cumulative exposure to risk factors during the industrialization and urbanization processes, the improvement of health service capacity and the increasing demand for cancer treatment. Surveillance data indicated that the cancer incidence and mortality rates are still on the rise and the turning point is not yet in sight in China (11). Without harsher and more extensive intervention measures, the period effect is expected to keep rising in the near future (12).

Cohort effect. Cohort effect explains the influence of unique risk factors for different birth cohorts. In urban areas, risk ratios increased among females born in 1938–1963, which was echoed in Guo’s research (10). Possible explanations include an increase in HPV infection and smoking rate and changing sexual behaviors in 1938–1963 cohorts (13). The risk ratios decreased among females born after 1963, which might be explained by the cancer intervention strategies implemented in recent years, including health education, the promotion of women’s health care and the implementation of extensive cervical cancer screening programs after 2009. In rural areas, we

observed no upward trends in cohort effects on incidence rate and decreased cohort effects on mortality rates, indicating that the cervical cancer intervention strategies in these areas have achieved promising effects. Increasing cohort effects were found in young generations in the Republic of Korea (14), Japan (15) and Russia (9) but were not observed in the present study. Considering that similar risk factors may also exist in China, corresponding public health measures for young generations should be implemented in advance.

In conclusion, the disease burden of cervical cancer in China is still on the rise, but the upward trend in young generations in urban areas is starting to slow down or even reverse. The decrease of cohort effects may reflect the effect of cervical cancer prevention and control strategies in China in recent years, which mainly affected females born after 1963 in urban areas and all females in rural areas. More comprehensive interventions for general female population with strengthened measures for young generations should be implemented in China.

Acknowledgments: Staffs of 22 population-based cancer registries for the effort they put in data collection, quality control and database creation, including Beijing Municipality; Cixian County in

Hebei Province; Dalian and Anshan cities in Liaoning Province; Nangang District in Heilongjiang Province; Shanghai Municipality; Qidong City, Huai'an District, and Yangzhong City in Jiangsu Province; Hangzhou City, Jiaxing City, Jiashan County, and Haining City in Zhejiang Province; Changle District in Fujian Province; Linqu County and Feicheng City in Shandong Province; Linzhou City in Henan Province; Wuhan City in Hubei Province; Guangzhou, Sihui, and Zhongshan cities in Guangdong Province; and Yanting County in Sichuan Province.

Conflicts of interest: No conflicts of interest.

Funding: Supported by CAMS Innovation Fund for Medical Sciences (2021-I2M-1-011) and Sanming Project of Medicine in Shenzhen (No.SZSM 20191015).

doi: 10.46234/ccdcw2022.216

* Corresponding authors: Wenqiang Wei, weiwq@cicams.ac.cn; Jie He, prof.hejie@263.net.

¹ National Central Cancer Registry, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Municipality, China; ² Shenzhen Center for Chronic Disease Control, Guangzhou City, Guangdong Province, China; ³ Department of Thoracic Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Municipality, China.

Submitted: October 26, 2022; Accepted: November 29, 2022

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. The cervical cancer incidence in China by age group and area, 2003–2017.

