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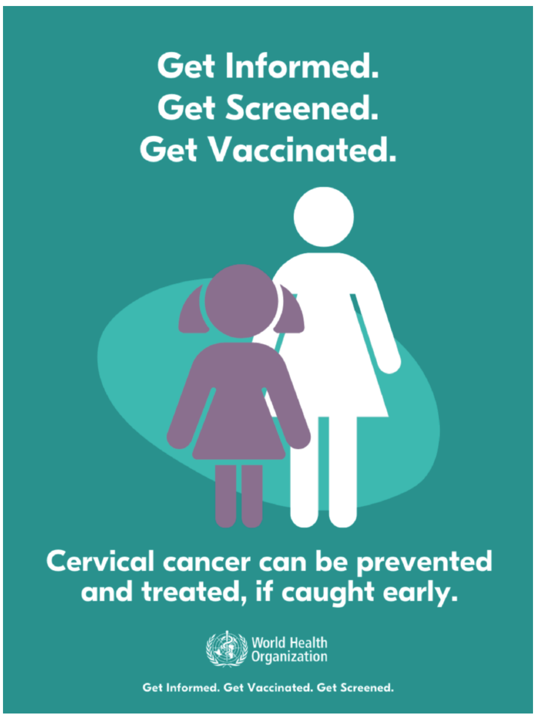


## CERVICAL CANCER PREVENTION AND CONTROL

### Foreword



### Vital Surveillances



### Preplanned Studies



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Cover Image: adapted from the World Health Organization, https://www.who.int/multi-media/details/get-informed.-get-screened.-get-vaccinated.

This week's issue was organized by Guest Editor Linhong Wang.

Foreword

# Accelerating Cervical Cancer Prevention and Control in China to Achieve Cervical Cancer Elimination Strategy Objectives

Linhong Wang[1,2,#]

Cervical cancer is one of many types of cancers that severely threaten women's health. Each year, 604,000 new cases of cervical cancer appear with 342,000 related deaths globally. China represents about 18% of global incidences and 17% of global deaths (*1*). The China Cancer Registry's annual report determined that, in 2020, world-standardized incidence rate of cervical cancer was 11.35 per 100,000 women — accompanied by a mortality rate of 3.42 per 100,000 women in China; further, both have demonstrated upward trends (*2*). Thus, China faces serious challenges with cervical cancer prevention and control: creating a major public health problem that severely threatens women's health.

China has long paid great attention to the prevention and treatment of cervical cancer. In 2009, China initiated a screening program for cervical cancer and breast cancer for rural women as a National Major Public Health Service Project (*3*), leading to the improvement of cervical cancer screening coverage nationwide. Following this initiative, free screening was provided to rural women aged 35–64 years in the same project areas. Relevant agencies explored options around building screening service systems suitable for local healthcare operations and optimized the screening program's implementation plan, which gradually formed institutionalized and standardized operation mechanisms for regular cervical cancer screening services. In recent years, different local provinces and regions have also been actively exploring effective models for comprehensive prevention and treatment of cervical cancer. In many regions, cervical cancer screening has been launched as a local public welfare project, with the aim of building a full-chain, closed-loop management model for cervical cancer prevention and treatment. In addition, big data has been used to promote scientific, standardized, and precise prevention and treatment of cervical cancer. In 2019, the national cervical cancer screening program became a National Basic Public Health Service Project in order to further expand screening coverage of cervical cancer. The Healthy China Action Plan (2019–2030) further specified objectives and strategies for gradually improving screening coverage of cervical cancer, promoting Human Papillomavirus (HPV) vaccination, and improving the accessibility of HPV vaccines (*4*).

With advances in science and technology, and improved prevention and control measures, it has been proven that the incidence and mortality of cervical cancer can be greatly reduced (or even eliminated) through multi-pronged prevention measures. In November 2020, the World Health Organization (WHO) officially released the Global Strategy for Accelerating the Elimination of Cervical Cancer as a Public Health Problem, which depicted the grand vision of eliminating cervical cancer by the end of this century. The strategy proposed the goal of "90-70-90", which stated that, by 2030, 90% of girls will have completed HPV vaccination by the age of 15; 70% of women will have been screened for high-precision tests by the age of 35–45; and 90% of women with cervical precancerous lesions and cervical cancer will have received treatment (*5*). China has actively responded to the WHO strategy and prioritized the prevention and control of cervical cancer. In the newly released China Women's Development Guidelines (2021–2030), China clearly identified objectives including raising women's awareness of cervical cancer prevention and treatment, continuously improving the prevention and treatment capacity for cervical cancer, and achieving 70% screening coverage of targeted female age groups (*6*). To effectively achieve these objectives, several strategies and measures were also recommended as follows. First, China must increase the dissemination of health knowledge among women and improve public awareness of core knowledge about cervical cancer prevention and treatment. Second, China needs to actively promote free HPV vaccination for school-aged girls in areas where conditions permit, while gradually increasing the HPV vaccination rate for girls aged 9−14 years, as well as promote pilots and accelerate public health campaign publicity. Third, China should continue to implement women's cervical cancer screening programs and comprehensively accelerate the improvement of cervical cancer screening rates among women. Fourth, China has to strengthen innovative applications of cervical cancer screening and diagnostic technologies, explore screening methods and strategies suitable for China, focus on improving the screening and service capacities of local institutions, strengthen the building of information management systems and big data applications, and strengthen quality control, monitoring, and evaluation. Finally, China needs to improve the tracking and management of those with abnormal screening results, strengthen the connectivity between screening and follow-up diagnosis and treatment services, and promote early diagnosis and treatment (*7*).

Given the massive number of women in China, as well as regional imbalances of health resources, it has been found that the provision of basic services in cervical cancer (vaccination, screening, and treatment) is still lacking. HPV vaccination has begun only recently and faces a supply shortage due to insufficient domestic production capacity, while HPV vaccination rate in the targeted 9–14 age groups remains quite low. Women's awareness of cervical cancer screening as well as screening coverage rates are both low, and gaps exist in the provision of high-precision screening techniques and system management that ensures quality control of screening and follow-up treatment. China still faces many challenges in trying to meet the objectives of the cervical cancer elimination strategy. It is essential that cervical cancer elimination models are adjusted to suit China's needs and current circumstances, accommodating the different developmental phases of regions in particular, in order to help achieve China's goal of the elimination of cervical cancer.

This Weekly issue convened a special issue on cervical cancer prevention and control. The China Cancer Registry team was invited to analyze age-specific characteristics and trends, as well as the age-period-cohort (APC) effects of incidence and mortality of cervical cancer in China using their long-term data (*8*). Wang's team applied China's Chronic Disease and Nutrition Surveillance data to estimate the latest screening coverage rates of cervical cancer in China, demonstrating regional and provincial differences as well as the effects of age, education, occupation, income, and health insurance on screening service utilization (*9*). Bao et al. multicentric clinical study aimed to evaluate the effects of multiple screening strategies and the prevalence of human papillomavirus infection in women with precancerous lesions (*10*). The study provides ample evidence for the future implementation of HPV-based screening and vaccination strategies at the population level. Qiu's team analyzed the distribution of high-risk HPV subtype infections using local HPV screening data (*11*). Characterizing the epidemiological trends of HPV subtypes is beneficial to the identification and follow-up of high-risk populations as well as provides scientific support for precise prevention and control measures for cervical cancer.

These articles provide evidence from multiple aspects of surveillance and research on the prevention and control of cervical cancer in China, including the trends and characteristics of cervical cancer incidence and mortality across different time periods and different regions (urban and rural areas), the distribution of high-risk HPV subtype infections across populations of women, the association between different HPV infection patterns with high-grade cervical precancerous lesions before the advent of large-scale HPV vaccinations, and the phased effect and gap of current implementation of cervical cancer screenings in China. These data and research recommendations are extremely important for identifying target population groups for prevention and control measures, exploring suitable screening strategies, achieving precise prevention and control, and proposing future, multi-tier cervical cancer prevention and control models that suit regions in different developmental phases in China. This special issue calls for the joint efforts of all parties to continue to reduce the threats of cervical cancer to women's health and lives so that one day cervical cancer might be eliminated for good.

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Vital Surveillances

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

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## 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

