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Epidemiological study of HPV infection in 24,588 rural women in Luonan, China

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ABSTRACT

Cervical cancer is a significant public health issue for women, with human papillomavirus (HPV) infection rates exhibiting regional variations throughout China. This study examined data from a cohort of 24,588 rural women who engaged in cervical cancer screening in Luonan County from 2021 to 2023, utilizing high-risk HPV (hrHPV) testing methodologies. The findings revealed an overall HPV positivity rate of 14.18 %, with hrHPV positivity rates of 13.99 % in 2021, 12.97 % in 2022, and 15.32 % in 2023. Infection rates increased with age, showing significant differences among age groups. Types 52, 16, and 58 were the most prevalent hrHPV types. Single-type infections were more common than multiple infections, with prevalent combinations such as HPV16 + HPV52, HPV52 + HPV58, and HPV51 + HPV16. The results highlight the imperative for improved screening, especially for women aged 60 to 64 residing in rural areas, and emphasize the importance of HPV vaccination and targeted screening for the prevention and eventual eradication of cervical cancer.

1. Introduction

Cervical cancer represents a significant challenge to global public health, with its incidence and mortality rates being intricately linked to socio-economic disparities.According to the data of the World Health Organization(WHO), 660,000 cases of cervical cancer were newly diagnosed in 2022, resulting in 350,000 deaths, of which more than 90 % of the new cases and deaths occurred in low-income and middle-income regions(Stelzle et al., 2021).China, although a lower-than-global-average incidence, represents 18.2 % of new cases and 17.3 % of fatalities due to its substantial population. The incidence and death rates of colorectal cancer are escalating, particularly in rural regions, with yearly increases of 6.0 % in rural areas and 2.2 % in urban areas(Li et al., 2017).

Human papillomavirus (HPV), a double-stranded DNA virus including over 400 known types, is the principal etiological agent of CC. Although the majority of HPV infections resolve spontaneously, chronic high-risk HPV (HR-HPV) infection can result in CC(Kombe Kombe et al., 2020).Vaccination and screening effectively decrease the incidence of and death from cervical cancer. Prevalent screening techniques encompass HPV nucleic acid testing, cytology (Pap smear and liquid-based), co-testing, and emerging methodologies such as methylation testing, HPV DNA load assessment, and artificial intelligence applications(Schiffman et al., 2016; Kong et al., 2020).

The WHO advocates adopting HPV genotyping as a screening method, supplemented by cytology and colposcopy for confirmed positive cases. U.S. recommendations recommend cervical cytology every three years for women aged 21 to 29 and either HR-HPV testing or co-testing every five years for those aged 30 to 65(Curry et al., 2018).In 2020, the WHO initiated a global effort to eradicate cervical cancer by 2030, a target incorporated into China's national health policy(Yan et al., 2024).The combination of HPV vaccination and screening can significantly reduce cervical cancer incidence(Sipp et al., 2018). Additionally, targeted vaccination based on specific HPV genotypes, along with educational outreach, can improve vaccine uptake and lower cancer rates(Yang et al., 2024).In rural regions like Luonan County, elements such as medical resources, legislation, and local public awareness have influenced screening efforts.

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2. Materials and Methods

2.1. Data Source

This retrospective analysis examined data from 24,588 women aged 35 to 64 who voluntarily engaged in cervical cancer screening at the Luonan County Maternal and Child Health Hospital from 2021 to 2023. The screening cycle lasted five years, with women tested in 2021 not invited for tests in 2022 or 2023. Eligible participants were citizens of Luonan County, Shaanxi Province, aged 35 to 64, having a history of sexual activity. The exclusion criteria were cervical lesions, previous conization or hysterectomy, pelvic radiation or chemotherapy, as well as pregnancy or nursing. The Ethics Committee of Xi'an Public Health Center accepted the study (Approval No. XPHC202408120002).