Area	Year	20–34 years			35–49 years			50–64 years			>65 years			All >20 years			
		No.	CR	ASIR	No.	CR	ASIR	No.	CR	ASIR	No.	CR	ASIR	No.	CR	ASIR	
All	2003	135	3.02	2.66	539	10.99	10.95	204	7.00	6.83	183	8.25	7.86	1,061	7.32	6.66	
	2004	221	4.51	3.95	805	14.76	14.71	349	10.68	10.29	244	9.89	9.34	1,619	10.06	9.18	
	2005	195	3.88	3.64	926	16.98	16.94	401	11.26	11.07	263	10.18	10.19	1,785	10.74	10.01	
	2006	210	4.04	3.75	1,049	18.68	18.65	531	14.33	14.03	263	10.12	10.00	2,053	12.00	11.18	
	2007	240	4.59	4.29	1,199	21.30	21.26	617	15.48	14.90	282	10.51	10.29	2,338	13.34	12.38	
	2008	205	3.82	3.65	1,260	23.00	22.98	740	16.99	16.54	303	10.69	10.75	2,508	13.91	13.07	
	2009	234	4.33	4.24	1,452	26.44	26.26	887	19.20	18.69	302	10.44	10.44	2,875	15.61	14.70	
	2010	210	3.96	3.83	1,376	25.20	24.87	972	20.18	19.89	313	10.56	10.82	2,871	15.48	14.44	
	2011	192	3.71	3.44	1,413	25.83	25.22	1,055	20.84	20.59	372	12.00	13.03	3,032	16.13	14.81	
	2012	218	4.21	3.75	1,500	27.66	26.99	1,178	22.69	22.75	377	11.74	12.54	3,273	17.22	15.86	
	2013	166	3.21	2.70	1,403	26.52	25.94	1,397	25.68	25.90	455	13.72	14.50	3,421	17.80	16.07	
	2014	203	3.87	3.26	1,318	25.32	24.91	1,450	25.97	26.11	482	13.88	15.02	3,453	17.70	16.08	
	2015	196	3.85	3.10	1,223	23.58	23.25	1,586	27.31	27.46	514	14.09	15.45	3,519	17.84	15.86	
	2016	248	5.03	3.94	1,204	23.00	22.83	1,747	30.21	30.59	561	14.63	15.80	3,760	19.00	16.76	
	2017	179	3.73	2.83	1,241	23.09	22.92	1,670	28.87	29.42	645	16.27	17.24	3,735	18.75	16.30	
	Urban	2003	123	3.42	3.07	484	11.99	11.93	156	6.44	6.27	144	7.69	7.28	907	7.60	6.91
		2004	209	5.17	4.65	749	16.38	16.32	284	10.32	9.92	198	9.37	8.89	1,440	10.68	9.79
2005		179	4.30	4.10	844	18.48	18.47	335	11.05	10.83	223	10.03	10.02	1,581	11.30	10.56	
2006		189	4.36	4.11	950	20.11	20.05	444	14.00	13.72	232	10.37	10.30	1,815	12.55	11.69	
2007		208	4.75	4.57	1,047	22.13	22.07	527	15.37	14.68	242	10.41	10.09	2,024	13.62	12.65	
2008		188	4.15	4.06	1,087	23.72	23.69	649	17.35	16.84	260	10.62	10.76	2,184	14.27	13.50	
2009		210	4.62	4.59	1,280	27.90	27.67	738	18.66	18.07	261	10.48	10.43	2,489	15.98	15.12	
2010		179	4.01	3.89	1,206	26.68	26.32	841	20.60	20.09	275	10.81	11.25	2,501	16.02	14.99	
2011		166	3.83	3.49	1,246	27.54	26.92	930	21.54	21.27	323	12.06	13.21	2,665	16.81	15.50	
2012		185	4.30	3.74	1,278	28.70	28.03	1,028	23.28	23.29	322	11.66	12.52	2,813	17.65	16.29	
2013		139	3.25	2.67	1,202	27.69	27.16	1,200	25.84	26.11	384	13.46	14.21	2,925	18.16	16.44	
2014		164	3.76	3.13	1,099	25.82	25.47	1,234	25.89	26.08	397	13.29	14.42	2,894	17.68	16.12	
2015		167	3.95	3.14	996	23.33	23.10	1,342	27.06	27.21	436	13.92	15.29	2,941	17.72	15.76	
2016		199	4.87	3.71	987	22.77	22.69	1,449	29.40	29.83	467	14.15	15.52	3,102	18.63	16.44	
2017		142	3.58	2.67	1,019	22.83	22.81	1,418	28.80	29.44	539	15.76	16.67	3,118	18.58	16.15	
Rural		2003	12	1.38	1.12	55	6.33	6.43	48	9.82	9.64	39	11.29	11.03	154	5.99	5.72
		2004	12	1.39	1.03	56	6.36	6.52	65	12.58	12.25	46	12.99	12.12	179	6.85	6.40
	2005	16	1.87	1.72	82	9.24	9.36	66	12.42	12.43	40	11.11	11.26	204	7.74	7.44	
	2006	21	2.44	2.17	99	11.11	11.19	87	16.28	15.95	31	8.58	8.17	238	8.99	8.56	
	2007	32	3.77	3.26	152	16.93	17.18	90	16.14	16.14	40	11.21	11.52	314	11.80	11.19	
	2008	17	2.04	1.80	173	19.34	19.38	91	14.76	14.63	43	11.12	10.86	324	11.87	10.91	
	2009	24	2.76	2.53	172	19.04	18.96	149	22.35	22.12	41	10.16	10.55	386	13.58	12.64	
	2010	31	3.68	3.48	170	18.11	17.94	131	17.89	18.14	38	9.09	8.63	370	12.63	11.59	
	2011	26	3.09	3.12	167	17.64	17.15	125	16.79	16.47	49	11.64	11.98	367	12.43	11.26	
	2012	33	3.76	3.79	222	22.91	22.18	150	19.31	19.60	55	12.24	12.82	460	14.97	13.79	
	2013	27	3.01	2.93	201	21.16	20.34	197	24.71	24.67	71	15.30	16.18	496	15.95	14.41	
	2014	39	4.42	4.21	219	23.09	22.46	216	26.48	26.40	85	17.46	18.42	559	17.84	16.15	
	2015	29	3.39	2.96	227	24.73	23.94	244	28.78	28.84	78	15.13	16.22	578	18.43	16.41	
	2016	49	5.78	5.10	217	24.11	23.54	298	34.88	34.85	94	17.58	17.70	658	20.97	18.55	
	2017	37	4.47	3.76	222	24.36	23.16	252	29.28	29.34	106	19.53	20.44	617	19.64	17.07	

Note: Urban: districts are defined as urban areas. Rural: Counties or county-level cities are defined as rural areas. Abbreviation: CR=crude rate; ASIR=age-standardized incidence rate.

SUPPLEMENTARY TABLE S2. Trends for age-standardized incidence rates of cervical cancer for any time segments identified in joinpoint analysis by age group and area, 2003 to 2017.

Age, years	Area	Trend1		Trend2		AAPC	
		Years	APC (95% CI)	Years	APC (95% CI)	2003–2017	2013–2017
20–34	All	2003–2017	-0.9 (-2.9, 1.1)	-	-	-0.9 (-2.9, 1.1)	-0.9 (-2.9, 1.1)
	Urban	2003–2017	-2.4* (-4.3, -0.4)	-	-	-2.4* (-4.3, -0.4)	-2.4* (-4.3, -0.4)
	Rural	2003–2017	9.3* (5.7, 13.0)	-	-	9.3* (5.7, 13.0)	9.3* (5.7, 13.0)
35–49	All	2003–2009	14.1* (10.8, 17.6)	2009–2017	-2.0* (-3.9, -0.1)	4.6* (3.1, 6.2)	-2.0* (-3.9, -0.1)
	Urban	2003–2009	13.4* (9.5, 17.4)	2009–2017	-2.7* (-4.8, -0.5)	3.9* (2.1, 5.7)	-2.7* (-4.8, -0.5)
	Rural	2003–2008	25.6* (17.9, 33.8)	2008–2017	2.8* (0.2, 5.5)	10.5* (7.8, 13.2)	2.8* (0.2, 5.5)
50–64	All	2003–2006	25.9* (14.3, 38.6)	2006–2017	7.5* (6.1, 8.9)	11.2* (8.9, 13.4)	7.5* (6.1, 8.9)
	Urban	2003–2006	29.0* (16.2, 43.3)	2006–2017	7.5* (6.0, 9.0)	11.8* (9.3, 14.3)	7.5* (6.0, 9.0)
	Rural	2003–2017	8.1* (6.4, 9.9)	-	-	8.1* (6.4, 9.9)	8.1* (6.4, 9.9)
>65	All	2003–2017	5.1* (4.3, 5.9)	-	-	5.1* (4.3, 5.9)	5.1* (4.3, 5.9)
	Urban	2003–2017	5.2* (4.4, 6.0)	-	-	5.2* (4.4, 6.0)	5.2* (4.4, 6.0)
	Rural	2003–2010	-1.1 (-5.9, 3.8)	2010–2017	11.1* (5.8, 16.7)	4.8* (1.7, 8.1)	11.1* (5.8, 16.7)
All >20	All	2003–2007	16.6* (11.0, 22.6)	2007–2017	2.6* (1.3, 3.8)	6.4* (4.9, 8.0)	2.6* (1.3, 3.8)
	Urban	2003–2009	11.8* (8.1, 15.5)	2009–2017	0.6 (-1.5, 2.8)	5.3* (3.5, 7.0)	0.6 (-1.5, 2.8)
	Rural	2003–2007	16.9* (9.5, 24.8)	2007–2017	5.7* (4.0, 7.4)	8.8* (6.7, 10.9)	5.7* (4.0, 7.4)

Note: "-" denotes no data.

