Human papillomavirus prevalence and genotype distribution landscapes in Shannan City, Tibet Tibetan Autonomous Region, China

Dilu Feng†, Sitian Wei†, Jun Chen, Zhicheng Yu, Yeshe Lhamo, Hongbo Wang and Xiaowu Zhu*

Abstract

Background: Data regarding human papillomavirus (HPV) prevalence and genotype distribution are limited in Shannan City, Tibet Tibetan Autonomous Region, China. The purpose of this study is to provide reliable data for guiding women in Shannan City in cervical cancer screening and HPV vaccine inoculation.

Methods: HPV testing was performed on women aged 16–109 years (mean age 44.03 ± 9.25 years) from Shannan City in 2019 and 2020, which was implemented technically by gynecological examination, vaginal discharge smear microscopy, cytology, and HPV detection. The overall prevalence, age-specific prevalence, and genotype distribution were analyzed.

Results: A total of 48,126 women received HPV testing, of which 3929 were detected human papillomavirus. The HPV-positive rate was 8.16% (3929/48,126), and the highest prevalence was in the ≤ 25-year-old age group (12.68%). After the age of 25, the prevalence rate decreased rapidly, and then slowly increased from 7.49% in the 46–55 age group to 9.82% in the ≥ 66 age group, showing a “U-shaped” pattern. The positive prevalence of HPV 16 or 18-only was 1.43%, that of other HPV genotypes except HPV 16 or 18 was 6.39%, and mixed HPV infections including HPV 16 or 18 was 0.34%.

Conclusions: The HPV infection rate in Shannan city is rather low, and the age-specific prevalence of HPV infection presents a “U” curve, suggesting the importance of screening among younger women and the necessity of detection among older women.

Keywords: Human papillomavirus, Cervical cancer, Prevalence, Genotype

© The Author(s) 2022. Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.
infection. Previous studies have shown that the HPV prevalence has obvious regional and age-specific distribution [6, 7]. Understanding the characteristics of HPV infection plays an important role in the prevention and treatment of cervical cancer. In this study, we collected basic information and HPV high-risk subtypes of patients from Shannan Maternal and Child Health Hospital from January 2019 to December 2020, and analyzed the HPV infection landscapes in different and continuous age groups to intervene early in cervical precancerous lesions and cervical cancer, thereby reducing the incidence rate of cervical cancer in Shannan city.

Shannan city is located in Southwest China, with an average altitude of about 3700 m. It is a vast and remote area composed of Tibetan, Han, Hui, and other nationalities. Cervical cancer is still a major public health problem for women living in Shannan city due to the lack of Health Science Popularization for HPV detection and prevention, insufficient local health conditions, scattered population, and ethnic culture. However, data on HPV infection rates in Shannan city are badly limited.

In the past few decades, cervical cancer vaccination has been carried out in more than 130 countries and regions around the world. In China, the HPV vaccine was approved for marketing on July 31, 2017. But so far, in China, especially in Tibet, only a few school-age women have been vaccinated against human papillomavirus-related diseases. So far, there is no large-scale sample study on the prevalence of human papillomavirus genotypes in Tibet.

Here, we examined the HPV infection rate of women in Shannan city and its relationship with age according to the data collected from female patients. These data will provide epidemiological evidence to support the development of a comprehensive and correct cervical cancer prevention program. We also aim to emphasize the need for complete, thorough and detailed data collection to increase our understanding of HPV infection rates.

Methods

Study population

A total of 48,126 females aged 16–109 years were enrolled in this study from January 2019 to December 2020. All participants were from Shannan Maternal and Child Health Hospital. Patients visited the hospital for various reasons, including physical examination, vaginitis, abnormal vaginal bleeding, Gynaecological tumors, etc. Clinical information was collected from the patients, and a molecular survey of HPVs was conducted. Eligible women were included in the study after signing an informed consent form.

Sample collection

Doctors from Wuhan Union Hospital (Wuhan, China) and local clinics were trained in the collection of cervical cell samples for HPV testing. All participants were informed to avoid sex within 24 h before collecting samples. With the help of a vaginal endoscope, the orificium externum isthmus was fully exposed and was scraped through clockwise 5 rotations gently using the HPV detection brush, so that the mucosa and secretions could adhere to the flat sides of the bristles. Then the tips of the cervical brush were put into a vial containing transport medium separately, which were stored at 2–8 °C until HPV DNA extraction and genotyping could be carried out. The HPV genotype detection of samples was completed within 48 h.

