



## OPEN Age distribution of high-risk HPV infection and cervical lesions in an unvaccinated adult Brazilian population within an organized screening program

Rafaella Moraes Rego, Diama Bhadra Vale, Cirbia Silva Campos, Leandro Vasconcelos, Eduardo Campos, Helena Cunha Lopes Lima, Michelle Garcia Discacciati, Luiz Carlos Zeferino & Julio Cesar Teixeira

High-risk human papillomavirus (hr-HPV) persistent infection is the necessary cause of cervical cancer, yet age-specific prevalence patterns in unvaccinated adult women remain insufficiently characterized in Brazil. This population-based study describes the distribution of hr-HPV infection and cervical lesions among 20,398 women aged 25–64 years screened during the first screening round of the PREVENTIVO organized program using HPV-DNA testing in Indaiatuba, Brazil (2017–2022). Overall hr-HPV prevalence was 12.8% (95% CI: 12.4–13.1), with a bimodal age pattern: a first peak at 25–26 years (26%) and a smaller second peak at 55–56 years (11.2%). HPV16, HPV18, and 12 other hr-HPV types were detected in 2.63%, 1.01%, and 10.72% of women, respectively, all showing significant age-related declines. Among hr-HPV positive women, 12.4% had CIN2+, including 29 cervical cancers. CIN2+ rates ranged from 11 to 17% between ages 25–49, decreased after, and showed a late HSIL peak at 61 years (8.2%). Cervical cancer peaked at 45–46 years, with no cases after age 55, reflecting the impact of early precursor detection within the program. These findings demonstrate a persistent burden of hr-HPV and high-grade lesions at older ages and provide essential baseline data for monitoring vaccination impact. They also support consideration of extended of screening strategies, including a potential hr-HPV “exit test” beyond age 64.

Cervical cancer remains a major cause of morbidity and mortality among women, particularly in vulnerable populations or in settings with limited access to healthcare services<sup>1–3</sup>. In Brazil, the annual estimate for 2023–2025 is 17,000 new cervical cancer cases and 6,000 deaths<sup>4</sup>. This cancer arises from persistent cervical infection with oncogenic high-risk human papillomavirus (hr-HPV). Cervical HPV infection is common among young adults, and although 90% of infections are transient, persistent infection increases the risk of developing precursor lesions and, eventually, cervical cancer. Approximately only 1% of all infections progress to cervical cancer<sup>5,6</sup>.

Established preventive measures include vaccination against the most relevant genotypes, especially HPV16 and HPV18, and regular screening for precursor lesions using cervical samples<sup>2,7–9</sup>. After decades of relying on cytology (Pap smear), molecular tests for hr-HPV DNA detection have become the standard in several countries<sup>8,10–12</sup>.

The global adjusted prevalence of HPV infection among women without cytological abnormalities is estimated at 11.7% (95% CI: 11.6–11.7)<sup>12</sup>. Rates vary by socioeconomic level and, more recently, by the impact of vaccination introduced in 2007<sup>13,14</sup>. While countries such as Australia and the United Kingdom report substantial declines in vaccine-type HPV prevalence, regions including Sub-Saharan Africa (24%), Eastern Europa (21.4%) e Latin America (16.1%) still show high rates<sup>1,7,12–14</sup>.

Age-specific hr-HPV distribution often displays a U-shaped or bimodal pattern, with a first peak in adolescence and young adulthood (25–40%), followed by a decline to baseline levels (5–15%) at ages 35–55 years, and, in some settings, a smaller second peak (15–20%) after age 50<sup>5,15–17</sup>. This late peak may reflect new

Department of Obstetrics and Gynecology, University of Campinas (UNICAMP), Campinas, SP 13098-340, Brazil.  
✉ email: juliotex@unicamp.br

exposures or reactivation of latent infections, potentially influenced by hormonal and immune changes during aging<sup>15</sup>.