Abbreviation: APC=annual percent change; AAPC=average annual percent change; CI=confidence interval.

*APC or AAPC with statistically significant trends, $P < 0.05$.

SUPPLEMENTARY TABLE S3. The cervical cancer mortality in China by age group and area, 2003–2017.

Area	Year	20–34			35–49			50–64			>65			All >20		
		No	CR	ASWR	No	CR	ASWR	No	CR	ASWR	No	CR	ASWR	No	CR	ASWR
All	2003	14	0.31	0.27	95	1.94	1.92	86	2.95	3.00	155	6.99	6.32	350	2.41	2.07
	2004	26	0.53	0.50	125	2.29	2.28	95	2.91	2.97	183	7.42	6.82	429	2.67	2.31
	2005	9	0.18	0.16	135	2.48	2.44	101	2.83	2.85	217	8.40	7.61	462	2.78	2.30
	2006	19	0.37	0.33	165	2.94	2.94	133	3.59	3.59	202	7.77	7.04	519	3.03	2.60
	2007	22	0.42	0.41	183	3.25	3.27	138	3.46	3.42	173	6.45	5.74	516	2.94	2.54
	2008	19	0.35	0.34	179	3.27	3.24	179	4.11	4.10	225	7.94	6.72	602	3.34	2.77
	2009	21	0.39	0.38	187	3.41	3.34	227	4.91	4.94	253	8.74	7.40	688	3.74	3.08
	2010	29	0.55	0.53	223	4.08	3.98	230	4.78	4.79	264	8.91	7.80	746	4.02	3.34
	2011	21	0.41	0.38	193	3.53	3.42	264	5.21	5.14	258	8.33	6.89	736	3.91	3.08
	2012	24	0.46	0.44	242	4.46	4.26	273	5.26	5.27	262	8.16	6.89	801	4.21	3.38
	2013	19	0.37	0.31	231	4.37	4.24	304	5.59	5.57	334	10.07	9.01	888	4.62	3.64
	2014	18	0.34	0.28	199	3.82	3.75	386	6.91	6.93	328	9.44	8.06	931	4.77	3.67
	2015	17	0.33	0.27	187	3.61	3.53	416	7.16	7.21	375	10.28	9.04	995	5.04	3.77
	2016	25	0.51	0.40	216	4.13	4.04	483	8.35	8.34	364	9.49	8.93	1,088	5.50	4.21
2017	25	0.52	0.38	229	4.26	4.19	444	7.68	7.73	410	10.34	9.35	1,108	5.56	4.16	
Urban	2003	11	0.31	0.27	75	1.86	1.84	59	2.43	2.41	122	6.51	5.87	267	2.24	1.86
	2004	24	0.59	0.56	112	2.45	2.44	67	2.43	2.47	145	6.86	6.17	348	2.58	2.19
	2005	8	0.19	0.17	108	2.37	2.32	76	2.51	2.42	180	8.09	7.23	372	2.66	2.13
	2006	16	0.37	0.34	134	2.84	2.82	94	2.96	2.95	165	7.38	6.69	409	2.83	2.39
	2007	14	0.32	0.30	162	3.42	3.44	100	2.92	2.87	140	6.02	5.17	416	2.80	2.37
	2008	15	0.33	0.33	147	3.21	3.17	140	3.74	3.69	197	8.05	6.70	499	3.26	2.65
	2009	16	0.35	0.35	162	3.53	3.45	180	4.55	4.53	220	8.84	7.55	578	3.71	3.03
	2010	22	0.49	0.48	185	4.09	3.97	188	4.60	4.59	226	8.88	7.78	621	3.98	3.27
	2011	17	0.39	0.36	156	3.45	3.35	211	4.89	4.80	222	8.29	6.80	606	3.82	2.97
	2012	20	0.46	0.43	203	4.56	4.34	226	5.12	5.14	219	7.93	6.47	668	4.19	3.33
	2013	14	0.33	0.26	191	4.40	4.27	252	5.43	5.41	277	9.71	8.59	734	4.56	3.55
	2014	14	0.32	0.25	173	4.06	4.01	333	6.99	7.01	253	8.47	7.01	773	4.72	3.63
	2015	12	0.28	0.22	150	3.51	3.46	360	7.26	7.31	309	9.86	8.53	831	5.01	3.70
	2016	21	0.51	0.41	173	3.99	3.93	396	8.03	8.00	297	9.00	8.34	887	5.33	4.04
2017	20	0.50	0.35	178	3.99	3.95	362	7.35	7.42	327	9.56	8.45	887	5.29	3.91	
Rural	2003	3	0.35	0.29	20	2.30	2.33	27	5.52	5.95	33	9.55	8.81	83	3.23	3.12
	2004	2	0.23	0.26	13	1.48	1.51	28	5.42	5.60	38	10.73	10.78	81	3.10	3.02
	2005	1	0.12	0.08	27	3.04	3.12	25	4.70	5.13	37	10.28	9.83	90	3.41	3.23
	2006	3	0.35	0.36	31	3.48	3.51	39	7.30	7.38	37	10.24	9.28	110	4.15	3.87
	2007	8	0.94	1.03	21	2.34	2.40	38	6.82	6.76	33	9.25	9.21	100	3.76	3.64
	2008	4	0.48	0.46	32	3.58	3.60	39	6.33	6.45	28	7.24	6.72	103	3.77	3.43
	2009	5	0.58	0.50	25	2.77	2.76	47	7.05	7.15	33	8.17	6.61	110	3.87	3.33
	2010	7	0.83	0.76	38	4.05	4.01	42	5.73	5.73	38	9.09	8.07	125	4.27	3.66
	2011	4	0.48	0.48	37	3.91	3.79	53	7.12	6.99	36	8.55	7.57	130	4.40	3.71
	2012	4	0.46	0.45	39	4.02	3.85	47	6.05	5.99	43	9.57	9.11	133	4.33	3.68
	2013	5	0.56	0.54	40	4.21	4.12	52	6.52	6.48	57	12.28	11.43	154	4.95	4.17
	2014	4	0.45	0.45	26	2.74	2.61	53	6.50	6.53	75	15.41	14.24	158	5.04	4.02
	2015	5	0.59	0.51	37	4.03	3.78	56	6.61	6.63	66	12.80	11.97	164	5.23	4.15
	2016	4	0.47	0.39	43	4.78	4.63	87	10.18	10.17	67	12.53	12.30	201	6.41	5.17
2017	5	0.60	0.51	51	5.60	5.30	82	9.53	9.53	83	15.29	14.73	221	7.03	5.56	