DNA extraction, PCR amplification, and HPV genotyping

HPV DNA was extracted from cervical samples using a viral nucleic acid extraction kit (Bioperfectus Technologies Co., Ltd., Taizhou, Jiangsu, China) was used for HPV DNA amplification and genotyping. The kit was used for the qualitative detection of 18 high-risk HPV (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58.59, 66, 68, 73.53, 82, and 26) nucleic acids in women’s cervical exfoliated cells in vitro, HPV16 and HPV18 were specifically distinguished, but the other 16 high-risk types were not specifically classified. This kit used real-time fluorescent PCR technology to label HPV16, HPV18, other 16 high-risk HPVs, and internal standard (β-globin) with FAM, VIC, ROX, and CY5 fluorescein respectively, so it could realize the specific distinction between HPV16 and HPV18. Primers were designed on 18 high-risk HPV-specific genes. The target genes designed by HPV primer probes were L1, L2, and E1 genes, and the length of each type of amplicon was no more than 200 bp. 5 μl DNA was added to format a 25 μl PCR reaction system. SLAN-96P real-time fluorescence quantitative PCR instrument (Hongshi Medical Technology Co., Ltd., Shanghai, China) was used for PCR amplification detection. The PCR reaction began with denaturation at 95 °C for 10 min, followed by 45 cycles, denaturation at 95 °C for 15 s, and annealing and extension at 58 °C for 50 s. Fluorescence was collected during the annealing extension phase. According to the verification with the comparative reagent clinical trial and the
third-party reagent, the receiver operating characteristic curve (ROC) was used to determine that the cutoff value of HPV16, HPV18, and other 16 high-risk types was 35.4, 34.6, and 33.6 respectively.

Quality control was carried out throughout the whole experiment, including PCR amplification and hybridization using the positive and negative controls provided by the kit. Experimental procedures were all followed by the manufacturer’s manual.

Statistical analysis
Analyses were done with SPSS (version 25.0) and Excel (version 2004). Descriptive statistical analysis was performed on the distribution of HPV genotypes using indicators such as frequency and prevalence. For comparisons among different age groups, the categorical variables were compared by using the Chi-square test. All the reported $P$ values were made based on two-sided tests with a significance level of 0.05.

Results
Prevalence and genotype distribution of human papillomavirus
From January 2019 to December 2020, a total of 48,126 human papillomavirus genotype samples were collected and detected in Shannan Maternal and Child Health Hospital. The subjects were aged 16–109 years, and the mean age was 44.03 ± 9.25 years. The genotype test showed that 3929 samples were HPV positive, so the overall prevalence of all types of human papillomavirus in the study population was 8.16%.

The details of genotypes distribution were shown in Tables 1 and 2. Notably, HPV 16-only infection rate was 0.52% (250/48,126). Correspondingly, HPV 16-total was 0.70% (339/48,126). HPV 18-only infection rate was 0.91% (440/48,126) and HPV 18-total was 1.09% (526/48,126), respectively. In addition, the HPV infection rate of other genotypes was 6.73% (3239/48,126), accounting for 82.44% (3239/3929) of all HPV-positive samples.

Prevalence of HPV grouped by age
Overall, 48,126 women (aged 16–109 years) were included in this study. All the participants were divided into six groups ranging from ≤25 years, 26–35 years, 36–45 years, 46–55 years, 56–66 years, and ≥66 years. There were significant differences in HPV infection rates among the six age groups ($P < 0.05$). Relevant data could be seen in Table 3.

The distribution of HPV infection rates in specific age groups presented a “U” curve. The first peak appeared in the youngest women (12.68%). However, the HPV infection rate decreased sharply after the first peak, and reached the bottom in the 46–55 age group (7.49%). On the contrary, it increased slowly, and finally reached the second peak at 9.82% in the oldest women group (Fig. 1).

Region-specific prevalence of HPV infection
The prevalence of HPV infection in Shannan city and in 19 different areas of China was compared separately (Table 4). There were significant differences in HPV prevalence among these areas ($P < 0.05$). The positive rate of HPV obtained in our study (Shannan City) was significantly different from those in other areas ($P < 0.05$). Moreover, the highest rate of HPV infection was in Henan Province (38.10%, 1536/4033) [8], whereas the lowest area was in Shannan City (8.16%, 3929/48,126). These results indicated that HPV infections were significantly region-specific.