In Brazil, hr-HPV prevalence and its age-specific distribution remain poorly characterized. Existing studies show regional heterogeneity and are often limited to specific age groups<sup>16–18</sup>. A meta-analysis by Colpani et al. (2020) reported a 25.6% prevalence in samples from the Southeast region<sup>17</sup>, while a study of 5,268 young Brazilian women (16–25 years) found a 38.6% prevalence<sup>20</sup>. However, consistent data for women over 25 years are lacking.

HPV vaccination was introduced in Brazil's national immunization program in 2014, and the first vaccinated cohort is expected to reach screening age in 2025. Brazil currently recommends cervical cancer screening for women aged 25–64 years, based on cytology every three years, offered in an opportunistic manner with minimal impact on mortality<sup>4,19</sup>.

To improve this scenario, the “PREVENTIVO” (PREvention of HPV Viruses in ENTire Indaiatuba by Vaccination and Organization of the screening) cervical cancer screening program was initiated in October 2017 as a population-based demonstration project within the public healthcare system, developed through cooperation between the city of Indaiatuba (Sao Paulo, Brazil) and the University of Campinas (UNICAMP, Campinas, SP, Brazil). Briefly, the screening program targets women aged 25–64y who have initiated sexual activity and includes hr-HPV DNA testing every five years. Its main achievements have been previously published<sup>20–22</sup> and have supported Brazil's ongoing transition to an organized HPV DNA-based screening program<sup>23</sup>.

With more than 20,000 women screened by hr-HPV DNA testing in the program first round, it is timely to describe hr-HPV prevalence in a predominantly unvaccinated adult population to support screening policy planning and provide baseline data for future evaluation of vaccination impact. This study aimed to describe the age-specific prevalence of hr-HPV infection and high-grade precursor lesions or cervical cancer in women aged 25 years or older participating in an organized screening program using hr-HPV DNA testing in the public health system.

## Results

A total of 20,398 women aged 25–64 years were screened, reaching 78% coverage of the target population. The overall hr-HPV prevalence was 12.8% (95% CI: 12.4–13.1;  $n=2,603$ ), and the overall rate of CIN2 or worse among hr-HPV-positive women was 12.4% ( $n=324$ ), comprising 154 (47.5%) CIN2, 141 (43.5%) CIN3, and 29 (9.0%) invasive cervical cancers.

### Age-group specific prevalence of hr-HPV and lesions

Five-year age group-specific hr-HPV prevalence among all screened women showed a progressive decline of 0.41% per year of age ( $p < 0.0009$ ; linear trend test; Fig. 1; Table 1), with a bimodal pattern consisting of an initial peak at age 25–26 years (26%) and a smaller second peak of 8.6% at ages 55–59. Using two-year age groups, the second peak reached 11.2% at ages 55–56 (Supplementary Figure S1). Lesion prevalence by five-years age group is shown in Table 2, with a significant decreasing trend for CIN2 (0.07% per year;  $p < 0.0001$ ) and CIN3 (0.04% per year;  $p = 0.0002$ ).

### HPV genotype prevalence by five-year age group

This analysis considered the different HPV detections and combinations; results are shown in Table 1. HPV16 was detected in 2.63%, HPV18 in 1.01% and the 12OT group in 10.72%. All HPV detections patterns showed a significant decreasing trend with increasing age ( $p < 0.05$ ), with the steepest declines observed for 12OT-only (1.4% per year;  $p = 0.001$ ) and 12OT-any infections (1.7% per year;  $p = 0.001$ ). Only the HPV16/18 co-infection group did not show a significant trend, likely due to its low frequency. Any hr-HPV prevalence decreased from 23.37% in women aged 25–29 years to 6.63% in women aged 60–64 years ( $-0.41\%$  per year;  $p = 0.0009$ ). Details about coefficient angular and percentage trend for each category are shown in Supplementary Table S1.