Note: Urban: Districts are defined as urban areas. Rural: Counties or county-level cities are defined as rural areas.
Abbreviation: CR=crude rate; ASWR=age-standardized mortality rate.

SUPPLEMENTARY TABLE S4. Trends in age-standardized mortality rates of cervical cancer for any time segments identified in joinpoint analysis by age group and area, 2003–2017.

Age (years)	Area	Trend1		Trend2		AAPC	
		Year	APC (95% CI)	Year	APC (95% CI)	2003–2017	2013–2017
20–34	All	2003–2017	1.0 (–2.9, 5.0)	–	–	1.0 (–2.9, 5.0)	1.0 (–2.9, 5.0)
	Urban	2003–2017	0.0 (–4.0, 4.3)	–	–	0.0 (–4.0, 4.3)	0.0 (–4.0, 4.3)
	Rural	2003–2017	5.3 (–1.7, 12.9)	–	–	5.3 (–1.7, 12.9)	5.3 (–1.7, 12.9)
35–49	All	2003–2007	14.7* (5.7, 24.6)	2007–2017	2.2* (0.2, 4.3)	5.6* (3.1, 8.2)	2.2* (0.2, 4.3)
	Urban	2003–2007	15.7* (4.7, 27.9)	2007–2017	1.9 (–0.6, 4.4)	5.7* (2.6, 8.8)	1.9 (–0.6, 4.4)
	Rural	2003–2017	5.2* (2.2, 8.4)	–	–	5.2* (2.2, 8.4)	5.2* (2.2, 8.4)
50–64	All	2003–2017	8.2* (7.2, 9.3)	–	–	8.2* (7.2, 9.3)	8.2* (7.2, 9.3)
	Urban	2003–2017	9.9* (8.8, 11.1)	–	–	9.9* (8.8, 11.1)	9.9* (8.8, 11.1)
	Rural	2003–2015	1.2 (–0.8, 3.3)	2015–2017	23.3 (–12.3, 73.4)	4.1 (–0.5, 9.0)	11.7 (–3.8, 29.8)
>65	All	2003–2017	2.6* (1.3, 3.8)	–	–	2.6* (1.3, 3.8)	2.6* (1.3, 3.8)
	Urban	2003–2017	2.4* (1.0, 3.9)	–	–	2.4* (1.0, 3.9)	2.4* (1.0, 3.9)
	Rural	2003–2009	–6.3 (–12.5, 0.5)	2009–2017	9.8* (5.0, 14.8)	2.6 (–0.9, 6.2)	9.8* (5.0, 14.8)
All >20	All	2003–2017	5.1* (4.5, 5.6)	–	–	5.1* (4.5, 5.6)	5.1* (4.5, 5.6)
	Urban	2003–2017	5.5* (4.7, 6.3)	–	–	5.5* (4.7, 6.3)	5.5* (4.7, 6.3)
	Rural	2003–2015	2.4* (1.2, 3.6)	2015–2017	17.4 (–3.7, 43.0)	4.4* (1.7, 7.2)	9.6* (0.5, 19.6)

Abbreviation: APC=annual percent change; AAPC=average annual percent change; CI=confidence interval.

*APC or AAPC with statistically significant trends, $P < 0.05$.

SUPPLEMENTARY TABLE S5. The age-period-cohort estimates for cervical cancer incidence in China by area, 2003–2017.