### Table 1 Frequency and prevalence of genotypes of HPV among women

| Genotype | Positive samples (n) | Proportion among 48,126 samples (%) | Proportion among 3929 HPV-positive samples (%) |
|----------|---------------------|-------------------------------------|-----------------------------------------------|
| 16       | 250                 | 0.52                                | 6.36                                          |
| 18       | 440                 | 0.91                                | 11.20                                         |
| Others*  | 3077                | 6.39                                | 78.32                                         |
| 16+others| 76                  | 0.16                                | 1.93                                          |
| 18+others| 73                  | 0.15                                | 1.86                                          |
| 16+18+others| 13            | 0.03                                | 0.33                                          |

* Other genotypes of HPV was HPV 31, 33, 35, 39, 45, 51, 52, 56, 58.59, 66, 68, 73.53, 82, and 26

### Table 2 Frequency and prevalence of HPV16, 18 and other genotypes among women

| Genotype | Positive samples (n) | Proportion among 48,126 samples (%) | Proportion among 3929 HPV-positive samples (%) |
|----------|---------------------|-------------------------------------|-----------------------------------------------|
| 16       | 339                 | 0.70                                | 8.63                                          |
| 18       | 526                 | 1.09                                | 13.39                                         |
| Others*  | 3239                | 6.73                                | 82.44                                         |

* Other genotypes of HPV was HPV 31, 33, 35, 39, 45, 51, 52, 56, 58.59, 66, 68, 73.53, 82, and 26
Discussion

HPV screening is very important for the prevention and detection of cervical cancer. However, cervical cancer screening started late in China, and there is still a big gap between the current promotion and developed countries. In addition, the data of HPV infection rate and genotype distribution in different regions are not comprehensive, especially in the remote areas in Western and Northern China. There is a lack of relevant data to guide the health education of cervical cancer. Therefore, collecting and analyzing the epidemiological evidence of local HPV infection can provide a reliable scientific basis for the prevention, treatment, and elimination of human papillomavirus infection-related diseases.

Shannan City of Tibet Tibetan Autonomous Region was located in Northwest China. Its economy was underdeveloped, and the prevention and screening of cervical cancer were also quite backward. Therefore, improving the screening of HPV in Tibet was particularly important for the primary prevention of cervical cancer in Tibet. This is not only conducive to women's health but also can save a lot of medical expenses for the country.

Table 3 Prevalence of HPV grouped by age groups

| Age group (years) | Mean age (years) | Total samples (n) | Positive samples (n) | Proportion among total samples (%) |
|------------------|------------------|------------------|----------------------|------------------------------------|
| ≤ 25             | 23.32±1.80       | 891              | 113                  | 12.68                              |
| 26–35            | 31.99±2.79       | 8289             | 726                  | 8.76                               |
| 36–45            | 40.35±2.85       | 17,640           | 1415                 | 8.02                               |
| 46–55            | 50.15±2.80       | 15,438           | 1157                 | 7.49                               |
| 56–65            | 58.76±2.35       | 5705             | 502                  | 8.80                               |
| ≥ 66             | 69.57±6.31       | 163              | 16                   | 9.82                               |
| Total            | 44.03±9.25       | 48,126           | 3929                 | 8.16                               |