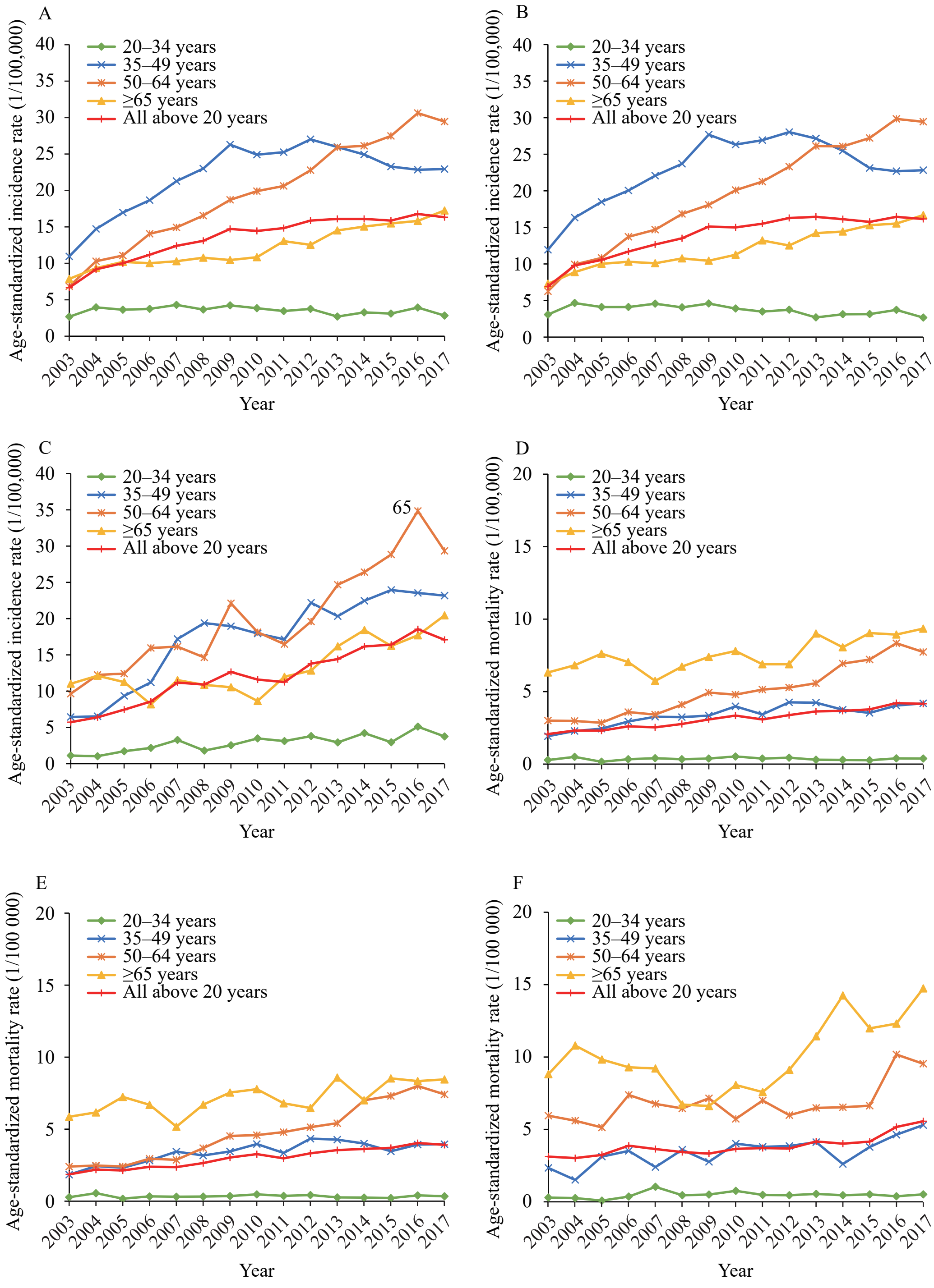


FIGURE 1. The trends of incidence and mortality rates of cervical cancer by age group and area, from 2003 to 2017. (A) Incidence rates in all areas, (B) Incidence rates in urban areas, (C) Incidence rates in rural areas, (D) Mortality rates in all areas, (E) Mortality rates in urban areas, (F) Mortality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

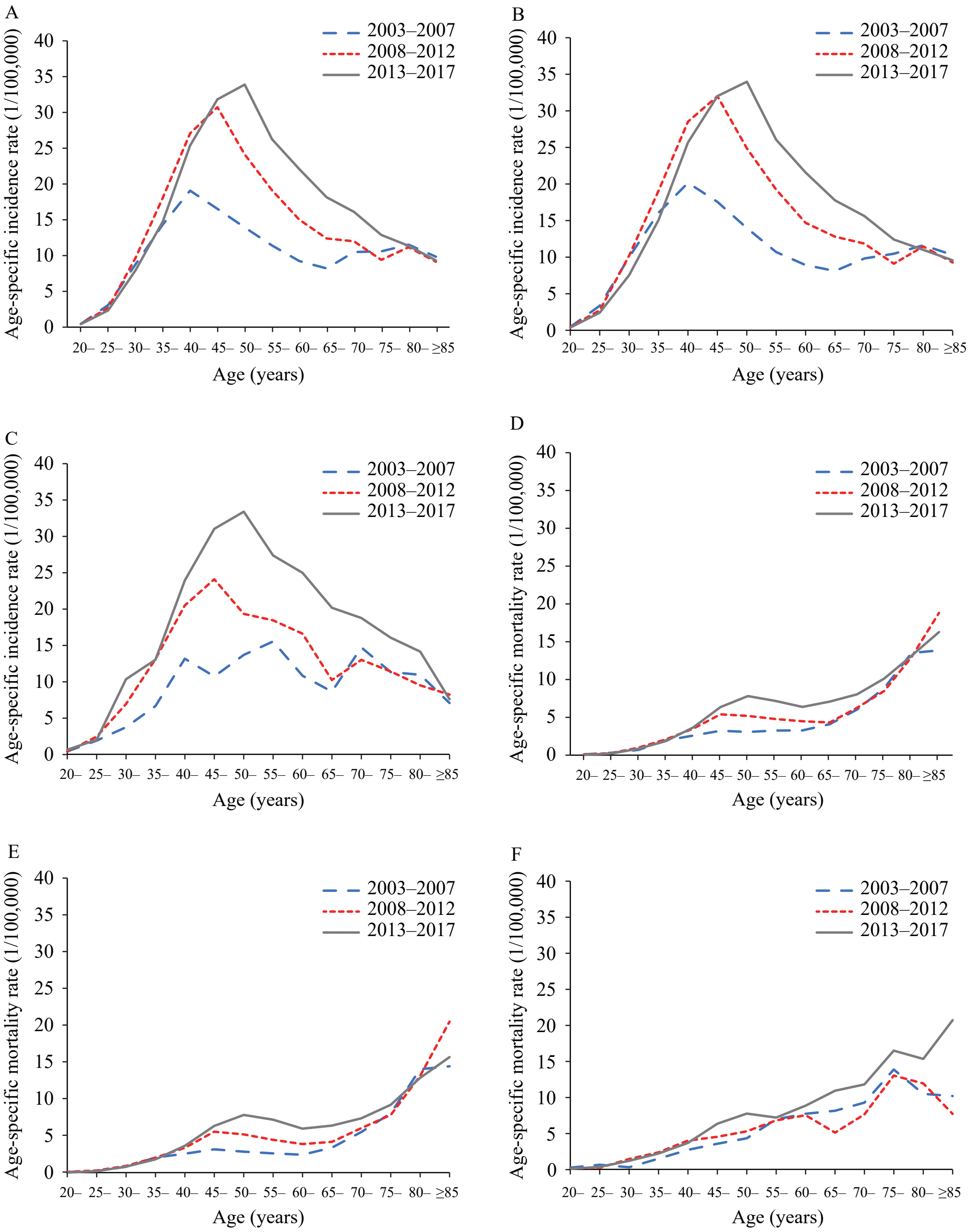


FIGURE 2. The age-specific incidence and mortality rates of cervical cancer, by time period and area. (A) Incident rates in all areas. (B) Incident rates in urban areas. (C) Incident rates in rural areas. (D) Mortality rates in all areas. (E) Mortality rates in urban areas. (F) Mortality rates in rural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

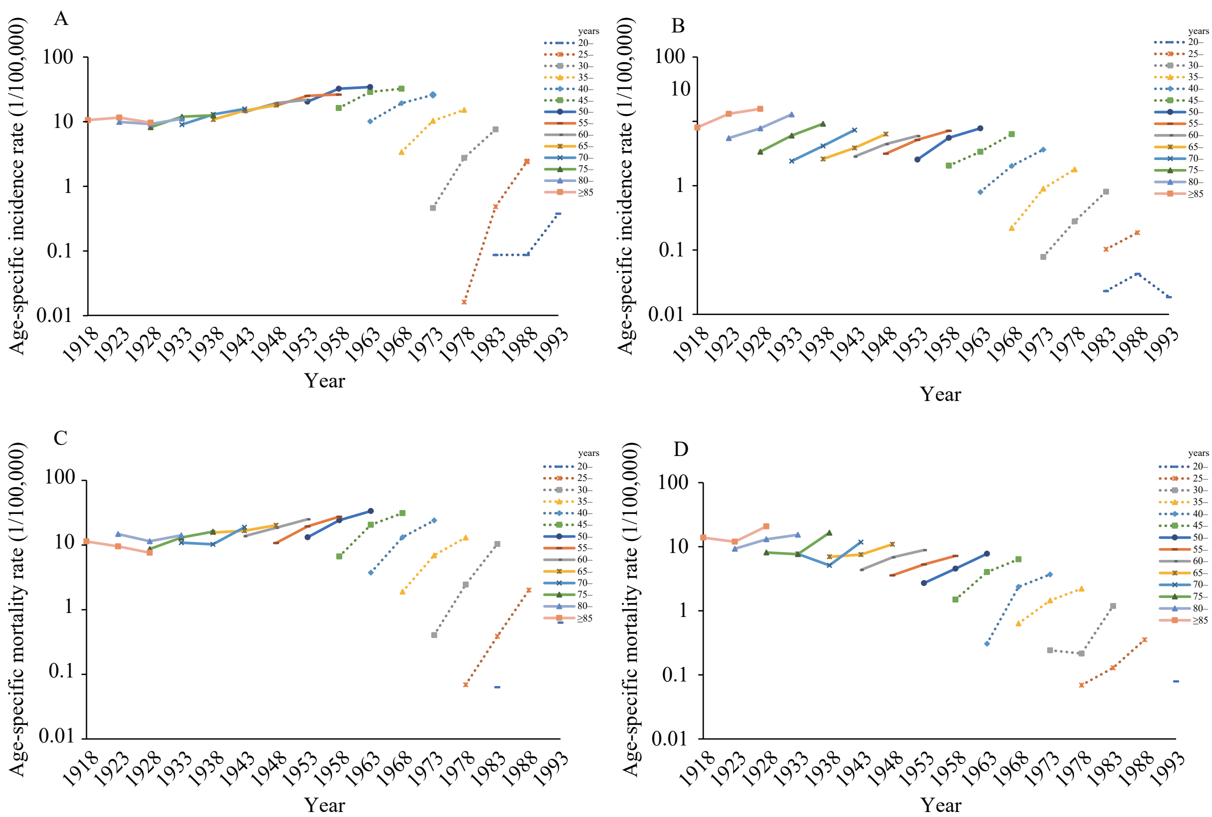


FIGURE 3. The birth cohort-specific incidence and mortality rates of cervical cancer, by area. (A) Incident rates in urban areas. (B) Incident rates in rural areas. (C) Mortality rates in urban areas. (D) Mortality rates in rural areas.
Note: Results are not shown in age group 20–24 if the age-specific 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