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard error	Z	P
	Age_20	-2.19 (-2.54, -1.85)	0.11 (0.08, 0.16)	0.18	-12.48	<0.001
	Age_25	-0.75 (-0.9, -0.6)	0.47 (0.41, 0.55)	0.08	-9.81	<0.001
	Age_30	0.06 (-0.05, 0.17)	1.06 (0.96, 1.18)	0.05	1.13	0.257
	Age_35	0.33 (0.24, 0.42)	1.39 (1.27, 1.53)	0.05	6.85	<0.001
	Age_40	0.52 (0.44, 0.61)	1.69 (1.55, 1.84)	0.04	11.85	<0.001
	Age_45	0.55 (0.46, 0.64)	1.73 (1.59, 1.89)	0.04	12.48	<0.001
	Age_50	0.5 (0.41, 0.59)	1.65 (1.51, 1.81)	0.05	10.78	<0.001
	Age_55	0.42 (0.32, 0.52)	1.52 (1.38, 1.68)	0.05	8.24	<0.001
	Age_60	0.37 (0.26, 0.48)	1.44 (1.29, 1.61)	0.06	6.53	<0.001
	Age_65	0.33 (0.21, 0.44)	1.39 (1.23, 1.56)	0.06	5.41	<0.001
	Age_70	0.38 (0.26, 0.50)	1.47 (1.30, 1.65)	0.06	6.29	<0.001
	Age_75	0.12 (-0.01, 0.24)	1.13 (0.99, 1.28)	0.06	1.87	0.061
	Age_80	-0.07 (-0.21, 0.08)	0.94 (0.81, 1.08)	0.07	-0.89	0.372
	Age_85	-0.57 (-0.78, -0.37)	0.56 (0.46, 0.69)	0.1	-5.51	<0.001
	Period_2003	-0.33 (-0.36, -0.30)	0.72 (0.70, 0.74)	0.02	-20.38	<0.001
	Period_2008	0.07 (0.05, 0.10)	1.08 (1.05, 1.10)	0.01	5.94	<0.001
All	Period_2013	0.25 (0.22, 0.28)	1.29 (1.25, 1.32)	0.01	17.88	<0.001
	Cohort_1918	0.91 (0.55, 1.26)	2.48 (1.73, 3.54)	0.18	4.98	<0.001
	Cohort_1923	0.5 (0.28, 0.71)	1.65 (1.33, 2.04)	0.11	4.57	<0.001
	Cohort_1928	0.23 (0.07, 0.38)	1.25 (1.08, 1.46)	0.08	2.91	0.004
	Cohort_1933	-0.08 (-0.22, 0.05)	0.92 (0.80, 1.05)	0.07	-1.20	0.229
	Cohort_1938	-0.18 (-0.31, -0.04)	0.84 (0.73, 0.96)	0.07	-2.52	0.012
	Cohort_1943	-0.14 (-0.27, 0)	0.87 (0.76, 1.00)	0.07	-1.94	0.052
	Cohort_1948	0.03 (-0.10, 0.16)	1.03 (0.90, 1.17)	0.07	0.39	0.693
	Cohort_1953	0.18 (0.06, 0.30)	1.2 (1.07, 1.36)	0.06	2.99	0.003
	Cohort_1958	0.32 (0.20, 0.43)	1.37 (1.23, 1.53)	0.06	5.52	<0.001
	Cohort_1963	0.5 (0.39, 0.60)	1.64 (1.48, 1.83)	0.05	9.27	<0.001
	Cohort_1968	0.39 (0.29, 0.50)	1.48 (1.34, 1.64)	0.05	7.47	<0.001
	Cohort_1973	0.18 (0.08, 0.29)	1.2 (1.08, 1.34)	0.05	3.44	0.001
	Cohort_1978	-0.15 (-0.27, -0.04)	0.86 (0.77, 0.96)	0.06	-2.62	0.009
	Cohort_1983	-0.55 (-0.68, -0.41)	0.58 (0.51, 0.66)	0.07	-8.02	<0.001
	Cohort_1988	-0.93 (-1.16, -0.71)	0.39 (0.31, 0.49)	0.11	-8.26	<0.001
	Cohort_1993	-1.2 (-1.89, -0.5)	0.3 (0.15, 0.61)	0.36	-3.36	0.001

TABLE S5. (Continued)

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard error	Z	P
	Age_20	-2.13 (-2.44, -1.82)	0.12 (0.09, 0.16)	0.16	-13.62	<0.001
	Age_25	-0.68 (-0.81, -0.55)	0.51 (0.44, 0.58)	0.07	-9.99	<0.001
	Age_30	0.11 (0.01, 0.20)	1.11 (1.01, 1.22)	0.05	2.20	0.028
	Age_35	0.34 (0.26, 0.43)	1.41 (1.3, 1.53)	0.04	8.03	<0.001
	Age_40	0.49 (0.42, 0.57)	1.64 (1.52, 1.77)	0.04	12.54	<0.001
	Age_45	0.5 (0.43, 0.58)	1.66 (1.53, 1.79)	0.04	12.82	<0.001
	Age_50	0.44 (0.36, 0.52)	1.55 (1.43, 1.69)	0.04	10.60	<0.001
	Age_55	0.35 (0.26, 0.44)	1.42 (1.30, 1.56)	0.05	7.64	<0.001
	Age_60	0.31 (0.21, 0.41)	1.37 (1.24, 1.51)	0.05	6.17	<0.001
	Age_65	0.32 (0.21, 0.43)	1.38 (1.24, 1.53)	0.05	5.89	<0.001
	Age_70	0.36 (0.25, 0.46)	1.43 (1.28, 1.59)	0.05	6.51	<0.001
	Age_75	0.12 (0.01, 0.23)	1.13 (1.01, 1.26)	0.06	2.06	0.039
	Age_80	-0.03 (-0.16, 0.10)	0.97 (0.85, 1.11)	0.07	-0.44	0.66
	Age_85	-0.51 (-0.69, -0.33)	0.6 (0.50, 0.72)	0.09	-5.56	<0.001
	Period_2003	-0.31 (-0.34, -0.29)	0.73 (0.71, 0.75)	0.01	-21.93	<0.001
	Period_2008	0.08 (0.06, 0.10)	1.09 (1.06, 1.11)	0.01	7.36	<0.001
Urban	Period_2013	0.23 (0.21, 0.26)	1.26 (1.23, 1.29)	0.01	18.30	<0.001
	Cohort_1918	0.88 (0.56, 1.19)	2.41 (1.76, 3.29)	0.16	5.50	<0.001
	Cohort_1923	0.45 (0.26, 0.64)	1.57 (1.30, 1.90)	0.1	4.65	<0.001
	Cohort_1928	0.21 (0.07, 0.34)	1.23 (1.07, 1.41)	0.07	2.97	0.003
	Cohort_1933	-0.13 (-0.26, -0.01)	0.88 (0.77, 0.99)	0.06	-2.06	0.039
	Cohort_1938	-0.18 (-0.31, -0.06)	0.83 (0.73, 0.94)	0.06	-2.90	0.004
	Cohort_1943	-0.12 (-0.24, 0.01)	0.89 (0.79, 1.01)	0.06	-1.83	0.067
	Cohort_1948	0.04 (-0.08, 0.16)	1.04 (0.92, 1.17)	0.06	0.61	0.544
	Cohort_1953	0.24 (0.13, 0.35)	1.27 (1.14, 1.42)	0.06	4.33	<0.001
	Cohort_1958	0.4 (0.30, 0.50)	1.5 (1.35, 1.66)	0.05	7.75	<0.001
	Cohort_1963	0.58 (0.48, 0.67)	1.78 (1.62, 1.96)	0.05	11.85	<0.001
	Cohort_1968	0.47 (0.38, 0.56)	1.6 (1.46, 1.76)	0.05	9.85	<0.001
	Cohort_1973	0.24 (0.15, 0.34)	1.27 (1.16, 1.40)	0.05	4.95	<0.001
	Cohort_1978	-0.14 (-0.24, -0.03)	0.87 (0.79, 0.97)	0.05	-2.56	0.011
	Cohort_1983	-0.62 (-0.74, -0.50)	0.54 (0.48, 0.61)	0.06	-9.98	<0.001
	Cohort_1988	-0.96 (-1.16, -0.76)	0.38 (0.31, 0.47)	0.1	-9.38	<0.001
	Cohort_1993	-1.36 (-2.03, -0.69)	0.26 (0.13, 0.50)	0.34	-3.98	<0.001