χ² 41.542

P < 0.05

Table 4 Comparison of HPV infection rates in different areas in China

| Regions                     | Total samples (n) | Positive samples (n) | Prevalence (%) | P-value |
|-----------------------------|-------------------|----------------------|----------------|---------|
| Shannan City                | 48,126            | 3929                 | 8.16           | –       |
| Beijing City [9]            | 29,436            | 3586                 | 12.18          | <0.001  |
| Shanghai City [10]          | 23,724            | 3816                 | 16.08          | <0.001  |
| Wuhan City [11]             | 13,775            | 2436                 | 17.68          | <0.001  |
| Xinjiang Province [12]      | 37,722            | 5287                 | 14.02          | <0.001  |
| Jiangxi Province [13]       | 71,435            | 16,065               | 22.49          | <0.001  |
| Sichuan Province [14]       | 14,185            | 3382                 | 23.84          | <0.001  |
| Yunnan Province [15]        | 17,898            | 3681                 | 21.94          | <0.001  |
| Zhejiang Province [11]      | 77,443            | 17,270               | 22.30          | <0.001  |
| Guangdong Province [16]     | 33,328            | 3526                 | 10.58          | <0.001  |
| Jiangsu Province [17]       | 62,317            | 16,775               | 26.92          | <0.001  |
| Shaanxi Province [18]       | 17,341            | 4559                 | 26.30          | <0.001  |
| Shandong Province [19]      | 94,489            | 26,839               | 28.40          | <0.001  |
| Henan Province [8]          | 4033              | 1536                 | 38.10          | <0.001  |
| Shanxi Province [20]        | 7640              | 1441                 | 18.86          | <0.001  |
| Liuzhou City [21]           | 2300              | 522                  | 22.70          | <0.001  |
| Jilin Province [16]         | 20,648            | 7095                 | 34.40          | <0.001  |
| Heilongjiang Province [22]  | 18,522            | 5011                 | 27.10          | <0.001  |
| Liaoning Province [23]      | 6479              | 667                  | 10.30          | <0.001  |
| Inner Mongolia [24]         | 2345              | 844                  | 36.00          | <0.001  |

χ² 18,795.358

P < 0.05
Studying the prevalence and genotype distribution of human papillomavirus in different regions and periods is highly important for cervical cancer screening and evaluating the effectiveness of the human papillomavirus vaccine for women. For the last 20 years, the world has made great efforts to generate epidemiological data on cervical HPV-DNA. In China, although certain studies have been performed to assess the prevalence and incidence rate of human papillomavirus genotypes in Tibet, they are based on small samples [25, 26]. Our study is the first large-scale sample study in Tibet.

80% of the high-risk HPV DNA detected in patients with cervical cancer were HPV16, 18, 45, and 31 [4]. Therefore, in this study, we mainly focused on the infection rates of HPV16 and 18. It could be seen that HPV16 and 18 positive accounted for 8.63% and 13.39% of 3929 HPV positive samples respectively. By now, all three existing vaccines could prevent HPV16 and 18 [27]. Therefore, for women in Shannan City, Tibet, no matter how much valent vaccine they chose, they could meet their needs for the prevention of cervical cancer. As expected in this study, clarifying the distribution of HPV genotype infection rate in specific areas was conducive to HPV vaccine development and clinical application.

Due to the differences in regional, population, living environment and lifestyle, and human papillomavirus DNA test methods, the reported results of global human papillomavirus distribution vary from study to study. A meta-analysis [28] of a total of 1,016,719 screening people included in 194 studies around the world showed that the adjusted infection rate of HPV in the global population with normal cytology was 11.7%, of which the infection rate was the highest in sub-Saharan Africa (24.0%), Eastern Europe (21.4%) and Latin America (16.1%) and the lowest in Western Asia (1.7%). According to research, the overall prevalence of human papillomavirus infection in China is 15.54% [29]. In our study, the rate of human papillomavirus infection among women in Shannan City, Tibet was 8.16%, lower than the global average, lower than the Chinese average, and lower than many other cities or regions in China. Some researchers speculated that the variability of HPV prevalence in China was due to China's large population and territory [29]. At the same time, the level of economic development and population migration also led to the differences in the distribution landscapes of human papillomavirus among regions. As shown in Table 4, both Beijing and Shanghai were economically developed cities, but the HPV infection rate varied greatly [9, 10]. The reason may be that Beijing, as China's political, cultural, and economic center, had good medical conditions and protection strategies. Otherwise, Shanghai's economic development level was also very high, but due to a large number of foreigners and migrant population, the city was expanding and the population composition was complex, resulting in a high rate of human papillomavirus infection. In Shannan City, although the economy and medical treatment were relatively backward, the HPV infection rate was the lowest. The reason behind it may be the simple folk customs, the majority of the people who believe in Tibetan Buddhism and the conservative traditional concept of sex, which was similar to Xinjiang Province. Another study on the HPV infection rate in Tibet which was 9.19% (279/3036), which supports this conclusion [25].