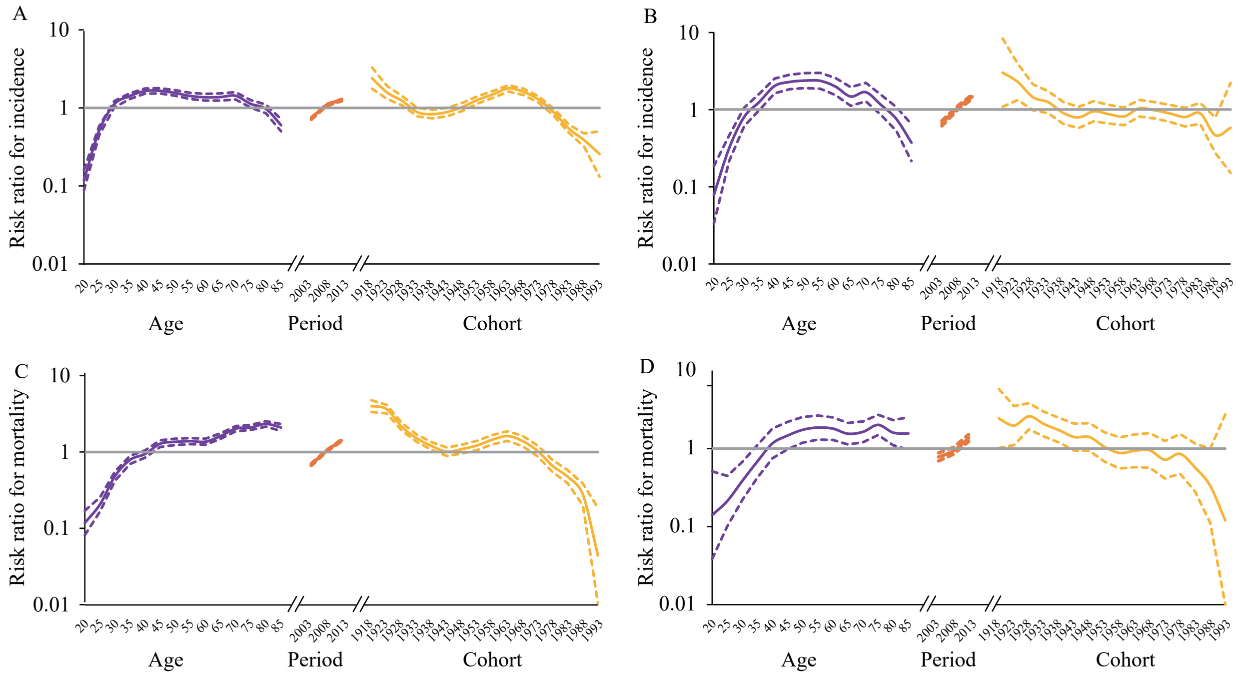


FIGURE 4. The result of age-period-cohort analysis of incidence and mortality rates of cervical cancer, by area. (A) Incident rates in urban areas; (B) Incident rates in rural areas; (C) Mortality rates in urban areas; (D) Mortality rates in rural areas.
Notes: Purple solid and dash lines represent the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

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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* |
|---|---|---|---|---|---|---|
| | 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 |
| All | 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 |

Preplanned Studies

# Cervical Cancer Screening Coverage — China, 2018–2019

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**Summary**

**What is already known about this topic?**

The World Health Organization set a 2030 target of 70% cervical cancer screening coverage for women aged 35–45 years. Coverage stood at 37% in China in 2015.

**What is added by this report?**

In 2018–2019, China's cervical cancer screening coverage reached 43.4% in women aged 35–44 years and 36.8% in women aged 35–64 years. Screening coverage was still lower in rural areas as well as central and western regions; large variations existed across provincial-level administrative divisions.

**What are the implications for public health practice?**

National and local policy and financial support should be maintained for cervical cancer screening, along with more targeted health education and outreach efforts and strengthened accessibility of health services in the rural areas and central and western regions.

Effective prevention and control measures have tamed cervical cancer in most parts of the world. In November 2020, the World Health Organization (WHO) set a 2030 target of 70% cervical cancer screening coverage for women aged 35–45 years. (*1*) China launched a national free screening program for rural women aged 35–64 years in 2009, in order to combat rising cervical cancer incidence, particularly in younger and rural populations, since the late 1990s (*2*) and an imbalanced disease burden in the central and western regions (*3*). It set a goal that screening coverage should reach 50% in women aged 35–64 years by 2025 (*4*). This study used the latest nationally and provincially representative survey data to estimate screening coverage in China and analyze its key sociodemographic and geographic factors via Rao Scott chi-square tests and logistic regression models. This study still suggests gaps in cervical cancer screening coverage with the WHO 2030 target. It also suggests that national and local policy and financial support should be maintained, health education and outreach efforts should be directed more toward the targeted age groups, and accessibility of health-related services should be further strengthened in the rural areas and central and western regions.

This study estimated China's latest cervical cancer screening uptake by using newly released national survey data from China Chronic Disease and Nutrition Surveillance in 2018–2019. Women aged 18 years and older were selected from 298 districts/counties across all 31 provincial-level administrative divisions (PLADs) in the mainland of China through multi-stage and cluster randomized sampling. Women were interviewed by trained local health staff about history of previous cervical cancer screening as well as the month and year of the most recent screening, if applicable. A total of 102,779 participants aged 20–64 years old completed the survey, yielding a 95.0% response rate. Among them, 27,471 female participants were excluded from the final analysis because of incomplete sociodemographic data, lack of response to the cervical cancer screening question, or age falling outside the targeted age groups. The screening rates of stratified sociodemographic groups were compared through chi-square tests, and predictors of screening uptake were investigated via multivariate logistic regression analysis. Standard errors (SE) were estimated by Taylor linearization with a finite population correction. Statistical significance was determined using two-sided $P<0.05$. All statistical analyses were performed over SAS (version 9.4, SAS Institute Inc., Cary, USA).

The final sample consists of 75,308 participants aged 20–64 years old. Participants were 40 years old on average with 44.6% from urban areas, 42.2% from the eastern region of China, 96.9% with health insurance coverage, and 43.8% with health check-ups done in the previous three years (Table 1).

The estimated results show that in 2018–2019, cervical cancer lifetime screening coverage (i.e., the percentage of women who had ever taken screening) reached 43.4% [95% confidence interval (*CI*): 41.5%–45.3%] in women aged 35–44 years, 39.6%

TABLE 1. Sociodemographic characteristics of female participants aged 20–64 years in the cervical cancer screening survey — China, 2018–2019.

| Characteristics | No. of participants (*N*=72,095) | Weighted proportion (%)* |
|---|---|---|
| Age (years) | | |
| 20–24 | 1,534 | 15.9 |
| 25–34 | 8,318 | 22.0 |
| 35–44 | 12,163 | 26.7 |
| 45–54 | 24,840 | 20.0 |
| 55–64 | 25,240 | 15.2 |
| Area type | | |
| Urban | 33,068 | 44.6 |
| Rural | 39,027 | 55.4 |
| Location | | |
| Eastern | 26,674 | 42.2 |
| Central | 21,147 | 32.4 |
| Western | 24,274 | 25.3 |
| Education | | |
| Primary or less | 34,596 | 31.6 |
| Middle school | 21,781 | 32.3 |
| High school | 9,553 | 16.1 |
| College or above | 6,165 | 20.0 |
| Income (CNY) | | |
| Q1 (<6,667) | 15,278 | 18.3 |
| Q2 (6,667–13,332) | 13,943 | 18.0 |
| Q3 (13,333–27,999) | 13,355 | 19.2 |
| Q4 (28,000+) | 14,142 | 23.0 |
| Don't know/refused | 15,377 | 21.5 |
| Employment | | |
| Employed | 47,155 | 69.1 |
| Housework | 14,835 | 18.3 |
| Retired | 6,541 | 4.3 |
| Unemployed | 3,564 | 8.3 |
| With health insurance | | |
| No | 1,462 | 3.1 |
| Yes | 70,633 | 96.9 |
| With health check–ups in the past 3 years | | |
| No | 40,195 | 51.9 |
| Yes | 31,900 | 48.1 |
| Self-assessed health status | | |
| Poor or fair | 41,913 | 56.5 |
| Good | 30,182 | 43.5 |

* Percentages are weighted to represent the national total population with poststratification for age and gender.

(95% *CI*: 37.9%–41.4%) in women aged 30–49 years, and 36.8% (95% *CI*: 35.1%–38.4%) in women aged 35–64 years. (Table 2) Screening coverage peaked at 45.0% in the 40–44 age group and declined to 18.8% in the 60–64 age group. About 90% of the screened women reported doing so within the previous three

TABLE 2. Sociodemographic stratifications and multivariate logistic regression results of cervical cancer screening coverage in China, 2018–2019.