TABLE S5. (Continued)

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard error	Z	P
	Age_20	-2.55 (-3.41, -1.69)	0.08 (0.03, 0.18)	0.44	-5.81	<0.001
	Age_25	-1.16 (-1.54, -0.78)	0.31 (0.21, 0.46)	0.19	-5.96	<0.001
	Age_30	-0.22 (-0.49, 0.05)	0.8 (0.61, 1.06)	0.14	-1.57	0.116
	Age_35	0.23 (-0.02, 0.47)	1.26 (0.98, 1.61)	0.12	1.84	0.066
	Age_40	0.7 (0.48, 0.92)	2.02 (1.62, 2.51)	0.11	6.25	<0.001
	Age_45	0.82 (0.61, 1.04)	2.28 (1.84, 2.82)	0.11	7.48	<0.001
	Age_50	0.86 (0.64, 1.08)	2.37 (1.89, 2.96)	0.11	7.59	<0.001
	Age_55	0.85 (0.62, 1.09)	2.35 (1.85, 2.98)	0.12	7.06	<0.001
	Age_60	0.68 (0.43, 0.94)	1.98 (1.54, 2.56)	0.13	5.28	<0.001
	Age_65	0.39 (0.11, 0.66)	1.47 (1.12, 1.94)	0.14	2.74	0.006
	Age_70	0.52 (0.24, 0.79)	1.68 (1.27, 2.21)	0.14	3.67	<0.001
	Age_75	0.14 (-0.16, 0.43)	1.14 (0.85, 1.54)	0.15	0.89	0.376
	Age_80	-0.28 (-0.63, 0.08)	0.76 (0.53, 1.08)	0.18	-1.54	0.124
	Age_85	-0.99 (-1.54, -0.44)	0.37 (0.21, 0.65)	0.28	-3.52	<0.001
	Period_2003	-0.41 (-0.49, -0.34)	0.66 (0.61, 0.71)	0.04	-10.42	<0.001
	Period_2008	0.03 (-0.03, 0.09)	1.03 (0.97, 1.10)	0.03	1.00	0.315
Rural	Period_2013	0.38 (0.32, 0.45)	1.46 (1.37, 1.56)	0.03	11.35	<0.001
	Cohort_1918	1.1 (0.08, 2.12)	3 (1.09, 8.31)	0.52	2.12	0.034
	Cohort_1923	0.82 (0.28, 1.36)	2.27 (1.33, 3.9)	0.28	2.99	0.003
	Cohort_1928	0.36 (-0.02, 0.75)	1.44 (0.98, 2.11)	0.2	1.86	0.063
	Cohort_1933	0.22 (-0.11, 0.55)	1.24 (0.90, 1.72)	0.17	1.30	0.193
	Cohort_1938	-0.11 (-0.43, 0.22)	0.9 (0.65, 1.25)	0.17	-0.64	0.522
	Cohort_1943	-0.24 (-0.55, 0.08)	0.79 (0.58, 1.08)	0.16	-1.46	0.144
	Cohort_1948	-0.05 (-0.35, 0.25)	0.95 (0.70, 1.28)	0.15	-0.35	0.723
	Cohort_1953	-0.14 (-0.42, 0.14)	0.87 (0.66, 1.15)	0.14	-1.00	0.32
	Cohort_1958	-0.2 (-0.47, 0.06)	0.82 (0.63, 1.06)	0.13	-1.52	0.128
	Cohort_1963	0.04 (-0.21, 0.28)	1.04 (0.81, 1.33)	0.13	0.29	0.772
	Cohort_1968	-0.02 (-0.27, 0.22)	0.98 (0.77, 1.25)	0.12	-0.19	0.852
	Cohort_1973	-0.12 (-0.37, 0.13)	0.89 (0.69, 1.14)	0.13	-0.91	0.361
	Cohort_1978	-0.23 (-0.50, 0.05)	0.8 (0.60, 1.05)	-1.59	0.112	
	Cohort_1983	-0.12 (-0.43, 0.20)	0.89 (0.65, 1.22)	0.16	-0.73	0.468
	Cohort_1988	-0.77 (-1.29, -0.24)	0.46 (0.27, 0.79)	0.27	-2.85	0.004
	Cohort_1993	-0.55 (-1.89, 0.79)	0.58 (0.15, 2.21)	0.68	-0.80	0.423

SUPPLEMENTARY TABLE S6. The age-period-cohort estimates for cervical cancer mortality in China by area, 2003–2017.