Information on the distribution of human papillomavirus infection in different age groups is extremely important for the design of human papillomavirus preventive vaccines in specific age groups [30]. What many studies have in common is that the first peak occurs in the younger age group (just after the beginning of sexual relations). In some areas, the second peak can be observed at the age of >45 or >55 or >65, while in some other areas, no second peak can be observed. In conclusion, age-specific HPV distribution is either shown as a bimodal curve (including "U" curve) [31, 32] or a left inclined unimodal distribution [26]. In this study, age-specific HPV distribution showed a "U" curve. The first peak of human papillomavirus infection occurred in the age group ≤25 years old (12.68%), then decreased gradually, reached the lowest in the age group 46–55 years old, and then increased gradually. The reason for this trend may be that young women were sensitive to human papillomavirus soon after sexual activity due to immature immune protection [33]. With the stimulation of immune response, a large part of primary HPV infection would be temporary and would be cleared spontaneously [34], so the HPV infection rate decreased gradually. The immune ability of elderly women decreased with age, especially in the premenopausal and postmenopausal women, which
resulted their ability to eliminate previous and new HPV infections being weakened. Furthermore, as past (latent) infections reappeared, both factors led to a higher HPV infection rate of elderly women [35]. Based on these findings, the earlier young women were vaccinated with HPV vaccine, the higher the antibody titer and the better the protection [36]. Once HPV infection was detected, HPV viral load should be continuously monitored and cervical biopsy should be performed regularly.

Although a variety of studies provided large-scale information on the recent HPV prevalence and genotype distribution in Shannan City, Tibet, China, there were still some limitations. First, most cervical screening tests received by patients did not carry out detailed HPV typing, nor did they be combined with cytology. Women included in some studies were unable to obtain cervical cytological or histological results. Therefore, it is impossible for doctors or researchers to associate HPV infection and genotype distribution with different cervical abnormalities. Secondly, the collection of personal information of patients was not complete. Tibet had a high altitude and a wide area. There was a variety of distinctive information about the nationality, living habits, reproductive history, climatic conditions cultural, and other backgrounds of the population in this area. Unfortunately, it was not recorded in this study so that we couldn’t specify the impact of these different backgrounds on the rate of HPV infection. In addition, some studies had shown that human papillomavirus infection may lead not only to cervical cancer but also to oropharyngeal cancer and head and neck cancer [37]. Therefore, it was suggested to also focus on the relationship between HPV infection and oropharyngeal cancer, and head and neck cancer in Tibetan women in future research. In addition, obtaining data on human papillomavirus infection in Tibetan men could be regarded as a potential direction for future research.

After all, our study revealed the HPV infection rate and genotype distribution of women from Shannan City, Tibet, China. This information may provide guidance and suggestions for the prevention of cervical cancer for women in this area. According to the current results, young women should be vaccinated with HPV vaccine as soon as possible, and elderly women should focus on crevice screening.