| Sociodemographic variables | Screen rates among 20–64 years old % (95% *CI*) | | | *P*-value* | 35–64 years old | |
|---|---|---|---|---|---|---|
| | Total | Urban | Rural | | Screen rates % (95% *CI*) | Screen *OR* (95% *CI*) |
| Total | 29.5 (28.1, 30.9) | 32.2 (30.2, 34.2) | 26.6 (24.9, 28.3) | <0.001 | 36.8 (35.1, 38.4) | |
| Age (years) | | | | | | |
| 20–24 | 8.6 (6.6, 10.6) | 7.8 (4.8, 10.9) | 9.5 (6.7, 12.3) | 0.473 | – | – |
| 25–29 | 19.2 (17.0, 21.3) | 21.8 (18.5, 25.1) | 15.7 (13.7, 17.7) | 0.001 | – | – |
| 30–34 | 29.7 (27.3, 32.1) | 32.3 (29.0, 35.6) | 26.1 (22.9, 29.3) | 0.012 | – | – |
| 35–39 | 41.7 (39.3, 44.1) | 47.3 (44.0, 50.5) | 34.9 (31.7, 38.2) | <0.001 | 41.7 (39.3, 44.1) | 2.82 (2.48, 3.22) |
| 40–44 | 45.0 (42.7, 47.2) | 48.3 (44.9, 51.6) | 41.6 (38.8, 44.3) | 0.002 | 45.0 (42.7, 47.2) | 3.51 (3.10, 3.98) |
| 45–49 | 40.1 (37.8, 42.4) | 43.6 (40.4, 46.7) | 36.7 (33.7, 39.6) | 0.001 | 40.1 (37.8, 42.4) | 3.02 (2.69, 3.39) |
| 50–54 | 34.5 (32.5, 36.4) | 38.6 (35.8, 41.4) | 30.4 (27.7, 33.2) | <0.001 | 34.5 (32.5, 36.4) | 2.33 (2.13, 2.55) |
| 55–59 | 27.5 (25.6, 29.3) | 30.9 (27.9, 33.9) | 24.5 (22.2, 26.7) | 0.001 | 27.5 (25.6, 29.3) | 1.60 (1.48, 1.74) |
| 60–64 | 18.8 (17.2, 20.5) | 21.4 (19.0, 23.8) | 16.7 (14.6, 18.8) | 0.005 | 18.8 (17.2, 20.5) | 1.00 [Reference] |
| $P_{trend}$ | <0.001 | <0.001 | <0.001 | | <0.001 | |
| 30–49 | 39.6 (37.9, 41.4) | 43.2 (40.7, 45.6) | 35.6 (33.6, 37.7) | <0.001 | – | – |
| 35–44 | 43.4 (41.4, 45.3) | 47.8 (44.9, 50.6) | 38.5 (36.3, 40.7) | <0.001 | – | – |
| Area type | | | | | | |
| Urban | 32.2 (30.2, 34.2) | – | – | | 41.1 (38.7, 43.4) | 0.92 (0.81, 1.00) |
| Rural | 26.6 (24.9, 28.3) | – | – | | 32.4 (30.5, 34.4) | 1.00 [Reference] |
| $P_{difference}$ | <0.001 | | | | <0.001 | |
| Geographic region | | | | | | |
| Eastern | 33.4 (31.1, 35.7) | 36.0 (33.1, 39.0) | 29.3 (26.6, 32.0) | <0.001 | 41.6 (38.9, 44.3) | 1.31 (1.12, 1.53) |
| Central | 28.1 (25.5, 30.7) | 29.9 (25.9, 33.9) | 26.6 (23.1, 30.0) | 0.242 | 34.9 (31.9, 38.0) | 1.11 (0.93, 1.32) |
| Western | 24.8 (23.1, 26.6) | 26.6 (24.0, 29.2) | 23.4 (21.3, 25.6) | 0.070 | 31.3 (28.9, 33.6) | 1.00 [Reference] |
| $P_{difference}$ | <0.001 | <0.001 | 0.023 | | <0.001 | |
| Education | | | | | | |
| Primary or less | 25.3 (23.6, 26.9) | 26.4 (23.4, 29.3) | 24.8 (23.0, 26.6) | 0.348 | 26.9 (25.2, 28.6) | 1.00 [Reference] |
| Middle school | 32.1 (30.1, 34.0) | 35.3 (32.4, 38.3) | 29.2 (27.1, 31.4) | <0.001 | 40.2 (38.2, 42.3) | 1.53 (1.40, 1.67) |
| High school | 33.5 (30.9, 36.1) | 36.0 (32.9, 39.1) | 28.1 (23.5, 32.8) | 0.011 | 46.5 (42.9, 50.1) | 1.81 (1.58, 2.08) |
| College or above | 28.9 (26.3, 31.5) | 30.2 (27.2, 33.2) | 22.4 (18.3, 26.6) | 0.006 | 55.7 (51.9, 59.4) | 1.85 (1.56, 2.20) |
| $P_{trend}$ | 0.005 | 0.489 | 0.493 | | <0.001 | |
| Household income per capita (CNY) | | | | | | |
| Q1 (<6,667) | 24.2 (22.3, 26.1) | 24.8 (20.0, 29.5) | 24.0 (22.0, 26.0) | 0.783 | 29.7 (27.5, 31.8) | 1.00 [Reference] |
| Q2 (6,667–13,332) | 27.6 (25.7, 29.5) | 29.6 (27.3, 31.9) | 26.0 (23.4, 28.6) | 0.038 | 34.2 (32.2, 36.1) | 1.09 (0.97, 1.23) |
| Q3 (13,333–27,999) | 32.4 (30.4, 34.4) | 34.0 (31.2, 36.7) | 30.2 (27.6, 32.8) | 0.054 | 40.2 (37.9, 42.4) | 1.15 (1.01, 1.31) |
| Q4 (>28,000) | 36.3 (33.9, 38.7) | 37.2 (34.4, 40.1) | 33.1 (29.5, 36.6) | 0.085 | 47.3 (44.6, 50.1) | 1.24 (1.07, 1.43) |
| Don't know/refused | 26.1 (23.9, 28.3) | 28.0 (24.7, 31.4) | 24.2 (21.7, 26.8) | 0.075 | 31.8 (28.8, 34.8) | 0.92 (0.80, 1.06) |
| $P_{trend}$ † | <0.001 | <0.001 | <0.001 | | <0.001 | |
| Employment status | | | | | | |
| Employed | 30.5 (29.1, 31.9) | 33.4 (31.2, 35.5) | 27.6 (25.9, 29.2) | <0.001 | 37.9 (36.2, 39.5) | 1.11 (0.96, 1.28) |
| Housework | 28.5 (25.9, 31.1) | 32.4 (28.5, 36.2) | 25.7 (23.1, 28.4) | 0.001 | 33.0 (30.4, 35.6) | 1.10 (0.94, 1.30) |
| Retired | 35.3 (31.7, 38.9) | 35.0 (31.3, 38.6) | 45.5 (35.8, 55.2) | 0.034 | 35.8 (32.2, 39.4) | 1.00 [Reference] |
| Unemployed | 20.3 (17.6, 23.0) | 21.7 (18.1, 25.3) | 18.1 (14.0, 22.1) | 0.215 | 37.0 (32.4, 41.5) | 1.07 (0.84, 1.38) |
| $P_{difference}$ | <0.001 | <0.001 | <0.001 | | 0.002 | |

TABLE 2. (Continued)

| Sociodemographic variables | Screen rates among 20–64 years old % (95% *CI*) | | | *P*-value* | 35–64 years old | |
|---|---|---|---|---|---|---|
| | Total | Urban | Rural | | Screen rates % (95% *CI*) | Screen *OR* (95% *CI*) |
| Health insurance | | | | | | |
| No | 15.4 (11.9, 18.9) | 15.9 (11.5, 20.3) | 14.4 (9.1, 19.7) | 0.678 | 21.3 (17.3, 25.4) | 1.00 [Reference] |
| Yes | 30.0 (28.6, 31.4) | 32.9 (30.9, 34.8) | 26.9 (25.1, 28.6) | <0.001 | 37.1 (35.4, 38.7) | 1.96 (1.57, 2.45) |
| $P_{difference}$ | <0.001 | <0.001 | 0.001 | | <0.001 | |
| Health check-up in the last 3 years | | | | | | |
| No | 20.2 (18.8, 21.5) | 20.5 (18.3, 22.7) | 19.9 (18.4, 21.4) | 0.654 | 24.5 (22.8, 26.1) | 1.00 [Reference] |
| Yes | 40.8 (39.1, 42.5) | 42.0 (39.8, 44.2) | 38.8 (36.2, 41.4) | 0.066 | 51.4 (49.3, 53.2) | 3.09 (2.84, 3.36) |
| $P_{difference}$ | <0.001 | <0.001 | <0.001 | | <0.001 | |
| Self-assessed health | | | | | | |
| Poor or fair | 31.4 (29.9, 32.9) | 34.5 (32.2, 36.9) | 28.3 (26.7, 29.9) | <0.001 | 37.2 (35.5, 38.8) | 1.00 [Reference] |
| Good | 27.5 (25.9, 29.1) | 29.9 (27.9, 32.0) | 24.5 (22.3, 26.7) | 0.001 | 36.2 (34.1, 38.3) | 0.85 (0.78, 0.93) |
| $P_{difference}$ | <0.001 | <0.001 | <0.001 | | 0.349 | |

Note: Screening rates are all weighted proportions to represent the national total population with poststratification for age and gender.

Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

* *P*-value denotes *P*-value for difference between urban screening coverage and rural screening coverage in women aged 20–64 years.

† Participants answering “Don’t know/refused” are not included in the calculation.

years.

Low screening uptake for the 20–64 age groups was found in women with the lowest education (25.3%; 95% *CI*: 23.6%–26.9%), income (24.2%; 95% *CI*: 22.3%–26.1%), without health insurance coverage (15.4%; 95% *CI*: 11.9%–18.9%), without health check-ups in the previous three years (20.2%; 95% *CI*: 18.8%–21.5%), and in the 20–24 age group (urban, 7.8%; 95% *CI*: 4.8%–10.9%, *vs*. rural, 9.5%; 95% *CI*: 6.7%–12.3%). Screening coverage for women aged 35–64 years in urban areas was 45.6% (95% *CI*: 42.0%–49.2%) in the eastern region, 37.9% (95% *CI*: 33.3%–42.5%) in the central region, and 35.3% (95% *CI*: 32.1%–38.5%) in the western region; for rural women aged 35–64 years, it was 36.0% (95% *CI*: 32.9%–39.1%) in the eastern region, 32.4% (95% *CI*: 28.5%–36.3%) in the central region, and 28.3% (95% *CI*: 25.8%–30.9%) in the western region.

Multivariate logistic regression results for women aged 35–64 years surprisingly revealed that the urban factor was statistically insignificant, if not negative, in predicting screening uptake compared to the rural areas [odds ratio (*OR*): 0.92; 95% *CI*: 0.81–1.00]. However, the likelihood of screening in the eastern region still prevailed over the western region (*OR*: 1.31; 95% *CI*: 1.12–1.53), whereas the central region showed an insignificant advantage over the western region (*OR*: 1.11; 95% *CI*: 0.93–1.32). The likelihood of screening was 96% higher in women with health insurance than in women without health insurance (*OR*: 1.96; 95% *CI*: 1.57–2.45), and 2.09 times higher in women with health check-ups during the past three years than in women without health check-ups (*OR*: 3.09; 95% *CI*: 2.84–3.36).

PLADs’ data showed that Beijing Municipality went beyond 70% in screening coverage, followed by Zhejiang Province at above 60%, Jiangsu Province at above 50%, Tianjin Municipality, Hunan Province, and Shanghai Municipality at nearly 50%, while Hebei Province, Xizang (Tibet) Autonomous Region and Guizhou Province fell under 25% in screening coverage (Figure 1).