2.2. HPV and Cytologic test Sampling, Detection, and colposcopy with cervical biopsy

Participants were instructed to abstain from sexual activity for three days, avoid vaginal medications, and schedule sampling outside menstruation. During the sampling process, participants were placed in the lithotomy position, and a speculum was used to fully expose the cervix. For HPV sampling, cervical secretions were first cleaned with 0.9 % saline solution, and a specialized HPV sampling brush was inserted 2–3 cm into the cervical canal, held for 5 s, and rotated 3–5 times clockwise. The brush head was then placed into a labeled transport vial for testing, and HPV DNA was extracted to detect 15 HPV subtypes, including high-risk types such as HPV16 and HPV18. Participants with positive results for HPV16/18 were directly referred for colposcopy and cervical biopsy. For ThinPrep Cytologic Test (TCT) sampling, primarily performed on patients with other high-risk HPV types, a specialized TCT sampling brush was placed parallel to the cervical os, with the central bristles gently inserted into the cervical canal. The brush was rotated clockwise for five gentle turns, after which the brush head was placed into a vial containing a cell-preserving solution, labeled with an ID number, and sealed for transport. The samples were processed by pathologists, who prepared slides for microscopic examination and classification. Patients with TCT results of $\geq$ ASC-US were referred for colposcopy and cervical biopsy. During colposcopy, specialists collected cervical tissue samples, which were sent to the pathology department for histological diagnosis. The pathological results were categorized as inflammation/condyloma-like alterations, low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), or cervical cancer.

2.3. Statistical Methods

Data analysis was conducted using SPSS 21.0 and R 4.4.1 software. Comparisons of categorical data among groups were performed using the chi-square test or Fisher's exact probability technique, with a significance level set at $P < 0.05$.

3. Results

3.1. Overall distribution of cervical cancer screening from 2021 to 2023

From 2021 to 2023, 24,588 women participated in cervical cancer screening utilizing HPV testing, with a mean age of 48.17 $\pm$ 7.73 years. The total HPV infection rate was 14.18 % (3,486/24,588), including 13.73 % high-risk HPV and 0.83 % low-risk HPV infections. The predominant high-risk HPV types were HPV52 (22.06 %), HPV16 (20.20 %), HPV58 (15.09 %), HPV51 (12.48 %), and HPV56 (9.50 %) (Fig. 1). In 2021, the inaugural free screening program produced the most substantial sample size, but 2022 had a diminished sample owing to COVID-19 limits. The rates of HPV positivity fluctuated markedly throughout the three-year period: 13.99 % in 2021, 12.97 % in 2022, and 15.32 % in 2023 ($p < 0.004$,95 % CI: 13.75 %-14.61 %).

3.2. Prevalence of HPV infection across various age groups

The results of this study demonstrate that the total HPV infection rate shows a considerable increase with advancing age, a tendency observed for both single and multiple infections. The infection rate for single infections was 10.98 % (2,700/24,588), significantly above the 3.20 % (786/24,588) recorded for multiple infections. Participants were divided into six age categories: 35–39 years, 40–44 years, 45–49 years, 50–54 years, 55–59 years, and 60–64 years, with HPV infection rates of 11.06 % (489/4,421), 11.48 % (452/3,937), 12.43 % (615/4,948), 14.62 % (802/5,484), 18.40 % (733/3,983), and 21.76 % (395/1,815), respectively. The findings demonstrate that the peak infection rate was observed in the 60–64 age cohort, whereas the minimum incidence was recorded in the 35–39 age cohort (Fig. 2).

An examination of the infection rates of HPV33, HPV45, HPV58, and HPV11 across various age groups revealed statistically significant variations ($p < 0.05$; Table 1). HPV infection rates, encompassing both single infections and overall positive, escalated with age, notably in the 50–54 and 55–59 age brackets.