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard Error	Z	P
All	Age_20	-2.11 (-2.55, -1.67)	0.12 (0.08, 0.19)	0.22	-9.44	<0.001
	Age_25	-1.57 (-1.82, -1.32)	0.21 (0.16, 0.27)	0.13	-12.15	<0.001
	Age_30	-0.78 (-0.95, -0.61)	0.46 (0.39, 0.54)	0.09	-8.94	<0.001
	Age_35	-0.27 (-0.42, -0.12)	0.77 (0.66, 0.89)	0.08	-3.5	<0.001
	Age_40	-0.02 (-0.15, 0.12)	0.98 (0.86, 1.12)	0.07	-0.29	0.774
	Age_45	0.29 (0.16, 0.41)	1.33 (1.18, 1.51)	0.06	4.58	<0.001
	Age_50	0.37 (0.25, 0.48)	1.44 (1.29, 1.62)	0.06	6.27	<0.001
	Age_55	0.4 (0.29, 0.51)	1.49 (1.34, 1.67)	0.06	7.15	<0.001
	Age_60	0.39 (0.28, 0.49)	1.47 (1.32, 1.64)	0.05	7.05	<0.001
	Age_65	0.47 (0.37, 0.57)	1.6 (1.44, 1.77)	0.05	8.99	<0.001
	Age_70	0.65 (0.56, 0.75)	1.92 (1.74, 2.11)	0.05	13.51	<0.001
	Age_75	0.72 (0.63, 0.81)	2.06 (1.88, 2.26)	0.05	15.52	<0.001
	Age_80	0.77 (0.67, 0.87)	2.16 (1.95, 2.40)	0.05	14.77	<0.001
	Age_85	0.69 (0.56, 0.82)	1.99 (1.75, 2.27)	0.07	10.53	<0.001
	Period_2003	-0.35 (-0.39, -0.31)	0.71 (0.68, 0.73)	0.02	-18.49	<0.001
	Period_2008	0.01 (-0.02, 0.04)	1.01 (0.98, 1.04)	0.01	0.88	0.377
	Period_2013	0.34 (0.30, 0.37)	1.4 (1.35, 1.44)	0.02	20.82	<0.001
	Cohort_1918	1.28 (1.07, 1.50)	3.61 (2.91, 4.47)	0.11	11.69	<0.001
	Cohort_1923	1.21 (1.06, 1.36)	3.34 (2.88, 3.88)	0.08	15.79	<0.001
	Cohort_1928	0.78 (0.65, 0.90)	2.17 (1.92, 2.47)	0.06	12.00	<0.001
	Cohort_1933	0.45 (0.33, 0.57)	1.57 (1.39, 1.77)	0.06	7.20	<0.001
	Cohort_1938	0.23 (0.10, 0.36)	1.26 (1.11, 1.43)	0.07	3.54	<0.001
	Cohort_1943	0.07 (-0.07, 0.21)	1.07 (0.93, 1.23)	0.07	0.97	0.333
	Cohort_1948	0.13 (-0.02, 0.27)	1.14 (0.98, 1.32)	0.07	1.71	0.086
	Cohort_1953	0.13 (-0.02, 0.28)	1.14 (0.98, 1.32)	0.08	1.66	0.097
	Cohort_1958	0.24 (0.09, 0.40)	1.27 (1.09, 1.49)	0.08	3.03	0.002
	Cohort_1963	0.36 (0.19, 0.52)	1.43 (1.21, 1.68)	0.08	4.25	<0.001
	Cohort_1968	0.24 (0.07, 0.41)	1.27 (1.07, 1.51)	0.09	2.72	0.007
	Cohort_1973	-0.04 (-0.23, 0.14)	0.96 (0.80, 1.15)	0.09	-0.45	0.65
Cohort_1978	-0.38 (-0.58, -0.17)	0.69 (0.56, 0.84)	0.10	-3.65	<0.001	
Cohort_1983	-0.72 (-0.95, -0.49)	0.49 (0.39, 0.61)	0.12	-6.17	<0.001	
Cohort_1988	-1.24 (-1.63, -0.86)	0.29 (0.20, 0.42)	0.20	-6.35	<0.001	
Cohort_1993	-2.72 (-4.15, -1.30)	0.07 (0.02, 0.27)	0.73	-3.74	<0.001	

TABLE S6. (Continued)

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard Error	Z	P
	Age_20	-2.13 (-2.50, -1.76)	0.12 (0.08, 0.17)	0.19	-11.34	<0.001
	Age_25	-1.58 (-1.79, -1.37)	0.21 (0.17, 0.26)	0.11	-14.51	<0.001
	Age_30	-0.72 (-0.86, -0.58)	0.48 (0.42, 0.56)	0.07	-10.11	<0.001
	Age_35	-0.23 (-0.36, -0.11)	0.79 (0.70, 0.89)	0.06	-3.74	<0.001
	Age_40	-0.06 (-0.17, 0.06)	0.95 (0.85, 1.06)	0.06	-0.98	0.326
	Age_45	0.25 (0.15, 0.35)	1.29 (1.17, 1.43)	0.05	4.95	<0.001
	Age_50	0.31 (0.21, 0.40)	1.36 (1.24, 1.49)	0.05	6.42	<0.001
	Age_55	0.33 (0.24, 0.42)	1.39 (1.27, 1.52)	0.05	7.12	<0.001
	Age_60	0.31 (0.22, 0.4)	1.37 (1.25, 1.50)	0.05	6.82	<0.001
	Age_65	0.48 (0.4, 0.57)	1.62 (1.49, 1.77)	0.04	11.13	<0.001
	Age_70	0.71 (0.63, 0.78)	2.03 (1.87, 2.19)	0.04	17.82	<0.001
	Age_75	0.74 (0.67, 0.82)	2.1 (1.95, 2.27)	0.04	19.44	<0.001
	Age_80	0.85 (0.77, 0.93)	2.34 (2.15, 2.54)	0.04	20.14	<0.001
	Age_85	0.74 (0.64, 0.84)	2.1 (1.89, 2.33)	0.05	14.10	<0.001
	Period_2003	-0.38 (-0.41, -0.35)	0.68 (0.66, 0.71)	0.02	-24.50	<0.001
	Period_2008	0.03 (0.01, 0.05)	1.03 (1.01, 1.06)	0.01	2.56	0.011
Urban	Period_2013	0.35 (0.32, 0.38)	1.42 (1.38, 1.46)	0.01	26.44	<0.001
	Cohort_1918	1.38 (1.21, 1.56)	3.99 (3.35, 4.76)	0.09	15.40	<0.001
	Cohort_1923	1.29 (1.16, 1.42)	3.65 (3.20, 4.15)	0.07	19.60	<0.001
	Cohort_1928	0.76 (0.65, 0.88)	2.15 (1.91, 2.41)	0.06	13.04	<0.001
	Cohort_1933	0.41 (0.30, 0.53)	1.51 (1.35, 1.69)	0.06	7.26	<0.001
	Cohort_1938	0.18 (0.06, 0.30)	1.2 (1.06, 1.34)	0.06	2.99	0.003
	Cohort_1943	0.01 (-0.12, 0.14)	1.01 (0.89, 1.15)	0.07	0.15	0.88
	Cohort_1948	0.09 (-0.04, 0.22)	1.1 (0.96, 1.25)	0.07	1.36	0.174
	Cohort_1953	0.2 (0.06, 0.34)	1.22 (1.07, 1.40)	0.07	2.88	0.004
	Cohort_1958	0.37 (0.23, 0.51)	1.45 (1.26, 1.67)	0.07	5.17	<0.001
	Cohort_1963	0.48 (0.34, 0.63)	1.62 (1.40, 1.88)	0.07	6.47	<0.001
	Cohort_1968	0.33 (0.18, 0.49)	1.4 (1.20, 1.63)	0.08	4.25	<0.001
	Cohort_1973	0.03 (-0.13, 0.20)	1.04 (0.88, 1.22)	0.08	0.42	0.678
	Cohort_1978	-0.42 (-0.60, -0.24)	0.66 (0.55, 0.79)	0.09	-4.62	<0.001
	Cohort_1983	-0.75 (-0.94, -0.55)	0.47 (0.39, 0.58)	0.10	-7.41	<0.001
	Cohort_1988	-1.28 (-1.61, -0.95)	0.28 (0.20, 0.39)	0.17	-7.60	<0.001
	Cohort_1993	-3.12 (-4.56, -1.68)	0.04 (0.01, 0.19)	0.73	-4.25	<0.001