## DISCUSSION

This study estimated that in 2018–2019, 43.4% of women aged 35–44 years, 39.6% of women aged 30–49 years, and 36.8% of women aged 35–64 years had ever participated in cervical cancer screening in China. These results reveal both progress and gaps in cervical cancer screening in China. On the one hand, screening coverage for women aged 35–64 years, the targeted range of China’s national screening program, rose continuously from about 25% in 2010 (*5*), 27% in 2013 (*6*), 31% in 2015 (*7*), to the current 37% in 2018–2019. The upward trend provides strong evidence for the positive impact of the national screening program. Screening coverage for women aged 30–49 years, the age groups recommended by the

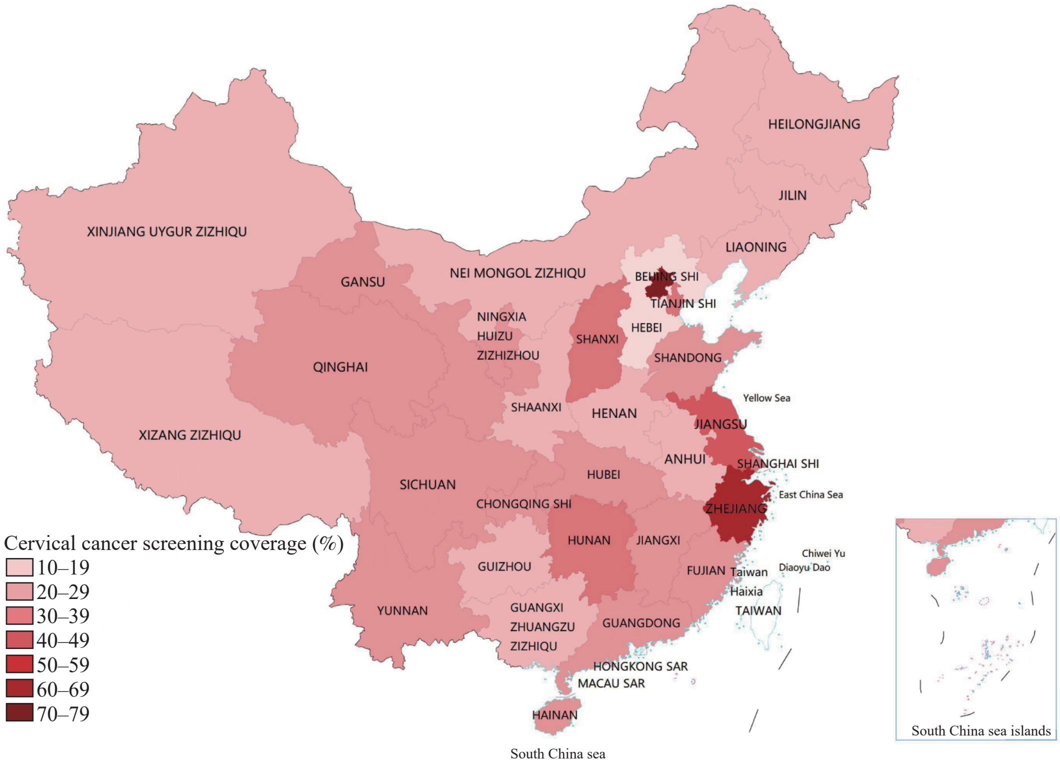


FIGURE 1. Provincial-level administrative divisions variations of cervical cancer screening coverage in women aged 35–64 years in China, 2018–2019.

WHO to monitor screening performance and results (*1*), also slightly exceeds the estimated worldwide screening coverage of 36% in 2019 (*8*). On the other hand, the 43% screening coverage for women aged 35–44 years is still far off the WHO 2030 target of 70% screening coverage.

One exciting finding of this study is that traditional disadvantages borne by the rural areas may have begun to dissipate as suggested by multivariate logistic analysis. It again points to the positive impact of the national free screening program in rural areas over the past decade. As the national screening program became the National Basic Public Health Service Program in 2019, national and local policy as well as financial support for cervical cancer screening should be continued to maintain ongoing progress in rural screening uptake. Furthermore, among individual socioeconomic and health-related disparities in screening uptake, which corroborate with previous studies in China and abroad (*9*), regular health-checkups had strong positive effects over screening uptake, which highlights the importance of strengthened access to health services and health education beyond cancer screening. Moreover, this study suggests excessive screening uptake in the 20–24 age group especially in rural areas, which falls outside the recommended age groups of national screening recommendations (*10*). To meet the WHO 2030 target, health education and outreach efforts should be directed more toward the targeted age groups.

This study is limited by inaccuracies of self-reported data, potential unequal representation of screening program areas across the sampling regions, and the lack of survey questions on sociopsychological factors of screening uptake. Future studies using administrative data will offer a more definitive look into screening coverage. Qualitative studies on the drivers and barriers of screening uptake will also be helpful in improving screening program design. Moreover, this study only addresses screening coverage without touching upon screening quality control, which is crucial to the effectiveness of any screening program.

In conclusion, this study provides the latest estimate of cervical cancer screening coverage in China based on nationally and provincially representative survey data in 2018–2019. Approximately 43.4% of women aged 35–44 years and 36.8% of women aged 35–64 years reported having had cervical cancer screening in China in 2018–2019. To close the gaps with the WHO target for 2030, national and local policy and financial support should be maintained for cervical cancer screening services, health education and outreach efforts should be focused on targeted age groups, and accessibility of health services should be strengthened in the rural areas and in central and western regions.

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Preplanned Studies

# Prevalence of High-Risk Human Papillomavirus in Cervical Intraepithelial Neoplasia in the Pre-Vaccine Era — China, 2017–2018

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**Summary**

### What is already known about this topic?

Human papillomavirus (HPV) type-specific strategies play a key role in the prevention of cervical intraepithelial neoplasia (CIN), but evidence on the HPV type-specific prevalence in CIN is limited.

### What is added by this report?

This multicentric study estimates the prevalence of high-risk HPV types in CIN cases and the associations of HPV infection patterns with high-grade CIN in China in 2017–2018.

### What are the implications for public health practice?

Population-based prevention strategies should give preference to HPV-16 and 18, and strategies for non-16/18 high-risk HPV are essential for the elimination of cervical cancer.

Persistent infection with high-risk human papillomavirus (HPV) leads to invasive cervical cancer (*1–2*). The World Health Organization calls for the elimination of cervical cancer through HPV vaccination, screening for progressive cervical intraepithelial neoplasia (CIN), and early treatment (*3*). Understanding the prevalence of high-risk HPV types in CIN cases can inform prevention strategies. Prevalence data, however, has not been updated in China since 2009 (*4*). This clinically multicentric study investigated the HPV prevalence in CIN cases in 2017–2018, which was prior to the introduction of HPV vaccines in the mainland of China. The results showed that more than 90% of CIN2/3 cases were in individuals positive for high-risk HPV. In particular, HPV-16/18 were significantly associated with an increased risk of high-grade lesions. This study provides evidence to inform HPV-based screening and vaccination strategies and suggests that HPV-16/18 prevention should be prioritized.

From March 2017 to October 2018, the study recruited women aged 20–64 years old who exhibited abnormalities during screenings or had genital tract symptoms. We selected eight tertiary hospitals or maternal and child healthcare hospitals from 7 provincial-level administrative divisions (PLADs) including Beijing, Shanxi, Shannxi, Jiangsu, Hunan, Guangdong, and Chongqing according to the geographic distribution and burden of cervical cancer in China. These hospitals were local centers for cervical prevention and treatment and were the designated hospitals for referred patients in a prior population-based screening (*5*). A clinician interviewed patients with a structured questionnaire and collected information on demographic characteristics, the history of screening and diseases, and genital symptoms. Then a cervical specimen was obtained by the clinician with a brush and stored in a reserve (Hologic, Bedford, MA, USA) for HPV testing and cytology examination. Cobas HPV assay (Cobas 4800, Roche Molecular Systems, Pleasanton, CA, USA) was used and reported for HPV-16, -18, and 12 other non-16/18 high-risk types (including HPV-31, -33, -35, -39, -45, -51, -52, -56, -58, -59, -66, and -68). Liquid-based technology (ThinPrep, Hologic, MA, USA) was used to generate slides for cytology examination. A panel of cytotechnicians examined these slides under the microscope and reported the results according to the Bethesda terminology. A skilled cytologist selected all the positive slides and randomly selected 20% of negative slides to review the results.

Each patient underwent a colposcopy examination, colposcopy-directed four-quadrant biopsy, histological confirmation, and endocervical curettage. Two pathologists from local hospitals reviewed the pathological sections and reported the results according to the CIN terminology. Two skilled pathologists independently reviewed the results to avoid false-negative or false-positive results. This study included cases with CIN grades 1, 2, and 3, and adenocarcinoma in situ (AIS). We classified AIS as CIN3 and defined CIN2/3 as high-grade lesions.

We estimated the overall and age-specific prevalence of high-risk HPV in all CIN cases and CIN2/3 cases, respectively. Fisher's exact method was used to estimate 95% confidence intervals (*CI*). To show the age-specific trends of HPV prevalence in CIN2/3, we used generalized additive models with quasibinomial distribution, adjusting for region and smoking status. Furthermore, we evaluated the association of different HPV infection patterns with high-grade CIN by multivariate ordinal or binomial logistic regression, adjusting for age, region, and smoking status. The former regarded the outcome as an ordinal variable, whereas the latter regarded CIN1 and CIN1/2 as reference groups, respectively. All analyses were done with SAS (version 9.4; SAS Institute, Cary, USA) and R software (version 3.5.3; R Foundation for Statistical Computing, Vienna, Austria).

There were 1,480 histologically confirmed CIN cases tested with HPV infection status, including 740 CIN1, 396 CIN2, and 344 CIN3 (Table 1). The median age was 37.6 years old for all CIN cases. The prevalence of 14 high-risk HPV types in all CIN cases was 85.1% (95% *CI*: 83.2%–86.9%). The prevalence of all HPV types and HPV-16/18 prevalence in CIN2/3 cases were 92.2% (95% *CI*: 90.0%–94.0%) and 52.0% (95% *CI*: 48.4%–55.7%), respectively, which is higher than in CIN1 cases (78.0%, 95% *CI*: 74.8%–80.9% and 25.4%, 95% *CI*: 22.3%–28.7%). In contrast, the prevalence of non-16/18 high-risk HPV types in CIN1 was 64.3%, 95% *CI*: 60.8%–67.8%), which was higher than in CIN2/3 (56.6%, 95% *CI*: 53.0%–60.2%). There were 50 cases with invalid cytology results. Among CIN2/3 cases with HPV positive results, 4.9% were classified as normal cytology, and these cases mostly occurred in those who were positive for non-16/18 HPV types.

The age-specific HPV-16/18 prevalence in CIN2/3 ranged from 49.4% to 65.9%, and non-16/18 HPV type prevalence ranged from 26.8% to 46.2% (Figure 1A). The highest HPV-16/18 prevalence was observed in individuals aged 20–29 years, whereas the highest prevalence of non-16/18 HPV types was observed in individuals aged 40–49 years. Overall, the non-linear models revealed HPV prevalence was equivalent across age groups for CIN2/3 (Figure 1B and 1C). Nonetheless, the association of HPV-16/18 with CIN2/3 was slightly more prevalent among younger (<30 years) and older (>50 years) women.