3.3. Single and multiple HPV infections

As the severity of lesions increases, the likelihood of a single HPV infection also increases.The rates of single HPV infections were 58.56 %

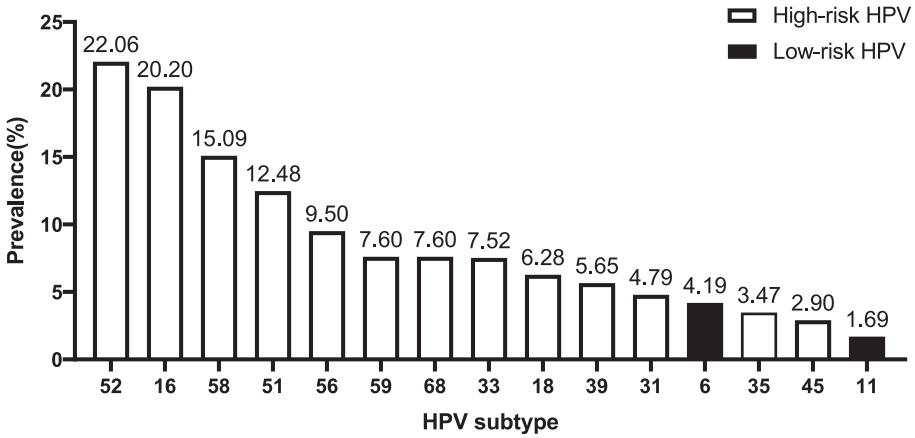

Fig. 1. Distribution of HPV Genotypes Among HPV-Positive Patients.

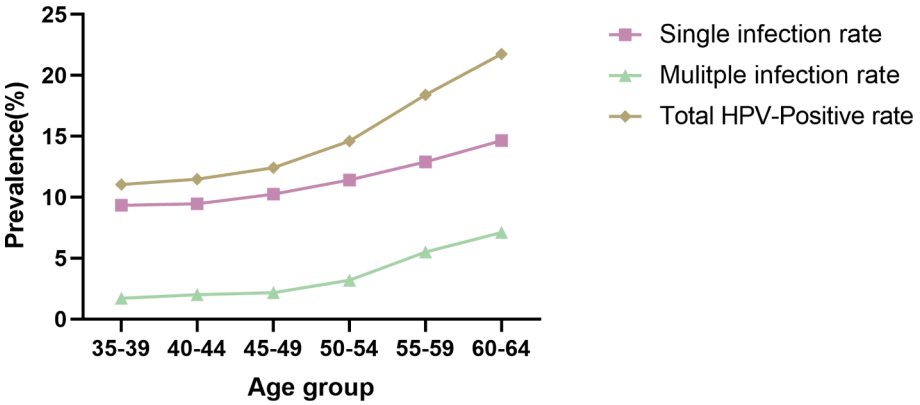

Fig. 2. Age-Specific Prevalence of HPV Infection in Luonan, China, from 2021 to 2023.

Table 1
Infection Rates of 15 HPV Subtypes Among Different Age Groups.