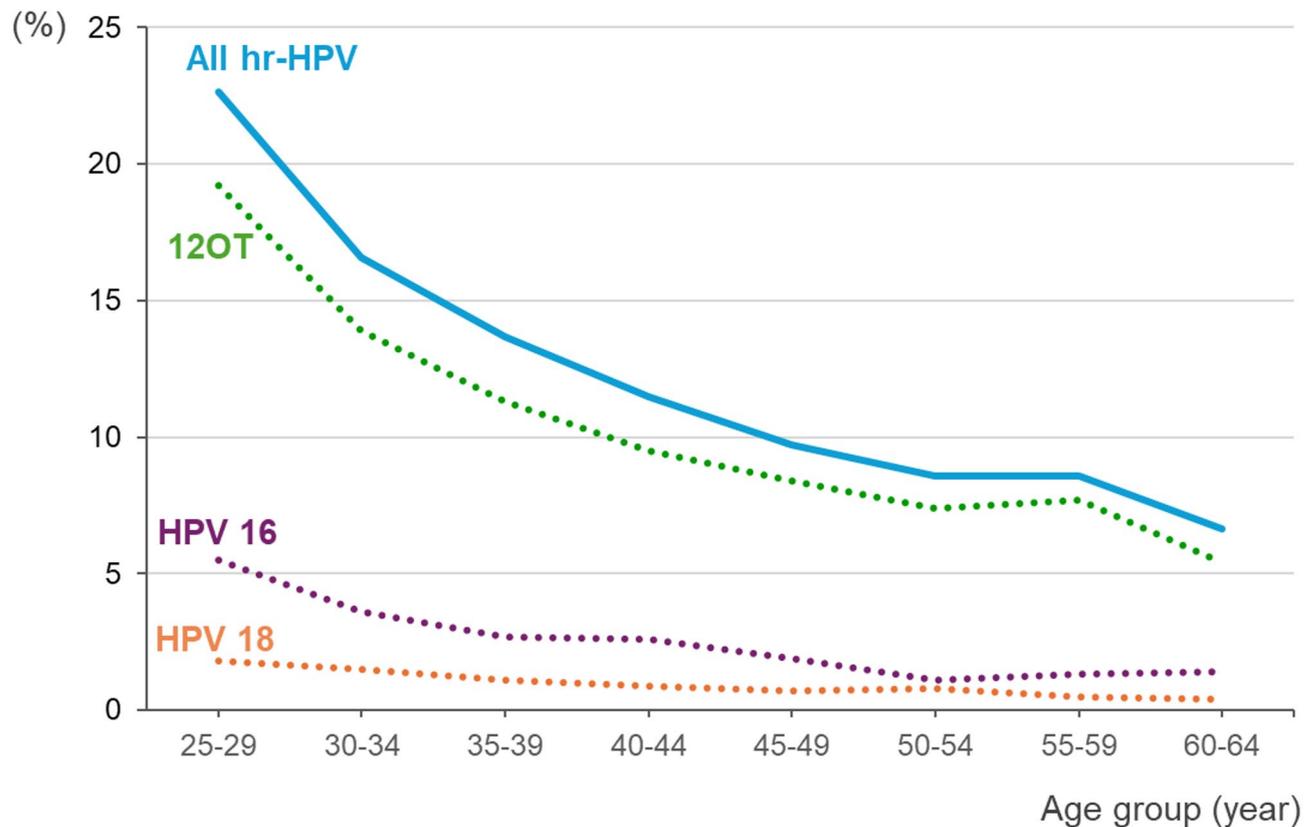
### Lesions detected among hr-HPV-positive women

The CIN2 or worse rate among hr-HPV-positive women ranged from 11 to 16.7% between ages 25–49 years, then declined to 7.7% at age 50–54 (Table 2). Three-year age group analysis (Fig. 2) showed a small second peak of HSIL (CIN2 plus CIN3) at age 61 (8.2%). Cervical cancer cases increased progressively from age 35, peaked at age 45–46, and no cases were detected after age 55, likely reflecting increased HSIL detection and treatment due to the screening program. Details about coefficient angular and percentage trend for each lesion category are shown in Supplementary Table S1.