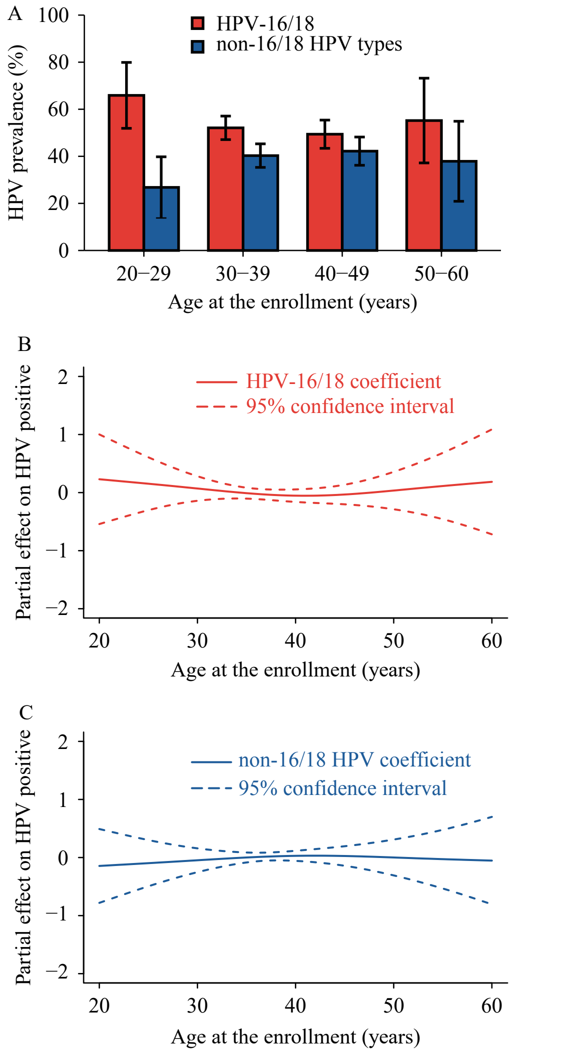


FIGURE 1. Age-specific HPV prevalence in cases with cervical intraepithelial neoplasia 2/3 and the association between HPV infection and age. (A) The prevalence of HPV-16/18 and non-16/18 high-risk HPV types in CIN2/3; (B) The non-linear association of age with HPV-16/18 positive in CIN2/3 cases; (C) The non-linear association of age with non-16/18 HPV types positive in CIN2/3 cases.
Abbreviation: HPV=human papillomavirus; CIN=cervical intraepithelial neoplasia.

The pattern of HPV infection was associated with an increased risk of high-grade CIN to a different extent (Table 2). Ordinal multivariate analyses revealed that patients with HPV-16/18 and non-16/18 HPV types had increased odds of 5.5 (*OR*=5.51, 95% *CI*: 3.92–7.73) and 2.1 (*OR*=2.14, 95% CI: 1.54–2.99) of developing CIN2/3, respectively, compared to patients negative for HPV. Furthermore, HPV-16-related infection was associated with a 7-fold increased risk of developing CIN2/3 (*OR*=6.96, 95% *CI*: 4.92–9.84). These results remained stable in binomial multivariate analyses.

TABLE 1. Prevalence of HPV types in cases with cervical intraepithelial neoplasia grade 1, 2, and 3.

| HPV types | All CIN (*n*=1,480) | | CIN 1 (*n*=740) | | CIN 2 (*n*=396) | | CIN 3 (*n*=344) | | CIN2/3 (*n*=740) | | *P* for CIN2/3 *vs*. CIN1 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Prevalence (95% *CI*) | *n* | Prevalence (95% *CI*) | *n* | Prevalence (95% *CI*) | *n* | Prevalence (95% *CI*) | n | Prevalence (95% *CI*) | |
| All HPV+ | 1,259 | 85.1 (83.2–86.9) | 577 | 78.0 (74.8–80.9) | 358 | 90.4 (87.1–93.1) | 324 | 94.2 (91.2–96.4) | 682 | 92.2 (90.0–94.0) | <0.001 |
| Normal | 106 | 7.2 (5.9–8.6) | 70 | 9.5 (7.5–11.6) | 24 | 6.1 (3.9–8.9) | 12 | 3.5 (1.6–5.4) | 36 | 4.9 (3.4–6.7) | <0.001 |
| ASC–US or worse | 1,120 | 75.7 (73.5–77.9) | 489 | 66.1 (62.5–69.5) | 328 | 82.8 (78.8–86.4) | 303 | 88.1 (84.2–91.3) | 631 | 85.3 (82.5–87.8) | <0.001 |
| HPV-16 | 496 | 33.5 (31.1–36.0) | 137 | 18.5 (15.8–21.5) | 165 | 41.7 (36.8–46.7) | 194 | 56.4 (51.0–61.7) | 359 | 48.5 (44.9–52.2) | <0.001 |
| Normal | 36 | 2.4 (1.7–3.4) | 17 | 2.3 (1.3–3.7) | 11 | 2.8 (1.4–4.9) | 8 | 2.3 (1.0–4.5) | 19 | 2.6 (1.6–4.0) | 0.745 |
| ASC–US or worse | 452 | 30.5 (28.2–33.0) | 119 | 16.1 (13.5–18.9) | 152 | 38.4 (33.6–43.4) | 181 | 52.6 (47.2–58.0) | 333 | 45.0 (41.4–48.7) | <0.001 |
| HPV-18 | 92 | 6.2 (5.0–7.6) | 57 | 7.7 (5.9–9.9) | 22 | 5.7 (3.5–8.3) | 13 | 3.8 (2.0–6.4) | 35 | 4.7 (3.3–6.5) | 0.018 |
| Normal | 15 | 1.0 (0.5–1.5) | 11 | 1.5 (0.7–2.6) | 4 | 1.0 (0.3–2.6) | NA | NA | 4 | 0.5 (0.2–1.4) | 0.069 |
| ASC–US or worse | 71 | 4.8 (3.8–6.0) | 42 | 5.7 (4.1–7.6) | 17 | 4.3 (2.5–6.8) | 12 | 3.5 (1.8–6.0) | 29 | 3.9 (2.6–5.6) | 0.114 |
| Other HPV types | 895 | 60.5 (57.9–63.0) | 476 | 64.3 (60.8–67.8) | 237 | 59.9 (54.8–64.7) | 182 | 52.9 (47.5–58.3) | 419 | 56.6 (53.0–60.2) | 0.002 |
| Normal | 69 | 4.7 (3.7–5.9) | 50 | 6.8 (5.1–8.8) | 13 | 3.3 (1.8–5.6) | 6 | 1.7 (0.6–3.8) | 394 | 2.6 (1.6–4.0) | <0.001 |
| ASC–US or worse | 804 | 54.3 (51.8–56.9) | 410 | 55.4 (51.7–59.0) | 221 | 55.8 (50.8–60.8) | 173 | 50.3 (44.9–55.7) | 19 | 53.2 (49.7–56.8) | 0.404 |
| HPV-16/18 | 573 | 38.7 (36.2–41.3) | 188 | 25.4 (22.3–28.7) | 184 | 46.5 (41.5–51.5) | 201 | 58.4 (53.0–63.7) | 385 | 52.0 (48.4–55.7) | <0.001 |
| Normal | 49 | 3.3 (2.5–4.4) | 26 | 3.5 (2.3–5.1) | 15 | 3.8 (2.1–6.2) | 8 | 2.3 (1.0–4.5) | 23 | 3.1 (2.0–4.6) | 0.663 |
| ASC–US or worse | 510 | 34.5 (32.0–36.9) | 157 | 21.2 (18.3–24.3) | 166 | 41.9 (37.0–47.0) | 187 | 54.4 (48.9–59.7) | 353 | 47.7 (44.1–51.3) | <0.001 |
| Other HPV types (no 16/18) | 686 | 46.4 (43.8–49.0) | 389 | 52.6 (48.9–56.2) | 174 | 43.9 (39.0–49.0) | 123 | 35.8 (30.7–41.1) | 297 | 40.1 (36.6–43.7) | <0.001 |
| Normal | 57 | 3.9 (2.9–5.0) | 44 | 6.0 (4.2–7.7) | 9 | 2.3 (1.0–4.3) | 4 | 1.2 (0.1–2.3) | 13 | 1.8 (0.9–3.0) | <0.001 |
| ASC–US or worse | 610 | 41.2 (38.7–43.8) | 332 | 44.9 (41.3–48.5) | 162 | 40.9 (36.0–45.9) | 116 | 33.7 (28.7–38.7) | 278 | 37.6 (34.1–41.2) | 0.004 |
| HPV-18 related (no 16) | 77 | 5.2 (4.1–6.3) | 51 | 6.9 (5.2–9.0) | 19 | 4.8 (2.9–7.4) | 7 | 2.0 (0.8–4.2) | 26 | 3.5 (2.3–5.1) | 0.003 |
| Normal | 13 | 0.9 (0.4–1.4) | 9 | 1.2 (0.6–2.3) | 4 | 1.0 (0.1–2.0) | NA | NA | 4 | 0.5 (0.2–1.4) | 0.164 |
| ASC–US or worse | 58 | 3.9 (3.0–5.0) | 38 | 5.1 (3.7–7.0) | 14 | 3.5 (1.7–5.4) | 6 | 1.7 (0.4–3.1) | 20 | 2.7 (1.5–3.9) | 0.016 |

Abbreviation: CIN=cervical intraepithelial neoplasia; HPV=human papillomavirus; *CI*=confidence interval; ASC–US=atypical squamous cells of undetermined significance; NA=not available.