HPV type	35–39(n = 4421)	40–44(n = 3937)	45–49(n = 4948)	50–54(n = 5484)	55–59(n = 3983)	60–64(n = 1815)	χ^2	*p*
	489(11.06 %)	452(11.48 %)	615(12.43 %)	802(14.62 %)	733(18.40 %)	395(21.76 %)	216.437	<0.001
High-risk HPV	477(10.79 %)	439(11.15 %)	593(11.98 %)	773(14.10 %)	707(17.75 %)	386(21.27 %)	3.142	0.680
16	98(2.22 %)	105(2.67 %)	125(2.53 %)	145(2.64 %)	153(3.84 %)	78(4.30 %)	5.082	0.406
18	33(0.75 %)	29(0.74 %)	32(0.65 %)	53(0.97 %)	50(1.26 %)	22(1.21 %)	2.258	0.813
31	19(0.43 %)	15(0.38 %)	27(0.55 %)	35(0.64 %)	44(1.10 %)	27(1.49 %)	9.544	0.089
33	16(0.36 %)	28(0.71 %)	40(0.81 %)	59(1.08 %)	65(1.63 %)	54(2.98 %)	38.196	<0.001
35	17(0.38 %)	9(0.23 %)	19(0.38 %)	30(0.55 %)	27(0.68 %)	19(1.05 %)	5.609	0.346
39	33(0.75 %)	24(0.61 %)	27(0.55 %)	41(0.75 %)	48(1.21 %)	24(1.32 %)	4.714	0.452
45	11(0.25 %)	6(0.15 %)	15(0.30 %)	24(0.44 %)	23(0.58 %)	22(1.21 %)	15.351	0.009
51	61(1.38 %)	43(1.09 %)	78(1.58 %)	100(1.82 %)	104(2.61 %)	49(2.70 %)	5.627	0.345
52	106(2.40 %)	102(2.59 %)	125(2.53 %)	166(3.03 %)	178(4.47 %)	92(5.07 %)	4.507	0.479
56	39(0.88 %)	41(1.04 %)	62(1.25 %)	65(1.19 %)	80(2.01 %)	44(2.42 %)	6.419	0.268
58	45(1.02 %)	62(1.57 %)	84(1.70 %)	128(2.33 %)	120(3.01 %)	87(4.79 %)	31.12	<0.001
59	40(0.90 %)	30(0.76 %)	43(0.87 %)	62(1.13 %)	63(1.58 %)	27(1.49 %)	2.536	0.772
68	45(1.02 %)	40(1.02 %)	45(0.91 %)	67(1.22 %)	44(1.10 %)	24(1.32 %)	7.481	0.187
Low-risk HPV	20(0.45 %)	21(0.48 %)	28(0.63 %)	54(1.22 %)	56(1.27 %)	24(1.32 %)	11.363	0.045
6	17(0.38 %)	17(0.43 %)	22(0.44 %)	38(0.69 %)	37(0.93 %)	15(0.83 %)	3.499	0.625
11	3(0.07 %)	4(0.10 %)	7(0.14 %)	16(0.29 %)	20(0.50 %)	9(0.50 %)	12.314	0.030

in the inflammatory group, 28.57 % in the LSIL group, 77.42 % in the HSIL group, and 84.62 % in the CC group. However, the rates of multiple infections dropped as the severity of the lesion increased, reaching 41.44 %, 71.43 %, 22.58 %, and 15.38 %, respectively. A statistically significant difference was noted between single and multiple infections ($p < 0.05$).Different types of HPV infectionsare clearly shown by the chord diagram. The most common combinations are HPV16 + HPV52 (66 cases), HPV52 + HPV58 (58 cases), and HPV51 + HPV16 (56 cases) (Fig. 3).

HPV16 (33.94 %, 241/710), HPV52 (9.86 %, 70/710), and HPV58 (8.73 %, 62/710) were identified as the predominant high-risk types, with HPV16 demonstrating the highest infection rates. This was particularly evident in the inflammatory (31.20 %, 185/593), high-grade squamous intraepithelial lesion (HSIL) (51.81 %, 43/83), and cervical cancer (CC) (68.75 %, 11/16) categories. HPV52 and HPV58 also showed increased infection rates, primarily within the HPV52 inflammatory (10.96 %, 65/593) and HPV58 HSIL (9.64 %, 8/83) groups. Other HPV types, such as HPV11 (1.13 %, 8/710), were less common,

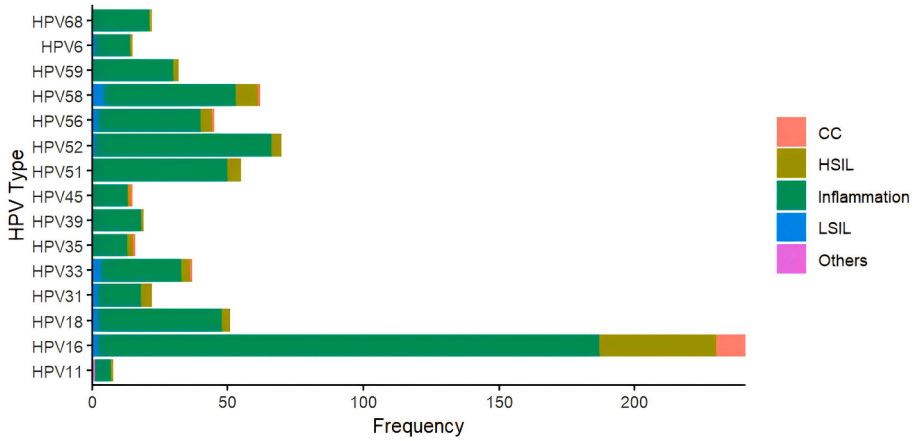

Fig. 3. HPV Type Correlations in Rural Women with Multiple Infections in Luonan,China.

with HPV11 (1.01 %, 6/593) being predominantly detected in the inflammatory cohort.(Fig. 4).