## Discussion

This study provides the first age-specific description of hr-HPV infection and cervical lesions in an unvaccinated adult female population within an organized screening program in Brazil. The overall hr-HPV prevalence (12.8%) aligns with global estimates for comparable age groups<sup>12–14</sup> and is lower than rates reported in Brazilian studies including younger women<sup>16–18</sup>, underscoring the influence of age and population characteristics on HPV epidemiology.

The hr-HPV age curve exhibited a bimodal pattern, with an early peak in younger women and a second smaller peak around age 55. Although not universal, this late peak has been documented in other populations and is attributed to new sexual exposure or reactivation of latent infections, potentially triggered by perimenopausal hormonal changes and immune senescence. Observing this pattern in a non-vaccinated, publicly screened population has direct policy implications, suggesting that older women remain at significant risk and should



**Fig. 1.** Five-year age group-specific prevalence of hr-HPV by woman (blue full line) among 20,398 screened between 25–64 years showing progressive declines with age ( $p < 0.0009$ ; linear trend test). At the age group 55–59 years the hr-HPV prevalence was 8.6% (11.2% considering the ages 55–56 years). Dotted lines represent prevalences of HPV16, HPV18 or the pooled 12 other hr-HPV genotypes (12OT: types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68), considering coinfections. All curves exhibited a five-year significant decreasing trend: all hr-HPV = 2.05% ( $p = 0.0009$ ); HPV16 = 0.54% ( $p = 0.002$ ); HPV18 = 0.19 ( $p = 0.001$ ).

be included in prevention strategies, particularly in settings with historically inconsistent or opportunistic screening.

The distribution of HSIL and cervical cancer showed distinct peaks. Cervical cancer peaked at 45–46 years, whereas HSIL showed a later second peak at age 61, approximately six years after the second infection peak (ages 55–56). These temporal gaps are consistent with the natural history of cervical carcinogenesis, which typically spans 10–15 years from infection to cancer<sup>5,6</sup>. According to this pattern, the sequential infection and lesion peaks observed in this study suggest that cervical cancer could occur after the age 64, beyond the current upper limit of screening. However, the low occurrence of cancer after age 55 in this population reflects the impact of prior screening and early detection resulting from the HPV DNA-based program, which has increased HSIL detection fourfold since its implementation in 2017<sup>24,25</sup>.

Previous regional data showed that 22.6% of cervical cancers in Brazil occurred in women over 65 years<sup>19,26</sup>, similar to U.S. reports (around 20%) which have prompted discussion about extending screening beyond age 65<sup>28</sup>. Strategies such as a one-time hr-HPV “exit test” beyond standard screening age should be considered, especially for women with limited prior screening. Ongoing studies in other countries are also exploring hr-HPV testing using self-collected or urine samples for women above the target screening age<sup>27–31</sup>.

These present findings complement previous evaluations of the PREVENTIVO program<sup>22</sup> and provide evidence to inform public health policy during Brazil’s transition to primary hr-HPV-based screening. Establishing baseline age-specific patterns in a non-vaccinated population will enable future assessment of vaccination impact as immunized cohorts enter screening age.

Study limitations include the lack of individual vaccination and behavioral data and the inability to distinguish between new infections and reactivations. Nevertheless, high population coverage and standardized diagnostic procedures strengthen the reliability of these findings.