TABLE 2. Association of HPV infection pattern with high-grade cervical intraepithelial neoplasia in cases.

| Model | Dependent variable | Ordinal logistic regression for CIN 1, 2, and 3 | | Binomial logistic regression for CIN2/3 *vs*. CIN1 | | Binomial logistic regression for CIN3 *vs*. CIN1/2 | |
|---|---|---|---|---|---|---|---|
| | | ***OR* (95% *CI*)** | ***P*** | ***OR* (95% *CI*)** | ***P*** | ***OR* (95% *CI*)** | ***P*** |
| Model 1 | HPV negative | Reference | | Reference | | Reference | |
| | Other HPV types (no HPV-16/18) | 2.14 (1.54−2.99) | <0.001 | 2.15 (1.54−3.02) | <0.001 | 2.12 (1.28−3.50) | 0.003 |
| | HPV-16/18 | 5.51 (3.92−7.73) | <0.001 | 5.74 (4.04−8.15) | <0.001 | 5.07 (3.09−8.32) | <0.001 |
| Model 2 | HPV negative | Reference | | Reference | | Reference | |
| | Other HPV types (no HPV-16/18) | 2.17 (1.55−3.02) | <0.001 | 2.17 (1.54−3.03) | <0.001 | 2.13 (1.29−3.52) | 0.003 |
| | HPV-16 related | 6.96 (4.92−9.84) | <0.001 | 7.48 (5.19−10.76) | <0.001 | 6.12 (3.71−10.08) | <0.001 |
| | HPV-18 related (no HPV-16) | 1.33 (0.76−2.31) | 0.305 | 1.40 (0.80−2.46) | 0.296 | 0.92 (0.37−2.29) | 0.864 |

Abbreviation: CIN=cervical intraepithelial neoplasia; HPV=human papillomavirus; *OR*=odds ratio; CI=confidence interval.

## DISCUSSION

This 2017–2018 study obtained histological confirmations from almost 1,500 CIN cases and is therefore the largest study in China to report the prevalence of HPV types in CIN cases in the country's pre-vaccine era. We estimated that more than 90% of CIN2/3 patients were positive for high-risk HPV, suggesting that HPV-focused strategies may be important for the prevention of cervical cancer. Furthermore, our results showed that HPV-16 and HPV-18 were significantly associated with an increased risk of high-grade lesions and that preventing these subtypes should be prioritized when designing cervical cancer vaccination and screening strategies.

Consistent with previous research, this study showed a high HPV prevalence (92%) in CIN and an association between high-risk HPV types and CIN2/3. These findings emphasize the importance of HPV-based screening and vaccination strategies to eliminate and mitigate cervical cancer in China. In this study, the HPV prevalence in CIN2/3 was slightly lower than in the previous multicentric study of China in 2009 (94.2% *vs*. 98.9%) (*4*). Both studies tested all high-risk HPV types and indicated the importance of HPV-based strategies for prevention of CIN. However, HPV-16 prevalence decreased by approximately 30% in CIN2/3 patients in our more recent study (48.5% *vs*. 68.7%). Given that HPV vaccination has not been implemented in the population, the reduction may be related to screening and subsequent treatment, which would protect against subsequent HPV infection by antigen-presenting effects (*6*). Our results showed a low prevalence of HPV-18 in CIN2/3 patients and an *OR* without significance. This could be explained by a smaller number of AIS cases in the study. Adenocarcinoma accounted for a small proportion of cervical cancer but was closely related to HPV-18 infection (*7–8*).

The proportion of non-16/18 high-risk HPV types in CIN2/3 was higher than in the study in 2009 (*4*). Although these non-16/18 HPV types have a lower risk of CIN2/3 than HPV-16/18, they are predominant in Chinese women, particularly HPV-52 and -58 (*9*). After the application of bivalent vaccines and screening based on HPV-16/18, these HPV types would gradually change to the predominant types. Among the CIN2/3 cases with non-16/18 HPV type positives, 1.8% were classified as normal cytology CIN2/3 and would be missed in the screening. Thus, primary HPV screening with HPV-16/18 genotyping was feasible but new stratification technology should be developed to reduce underdiagnosis.

The bimodal pattern of HPV prevalence in the population was identified by many studies in China (*9–10*). Nonetheless, our age-specific analyses showed that the roles of different HPV types were equivalent across the age spectrum. Furthermore, these results indicate that HPV vaccinations before the age of 20 should provide benefits that last until patients are 60 years old.

The key limitation was that results for HPV infection were from cervical scraping rather than paraffin-embedded biopsy specimens, which could lead to misclassification bias or false-negative results. A small spectrum of 14 HPV types also increased the likelihood of false negatives. Nonetheless, a high-sensitive PCR-based assay would reduce the risk of misclassification, and the proportion of HPV-negative CIN2+ in our study was similar to previous studies (*11–12*).

In conclusion, HPV-based screening and HPV vaccination strategies greatly influence the prevention of cervical cancer in China. HPV-16 and HPV-18 should be priority vaccinations in China, and the prevention of non-16/18 high-risk HPV types will be essential to eliminate cervical cancer in the future.

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Preplanned Studies

# Prevalence of High-Risk Human Papillomavirus by Subtypes Among Rural Women Aged 35–64 Years — Guangzhou City, Guangdong Province, China, 2019–2021

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**Summary**

**What is already known about this topic?**

Little is known about the infection pattern for high-risk human papillomavirus (hrHPV) subtypes in rural areas in southern China.

**What is added by this report?**

The prevalence of HPV-16, 18, and the other 12 hrHPV subtypes were 0.71%, 0.34%, and 4.50%, respectively, among rural women in Guangzhou. The prevalence of HPV-16 and the other 12 hrHPV subtypes increased with age, but there was no evident age trend for HPV-18 prevalence.

**What are the implications for public health practice?**

Epidemiological characteristics of hrHPV prevalence in rural Guangzhou should be considered to identify high-risk populations of hrHPV infection and determine follow-up strategies.

Cervical cancer, the fourth most common cancer and the fourth leading cause of cancer death in women worldwide (*1*), is preventable through effective screening and vaccination. Human papillomavirus (HPV) testing is now recommended as the primary method in cervical cancer screening (*2*). HPV-16 and 18 are the most carcinogenic high-risk (hrHPV) subtypes and account for approximately 70% of cervical cancers (*3*). Understanding the prevalence patterns of different hrHPV subtypes is important to identify target populations for screening and vaccination. However, the age-specific prevalence of different hrHPV subtypes remains unclear among women in rural areas in southern China. A total of 159,251 women aged 35–64 years who participated in a cervical cancer screening program in rural areas in Guangzhou City, Guangdong Province, China, from 2019–2021 were included in this population-based study. All women received the hrHPV test using Roche Cobas 4800 (Roche Molecular Systems, Pleasanton, USA). We found that the prevalences of HPV-16, 18, and the other 12 hrHPV types were 0.71%, 0.34%, and 4.50%, respectively, among rural women in Guangzhou. We observed the prevalence of HPV-16 declined in the age group of 35–49 years and increased by age group afterwards, whereas the prevalence of the other 12 hrHPV subtypes increased with age from 40–44 years old ($P_{trend}$<0.01), but there was no evident trend for HPV-18 prevalence across the age groups ($P_{trend}$=0.70). Our findings might have implications in the identification and follow-up for high-risk population of hrHPV infection.

This study was based on a population-based cervical cancer screening program covering all seven rural administrative districts in Guangzhou during 2019–2021. All screened women aged 35–64 years with rural registered permanent residence in Guangzhou were included in the study. All women received a gynecological examination and the hrHPV test using Roche Cobas 4800 (Roche Molecular Systems, Pleasanton, USA) HPV Detection (Cobas). Cobas could specifically identify HPV-16 and HPV-18 while concurrently detecting the other 12 hrHPV types (HPV-31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). All women provided written informed consent before screening. Age-specific prevalence of hrHPV infection was calculated by five-year age groups. The Cochran-Armitage test was used to examine the overall linear trends of the prevalence of hrHPV subtypes across age groups. The two-sided Poisson test was used to compare the prevalence ratios (PR) across age-groups and calculate the 95% confidence interval (*CI*). Stratified analyses of prevalence of hrHPV subtypes were performed among women who were first time to participate in HPV screening or not. Analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA) or R (version 4.0.3; R Core Team, Vienna, Austria).

A total of 159,251 women aged 35–64 years (mean: 46.51 years) were included in the study. Women aged

35–39 years old accounted for 23.18% of the participants while 5.04% of women were 60–64 years old. Of the included participants, 8,465 (5.32%) women were detected as hrHPV positive, with 1,130 (0.71%) positive for HPV-16, 538 (0.34%) positive for HPV-18 and 7,168 (4.50%) positive for the other 12 hrHPV types (Table 1). Among women who tested as hrHPV positive, 13.35% were positive for HPV-16, 6.36% for HPV-18, and 84.68% for the other 12 hrHPV subtypes.

Age-specific prevalence for hrHPV subtypes is shown in Table 2. The prevalence of HPV-16 slightly declined from 35–49 years group and increased with age afterwards, indicating an overall upward trend ($Z$=−3.19, $P_{trend}$<0.01, Figure 1). Highest prevalence of HPV-16 was observed among women of 60–64 years, with a PR of 1.34 (95% *CI*: 1.02–1.73) compared with those of 35–39 years (Table 2). Women at 60–64 years also had the highest prevalence of HPV-18, but there was no evident trend for HPV-18 prevalence across the age groups ($Z$=−0.39, $P_{trend}$=0.70). The other 12 hrHPV subtypes also had an increasing prevalence along with age ($Z$=−6.16, $P_{trend}$<0.01), with the highest prevalence observed among women at 60–64 years (PR, 1.39; 95% *CI*: 1.26–1.54). Stratified analysis showed similar age-specific prevalence patterns between women undergoing HPV screening for the first time and those who had participated before (Supplementary Figure S1, available in http://weekly.chinacdc.cn).

TABLE 1. The prevalence of hrHPV subtypes in rural Guangzhou, China, 2019–2021.

| Infection patterns | No. of positive | Prevalence (%) (95% *CI*) | Proportion of hrHPV (%) |
|---|---|---|---|
| Any types of infection | | | |
| Any hrHPV subtypes | 8,465 | 5.32 (5.21–5.43) | 100.00 |
| Any HPV-16 | 1,130 | 0.71 (0.67–0.75) | 13.35 |
| Any HPV-18 | 538 | 0.34 (0.31–0.37) | 6.36 |
| Any pooled 12 hrHPV types | 7,168 | 4.50 (4.40–4.60) | 84.68 |
| HPV-16 or HPV-18 | 1,651 | 1.04 (0.99–1.09) | 19.50 |
| Co-infection | | | |
| HPV-16 + Other hrHPV types* | 249 | 0.16 (0.14–0.18) | 2.94 |
| HPV-18 + Other hrHPV types† | 134 | 0.08 (0.07–0.10) | 1.58 |
| HPV-16 + 18 | 12 | 0.008 (0.004–0.014) | 0.14 |
| HPV-16 +18 + Pooled 12 hrHPV types | 5 | 0.003 (0.001–0.007) | 0.06 |

Abbreviation: hrHPV=high-risk human papillomavirus, *CI*=confidence interval.
* Other hrHPV types means pooled 12 hrHPV types or HPV-18.
† Other hrHPV types means pooled 12 hrHPV types or HPV-16.