TABLE S6. (Continued)

Area	Factor	Coefficient (95% CI)	Risk ratio (95% CI)	Standard Error	Z	P
	Age_20	-1.96 (-3.25, -0.67)	0.14 (0.04, 0.51)	0.66	-2.98	0.003
	Age_25	-1.55 (-2.29, -0.81)	0.21 (0.10, 0.45)	0.38	-4.09	<0.001
	Age_30	-0.95 (-1.52, -0.39)	0.39 (0.22, 0.68)	0.29	-3.32	0.001
	Age_35	-0.38 (-0.86, 0.10)	0.68 (0.42, 1.11)	0.25	-1.54	0.123
	Age_40	0.15 (-0.29, 0.59)	1.17 (0.75, 1.81)	0.22	0.69	0.492
	Age_45	0.38 (-0.02, 0.79)	1.47 (0.98, 2.20)	0.21	1.87	0.062
	Age_50	0.55 (0.17, 0.93)	1.74 (1.19, 2.54)	0.19	2.86	0.004
	Age_55	0.62 (0.26, 0.97)	1.86 (1.30, 2.65)	0.18	3.42	0.001
	Age_60	0.59 (0.26, 0.92)	1.8 (1.29, 2.51)	0.17	3.48	0.001
	Age_65	0.44 (0.12, 0.76)	1.55 (1.13, 2.13)	0.16	2.70	0.007
	Age_70	0.49 (0.19, 0.80)	1.64 (1.2, 2.23)	0.16	3.14	0.002
	Age_75	0.7 (0.40, 1.00)	2.01 (1.49, 2.71)	0.15	4.59	<0.001
	Age_80	0.47 (0.10, 0.84)	1.6 (1.11, 2.32)	0.19	2.49	0.013
	Age_85	0.45 (-0.03, 0.93)	1.56 (0.97, 2.52)	0.24	1.82	0.068
	Period_2003	-0.25 (-0.37, -0.13)	0.78 (0.69, 0.88)	0.06	-4.08	<0.001
	Period_2008	-0.07 (-0.17, 0.04)	0.94 (0.84, 1.04)	0.05	-1.25	0.21
Rural	Period_2013	0.31 (0.21, 0.42)	1.37 (1.23, 1.52)	0.05	5.93	<0.001
	Cohort_1918	0.89 (0.02, 1.76)	2.43 (1.02, 5.80)	0.44	2.00	0.045
	Cohort_1923	0.68 (0.10, 1.25)	1.97 (1.11, 3.51)	0.29	2.31	0.021
	Cohort_1928	0.95 (0.57, 1.34)	2.59 (1.76, 3.81)	0.20	4.84	<0.001
	Cohort_1933	0.72 (0.35, 1.08)	2.05 (1.43, 2.96)	0.19	3.86	<0.001
	Cohort_1938	0.54 (0.18, 0.90)	1.72 (1.19, 2.47)	0.19	2.90	0.004
	Cohort_1943	0.34 (-0.06, 0.74)	1.4 (0.94, 2.09)	0.20	1.68	0.093
	Cohort_1948	0.34 (-0.07, 0.75)	1.41 (0.93, 2.12)	0.21	1.63	0.103
	Cohort_1953	0.05 (-0.38, 0.48)	1.05 (0.68, 1.62)	0.22	0.22	0.826
	Cohort_1958	-0.13 (-0.59, 0.33)	0.88 (0.55, 1.39)	0.24	-0.55	0.584
	Cohort_1963	-0.06 (-0.55, 0.42)	0.94 (0.58, 1.52)	0.25	-0.26	0.793
	Cohort_1968	-0.05 (-0.56, 0.46)	0.95 (0.57, 1.58)	0.26	-0.20	0.841
	Cohort_1973	-0.33 (-0.88, 0.22)	0.72 (0.41, 1.25)	0.28	-1.17	0.242
	Cohort_1978	-0.16 (-0.74, 0.43)	0.86 (0.48, 1.53)	0.30	-0.52	0.602
	Cohort_1983	-0.56 (-1.27, 0.15)	0.57 (0.28, 1.16)	0.36	-1.54	0.123
	Cohort_1988	-1.1 (-2.19, 0)	0.33 (0.11, 1.00)	0.56	-1.96	0.05
	Cohort_1993	-2.12 (-5.25, 1.01)	0.12 (0.01, 2.74)	1.60	-1.33	0.184