4. Discussion

In 2022, around 296,300 new cases of gynecological malignancies were reported among women in China, representing 12.93 % of all newly diagnosed female cancers. The incidence rate in rural areas was markedly greater than in metropolitan districts(Sun et al., 2024).Cervical cancer had the greatest prevalence among these instances, with 150,700 new cases documented. In 2019, the cervical cancer screening rate in China was at 33 %, falling short of the global average of 36 %, and exhibiting significant regional variances. The screening coverage was 48 % in upper-middle-income nations, 84 % in high-income countries, and just 9 % and 11 % in lower-middle-income and low-income countries, respectively(Zhang et al., 2022).The incidence of high-risk human papillomavirus (HPV) infection was observed to be greatest among women in northern China, presumably due to lagging economic growth and inadequate awareness of preventive measures in some regions(Li et al., 2019).Standardized HPV and cervical cancer screening programs can efficiently identify high-risk groups and provide early therapies, therefore decreasing the incidence and death of cervical cancer.

This study examined the frequency of HPV infection and genotype distribution using cervical cancer screening data gathered from rural regions of Luonan County, Shaanxi Province, China, between 2021 and 2023. The findings indicated that the HPV infection rate in Luonan County was 14.18 %, which is below the province average of 30.21 % (Cao et al., 2017).The prevalence of high-risk HPV infection was 13.73 %, which is lower than the 20–25 % reported in both domestic and foreign research. Nonetheless, it surpassed the rates in many domestic areas, like Suzhou (10.2 %) and Xinjiang (7.3 %), although it was inferior to those in Beijing (22.7 %) and Qingdao (32.2 %)(Zhu et al., 2021; Wang et al., 2023).The regional disparities may be ascribed to China's substantial population and geographical heterogeneity, since there are variances in the features of high-risk HPV infections and predominant subtypes across different areas. In Luonan County, the predominant HPV genotypes were HPV52, HPV16, and HPV58, aligning with national trends.

HPV infections were detected in all age demographics, with prevalence rates rising with advancing age. The largest incidence was in women aged 60–65, maybe linked to diminished immune function, hormonal alterations following menopause, and the reactivation of latent infections(Jiang et al., 2019).The age distribution of rural women in Luonan County exhibited a unimodal pattern, contrasting with the U-shaped bimodal distribution found in other areas, possibly due to the exclusion of women under 35 years from this research. The 60–64 age demographic had the greatest infection incidence at 21.76 % in this research, indicating that future initiatives could consider broadening cervical cancer screening to include those aged 65 and older.The 35–39 age range exhibited the lowest infection rate, possibly attributable to enhanced immune function and more consistent sexual practice within this demographic(Yi et al., 2023).Infection rates for genotypes such as HPV33, HPV45, and HPV58 have considerably risen in older women, highlighting the necessity for age-specific screening and management techniques.

Single HPV infections were the most common kind of HPV infections among rural women in Luonan County, with HPV16 being the most frequent, especially in patients with cervicitis, HSIL and CC. Women with numerous infections exhibited a higher likelihood of developing cervical lesions and cancer.Multiple infections, particularly the HPV16 and HPV52 combination, were most common, consistent with findings from Guangzhou,China(Yang et al., 2023),Co-infection is linked to