**Conclusion**

In summary, this study analyzed the prevalence of HPV in women and its difference with age distribution characteristics in Shannan City, Tibet from 2019 to 2020. Moreover, the differences of HPV infection rate between Shannan city and other regions in China were also compared. The results in our study will provide helpful information for cervical cancer screening and human papillomavirus vaccination in women in Shannan City, Tibet.
8. Zhao JW, et al. Prevalence and genotype distribution of human papillomavirus: implications for cancer screening and vaccination in Henan province. China Rev Soc Bras Med Trop. 2016;49(2):237–40.
9. Yu H, et al. Prevalence and genotype distribution of human papillomavirus among healthy females in Beijing, China, 2016–2019. Infect Drug Resistance. 2021;14:173–82.
10. Li P, et al. Characteristics of human papillomavirus infection among women with cervical cytoligical abnormalities in the Zhoupu District, Shanghai City, China, 2014–2019. Virol J. 2021;18(1):51.
11. Xiang F, et al. Distribution characteristics of different human papillomavirus genotypes in women in Wuhan, China. J Clin Lab Anal. 2018;32(8):e22581.
12. Pan Z, et al. Screening for HPV infection in exfoliated cervical cells of women from different ethnic groups in Yili, Xinjiang, China. Sci Rep. 2019;9(1):3468.
13. Zhong TY, et al. Prevalence of human papillomavirus infection among 71,435 women in Jiangxi Province. China J Infect Public Health. 2017;10(6):783–8.
14. Luo Q, et al. Prevalence and genotype distribution of HPV and cervical pathological results in Sichuan Province, China: a three years surveys prior to mass HPV vaccination. Virol J. 2020;17(1):100.
15. Baloch Z, et al. Epidemiologic characterization of human papillomavirus (HPV) infection in various regions of Yunnan Province of China. BMC Infect Dis. 2016;16:228.
16. Li M, et al. Incidence, persistence and clearance of cervical human papillomavirus among women in Guangdong, China 2007–2018: a retrospective cohort study. J Infect Public Health. 2021;14(1):42–9.
17. Zhang C, et al. Distribution of human papillomavirus infection: a population-based study of cervical samples from Jiangsu Province. Virol J. 2019;16(1):67.
18. Li J, et al. Distribution of human papillomavirus genotypes in western China and their association with cervical cancer and precancerous lesions. Arch Virol. 2021;166(3):853–62.
19. Jiang L, et al. HPV prevalence and genotype distribution among women in Shandong Province, China: analysis of 94,489 HPV genotyping results from Shandong's largest independent pathology laboratory. PLoS ONE. 2019;14(1):e0210311.
20. Li J, et al. Analysis of human papillomavirus infection and typing in Shanxi province. Zhonghua Yu Fang Yi Xue Za Zhi. 2017;51(4):397–401.
21. Wu X, et al. Prevalence of type-specific human papillomavirus infection among 18–45 year-old women from the general population in Liuzhou, Guangxi Zhuang Autonomous Region: a cross-sectional study. Zhonghua Liu Xing Bing Xue Za Zhi. 2017;38(4):467–71.
22. Liu J, et al. Epidemiology and persistence of cervical human papillomavirus infection among outpatient women in Heilongjiang province: a retrospective cohort study. J Med Virol. 2020;92:3784–92.
23. Xue H, et al. Prevalence and genotype distribution of human papillomavirus infection in asymptomatic women in Liaoning province. China J Med Virol. 2015;87(7):1248–53.
24. Ji Y, et al. The burden of human papillomavirus and chlamydia trachomatis coinfection in women: a large cohort study in Inner Mongolia. China J Infect Dis. 2019;12(2):206–14.
25. Jin Q, et al. Prevalence of human papillomavirus infection in women in Tibet Autonomous Region of China. Zhonghua Fu Chan Ke Za Zhi. 2009;44(12):898–902.
26. Chen L, et al. The genomic distribution map of human papillomavirus in Western China. Epidemiol Infect. 2021;149:e135.
27. Suresh A, et al. Prevalence of high-risk HPV and its genotypes: Implications in the choice of prophylactic HPV vaccine. J Med Virol. 2021;93(8):5188–92.
28. Bruni L, et al. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. J Infect Dis. 2010;202(12):1789–99.
29. Zhu B, et al. The prevalence, trends, and geographical distribution of human papillomavirus infection in China: the pooled analysis of 1.7 million women. Cancer Med. 2019;8(11):5373–85.
30. Skinner SR, et al. Efficacy, safety, and immunogenicity of the human papillomavirus 16/18 AS04-adjuvanted vaccine in women older than 25 years: 4-year interim follow-up of the phase 3, double-blind, randomised controlled VIVIANE study. Lancet. 2014;384(9961):2213–27.
31. Xue Y, et al. "U" shape of age-specific prevalence of high-risk human papillomavirus infection in women attending hospitals in Shanghai, China. Eur J Obstet Gynecol Reprod Biol. 2009;145(2):214–8.
32. Liao G, et al. Multi-infection patterns and co-infection preference of 27 human papillomavirus types among 137,943 gynecological outpatients across China. Front Oncol. 2020;10:449.
33. Alder S, et al. Acceptance of human papillomavirus (HPV) vaccination among young women in a country with a high prevalence of HPV infection. Int J Oncl. 2013;43(4):1310–8.
34. Rodríguez AC, et al. Rapid clearance of human papillomavirus and implications for clinical focus on persistent infections. J Natl Cancer Inst. 2008;100(7):513–7.
35. González P, et al. Behavioral/lifestyle and immunologic factors associated with HPV infection among women older than 45 years. Cancer Epidemiol Biomark Prev. 2010;19(12):3044–54.
36. Spinner C, et al. Human papillomavirus vaccine effectiveness and herd protection in young women. Pediatrics. 2019;143(2).
37. Manur S, et al. HPV-associated head and neck cancer: a virus-related cancer epidemic. Lancet Oncol. 2010;11(8):781–9.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.