TABLE 2. The prevalence of HPV-16, HPV-18, and the other 12 hrHPV subtypes by age group during 2019–2021 in rural Guangzhou, China ($N$=159,251).

| Age group | Total participants (%) | HPV-16 | | | HPV-18 | | | Pooled 12 hrHPV | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of positive | Positive rate (%) (95% *CI*) | Prevalence ratio (95% *CI*) | No. of positive | Positive rate (%) (95% *CI*) | Prevalence ratio (95% *CI*) | No. of positive | Positive rate (%) (95% *CI*) | Prevalence ratio (95% *CI*) |
| 35–39 | 36,914 (23.18) | 262 | 0.71 (0.63–0.80) | 1.00 | 136 | 0.37 (0.31–0.44) | 1.00 | 1,623 | 4.40 (4.19–4.61) | 1.00 |
| 40–44 | 29,917 (18.78) | 190 | 0.64 (0.55–0.73) | 0.89 (0.74–1.08) | 93 | 0.31 (0.25–0.38) | 0.84 (0.64–1.11) | 1,243 | 4.15 (3.93–4.39) | 0.94 (0.88–1.02) |
| 45–49 | 34,974 (21.96) | 206 | 0.59 (0.51–0.68) | 0.83 (0.69–1.00) | 104 | 0.30 (0.24–0.36) | 0.81 (0.62–1.05) | 1,511 | 4.32 (4.11–4.54) | 0.98 (0.92–1.05) |
| 50–54 | 31,151 (19.56) | 232 | 0.75 (0.65–0.85) | 1.05 (0.88–1.26) | 112 | 0.36 (0.30–0.43) | 0.98 (0.75–1.26) | 1,364 | 4.38 (4.16–4.61) | 1.00 (0.93–1.07) |
| 55–59 | 18,275 (11.48) | 164 | 0.90 (0.77–1.05) | 1.26 (1.03–1.54) | 53 | 0.29 (0.22–0.38) | 0.79 (0.56–1.09) | 936 | 5.12 (4.81–5.45) | 1.16 (1.07–1.26) |
| 60–64 | 8,020 (5.04) | 76 | 0.95 (0.75–1.19) | 1.34 (1.02–1.73) | 40 | 0.50 (0.36–0.69) | 1.35 (0.93–1.94) | 491 | 6.12 (5.61–6.67) | 1.39 (1.26–1.54) |
| Total | 159,251 | 1,130 | 0.71 (0.67–0.75) | – | 538 | 0.34 (0.31–0.37) | – | 7,168 | 4.50 (4.40–4.60) | – |

Abbreviation: hrHPV=high-risk human papillomavirus; *CI*=confidence interval.
"–" means not applicable.

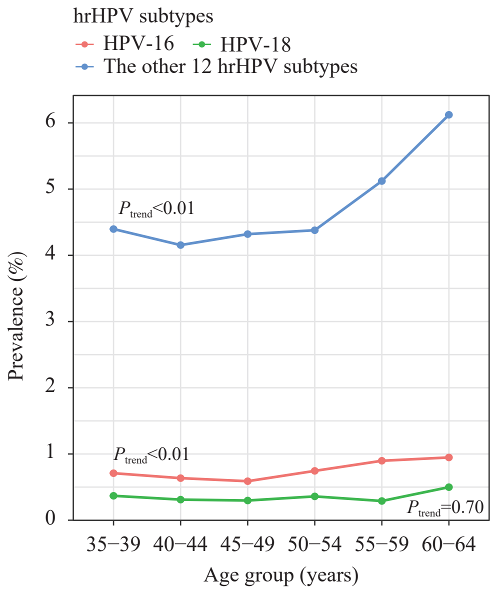


FIGURE 1. The prevalence and trend of hrHPV subtypes by age group during 2019–2021 in rural Guangzhou, China (*N*=159,251).
Abbreviation: hrHPV=high-risk human papillomavirus.

## DISCUSSION

In this study, we characterized the prevalence pattern of hrHPV subtypes among rural women in Guangzhou, China. We found the prevalences of HPV-16, HPV-18, and the other 12 hrHPV subtypes were 0.71%, 0.34%, and 4.50%, respectively. An overall upward trend in prevalence was observed for both HPV-16 and the other 12 hrHPV across age groups. Although there was no significant age trend for HPV-18, women at 60–64 years appeared to have the highest prevalence of HPV-18.

It has been well documented that HPV-16 and HPV-18 have a higher likelihood of persistence and progression to cervical lesions compared with other oncogenic types, accounting for approximately 70% of cervical cancers globally (*3*). Understanding the prevalence of hrHPV subtypes is beneficial for decision making for both screening strategies and vaccination. The distribution of HPV-16 and HPV-18 in general population varies across continents: 5.8% and 2.3% in northern America, 4.8% and 0.9% in Europe, and 2.5% and 1.4% in Asia (mostly from India) (*4*). Even within China, the prevalence of hrHPV subtypes varies among different regions. For example, the prevalence of HPV-16 ranges from 0.71% in Guangdong Province to 3.62% in Zhejiang Province, whereas the prevalence of HPV-18 ranges from 0.28% in Jiangxi Province to 1.48% in Zhejiang Province (*5*–*7*). These differences in hrHPV prevalence across regions could be due to different HPV testing approaches or different age structure of the population under investigation and might reflect actual geographic variations in hrHPV prevalence. Using the same method (i.e., Cobas) for a close age-distributed population (older than 30 years old) as this study, Guo revealed rates of 0.71% and 0.30% for HPV-16 and HPV-18 among a small sample (*n*=986) in Guangdong Province (*6*), while another study in Hubei Province (*n*=313,704) found that the prevalences of HPV-16 and HPV-18 were 1.51% and 0.46%, respectively (*8*).

This study found that different hrHPV subtypes presented different patterns for age distribution. It has been reported that the prevalence of HPV-16/18 gradually increased among 35–50 age group in general population in Guangdong Province, China (*7*). However, the prevalence of HPV-16 decreased to the lowest point in the 45–49 age group and then went upward in the current study. As for the prevalence of the other 12 hrHPV subtypes, a significant increase across age groups was observed in the rural women of Guangzhou. Another study also found a similar trend for HPV-52 and HPV-58 in Guangdong Province, China, which are the most common types in the other 12 hrHPV subtypes (*7*).

The findings of this study might have important implications in public health. First, the variability in prevalence patterns for different hrHPV subtypes across age groups indicates that women at different ages might have different risk factors for hrHPV infection. It provides a better understanding for the epidemiological characteristics of hrHPV in rural Guangzhou. Second, we found that women at an older age have a higher prevalence of HPV-16 and the other 12 hrHPV subtypes than those at a younger age. This suggests that elderly women deserve additional concern because most national guidelines recommend stopping cervical cancer screening at age 65 (*9*). Whether the high prevalence of hrHPV subtypes also translates into a higher cervical intraepithelial neoplasia burden in elderly women needs further investigation.

Although this study had the advantage of a large sample size, limitations remain. First, we are unable to identify the prevalence of each of the other 12 hrHPV because Cobas detects them concurrently. Second, pathological data were not available; thus, the association between HPV subtypes and cervical cancer or precancerous lesions could not be examined. Furthermore, only data from Guangzhou were included in this study, it cannot be extrapolated to the whole rural area of China. Multiarea data are needed to characterize the prevalence of hrHPV subtypes in rural China.

In conclusion, we found that different hrHPV subtypes had different age-specific prevalence patterns and women at an older age had significantly higher prevalence of HPV-16 and the other 12 hrHPV subtypes. This information is helpful for better understanding the epidemiological characteristics of hrHPV subtypes in rural Guangzhou and provides a scientific basis for identification and follow-up of high-risk populations. Further investigations are warranted to investigate the prevalence and health effects of HPV-16 and the other 12 hrHPV subtypes in elderly women.

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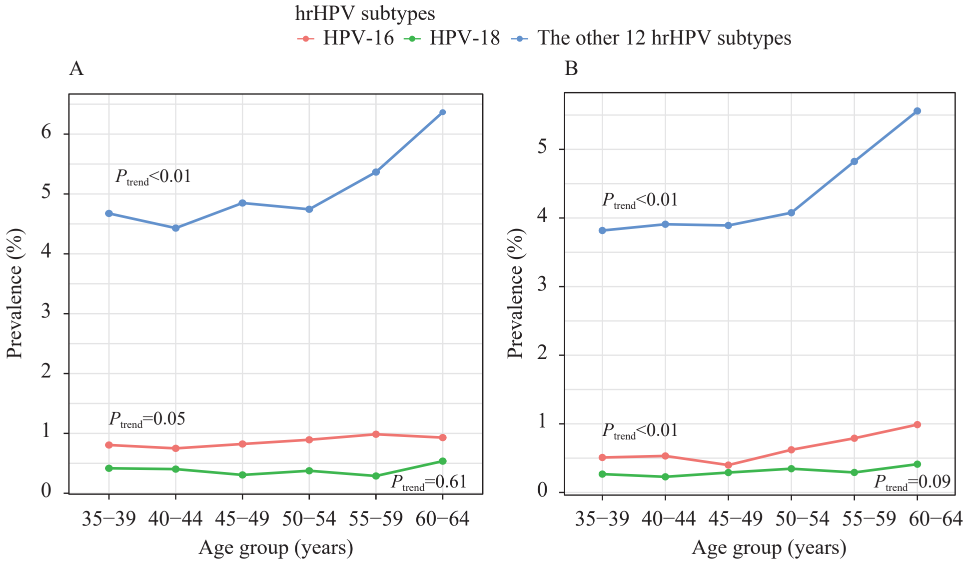


SUPPLEMENTARY FIGURE S1. The prevalence and trend of hrHPV subtypes by age group in rural Guangzhou, China. (A) For women who participated in HPV screening for the first time ($N$=84,486); (B) For women who had previously participated in HPV screening ($N$=74,765).
Abbreviation: hrHPV=high-risk human papillomavirus.

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