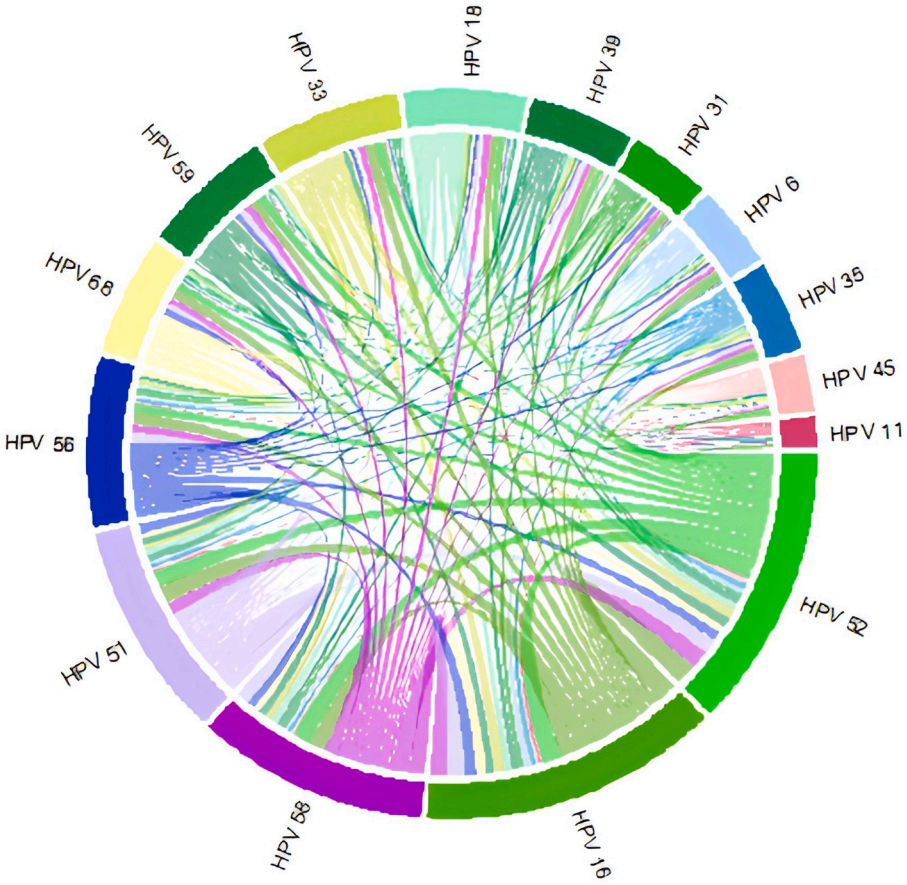

Fig. 4. Frequency Distribution of HPV Types in Different Disease Categories.

higher viral loads, which predict cervical intraepithelial neoplasia (CIN) and cervical cancer(van der Weele et al., 2016). Multiple high-risk HPV infections are associated with low-grade cytological abnormalities but not HSIL(Tong et al., 2024). Clinical focus should prioritize patients with multiple infections and high-risk genotypes(Tang et al., 2023).

The HPV infection rate among rural women in Luonan County was below the provincial norm, but high-risk genotypes such as HPV52, HPV16, and HPV58 were prevalent. Advocating for the nine-valent HPV vaccine is crucial for women in this region. Future efforts should focus on improving HPV screening and vaccination programs, leveraging artificial intelligence for efficient cervical cancer screening, and implementing targeted treatments for high-risk groups. This study, based on three years of HR-HPV genotyping and TCT pathology data, supports enhanced prevention and vaccination strategies, highlights the importance of free screenings, and aims to reduce the cervical cancer burden while improving screening accessibility.

CRediT authorship contribution statement

Xin Zhao: Writing – review & editing, Writing – original draft, Conceptualization, Data curation, Software, Supervision, Validation, Visualization. **Shi Shen:** Writing – original draft, Investigation. **Cailing Su:** Investigation. **Juan Chang:** Investigation, Data curation. **Yunfang Yan:** Supervision, Investigation. **Jianmin Zhao:** Writing – review & editing, Supervision, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101669.

References

Cao, D., Zhang, S., Zhang, Q., et al., 2017. Prevalence of high-risk human papillomavirus infection among women in Shaanxi province of China: A hospital-based investigation [J]. J Med Virol 89 (7), 1281–1286.
Curry, S.J., Krist, A.H., Owens, D.K., et al., 2018. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement [J]. Jama 320 (7), 674–686.
Jiang, L., Tian, X., Peng, D., et al., 2019. 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 [J]. PLoS One 14 (1), e0210311.
Kombe Kombe, A.J., Li, B., Zahid, A., et al., 2020. Epidemiology and Burden of Human Papillomavirus and Related Diseases, Molecular Pathogenesis, and Vaccine Evaluation [J]. Front. Public Health 8, 552028.
Kong, L., Wang, L., Wang, Z., et al., 2020. DNA methylation for cervical cancer screening: a training set in China [J]. Clin Epigenetics 12 (1), 91.
Li, K., Li, Q., Song, L., et al., 2019. The distribution and prevalence of human papillomavirus in women in mainland China [J]. Cancer 125 (7), 1030–1037.
Li, X., Zheng, R., Li, X., et al., 2017. Trends of incidence rate and age at diagnosis for cervical cancer in China, from 2000 to 2014 [J]. Chin J Cancer Res 29 (6), 477–486.
Schiffman, M., Doorbar, J., Wentzensen, N., et al., 2016. Carcinogenic human papillomavirus infection [J]. Nat Rev Dis Primers 2, 16086.
Sipp, D., Frazer, I.H., Rasko, J.E.J., 2018. No Vacillation on HPV Vaccination [J]. Cell 172 (6), 1163–1167.
Stelzle, D., Tanaka, L.F., Lee, K.K., et al., 2021. Estimates of the global burden of cervical cancer associated with HIV [J]. Lancet Glob Health 9 (2), e161–e169.
Sun, K., Han, B., Zeng, H., et al., 2024. Incidence and Mortality of Cancers in Female Genital Organs - China, 2022 [J]. China CDC Wkly 6 (10), 195–202.
Tang, X., Zhang, H., Wang, T., et al., 2023. Single and Multiple High-Risk Human Papillomavirus Infections in Histopathologically Confirmed Cervical Squamous Lesions: Incidences, Distribution, and Associated Detection Rates for Precancerous and Cancerous Lesions [J]. Lab Invest 103 (11), 100234.
Tong, T., Su, D., Yang, Q., et al., 2024. Multiple high-risk HPV infections probably associated with a higher risk of low-grade cytological abnormalities but not with high-grade intraepithelial lesions of the cervix [J]. World J Surg Oncol 22 (1), 79.
van der Weele, P., van Logchem, E., Wolffs, P., et al., 2016. Correlation between viral load, multiplicity of infection, and persistence of HPV16 and HPV18 infection in a Dutch cohort of young women [J]. J Clin Virol 83, 6–11.
Wang, T., Luan, L., Deng, J., et al., 2023. Prevalence and human papillomavirus (HPV) genotype distribution in Suzhou, China [J]. Hum Vaccin Immunother 19 (2), 2241309.
Yan, H., Wang, Q., Qiao, Y., 2024. Cervical cancer prevention in China: where are we now, and what's next? [J]. Cancer Biol Med 21 (3), 213–217.
Yang, X., Li, Y., Tang, Y., et al., 2023. Cervical HPV infection in Guangzhou, China: an epidemiological study of 198,111 women from 2015 to 2021 [J]. Emerg Microbes Infect 12 (1), e2176009.
Yang, S.T., Wang, P.H., Liu, H.H., et al., 2024. Cervical cancer: Part I human papilloma virus vaccination in Taiwan [J]. Taiwan J Obstet Gynecol 63 (3), 320–328.
Yi, J., Li, X., Zhang, R., et al., 2023. The impact of the COVID-19 pandemic on the prevalence and genotype distribution of HPV infection in Beijing, China [J]. J Med Virol 95 (10), e29155.
Zhang, M., Zhong, Y., Wang, L., et al., 2022. Cervical Cancer Screening Coverage - China, 2018-2019 [J]. China CDC Wkly 4 (48), 1077–1082.
Zhu, X., Wang, Y., Lv, Z., et al., 2021. Prevalence and genotype distribution of high-risk HPV infection among women in Beijing, China [J]. J Med Virol 93 (8), 5103–5109.