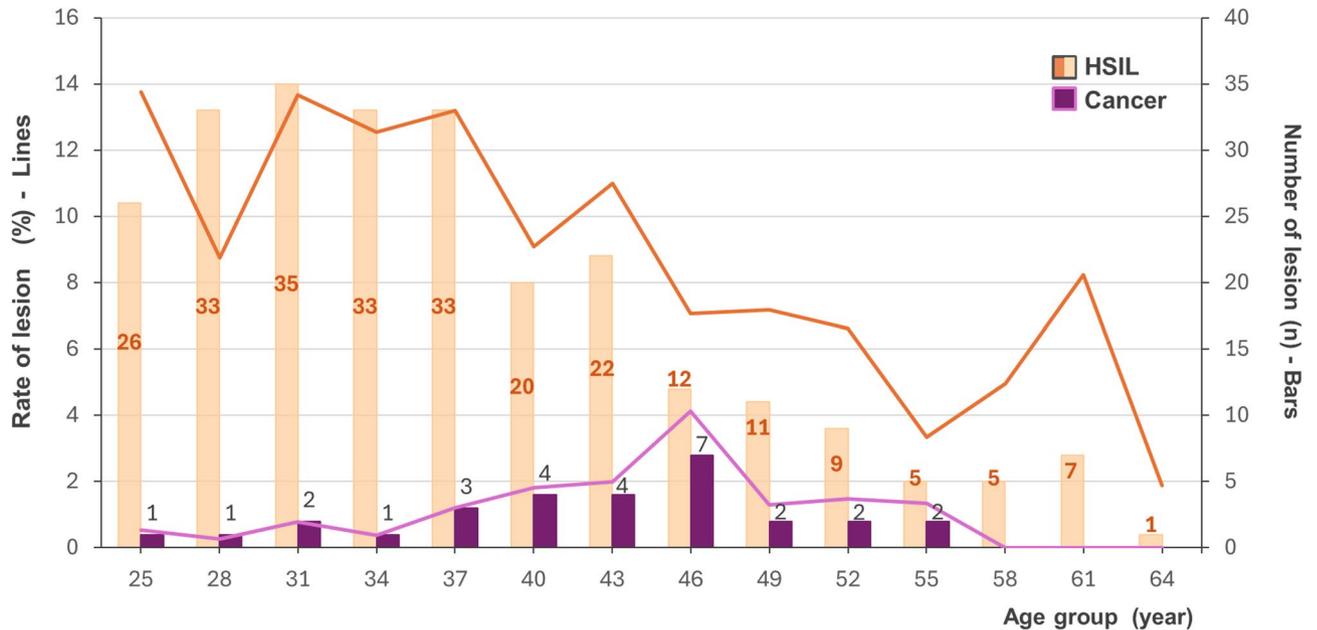
In summary, the age-specific distribution of hr-HPV infection and HSIL in an unvaccinated adult female population showed a bimodal pattern, with early peaks in younger ages and a smaller second infection peak at ages 55–56, followed by a late HSIL peak at age 61. These findings support maintaining screening strategies into older ages in new HPV DNA testing programs, including consideration of an hr-HPV “exit test” beyond the current upper age limit, and provide essential baseline parameters for monitoring future vaccination impact in Brazil.

		Population screened by age group and prevalence of high-risk HPV detection															
		25-29y		30-34y		35-39y		40-44y		45-49y		50-54y		55-59y		60-64y	
HPV detected	Total (N = 20398)	n	Prev (%)	n	Prev (%)	n	Prev (%)	n	Prev (%)	n	Prev (%)	n	Prev (%)	n	Prev (%)	n	Prev (%)
		HPV16 only	309 (1.35-1.68)	88 (3.11)	(2.47-3.75)	51 (2.0)	(1.46-2.54)	49 (1.67)	(1.21-2.13)	45 (1.59)	(1.13-2.06)	28 (1.01)	(0.64-1.39)	18 (0.70)	(0.38-1.03)	13 (0.57)	(0.26-0.88)
HPV18 only	96 (0.38-0.56)	24 (0.85)	(0.51-1.18)	16 (0.63)	(1.46-2.54)	19 (0.65)	(1.21-2.13)	11 (0.39)	(0.16-0.62)	7 (0.25)	(0.07-0.44)	11 (0.43)	(0.18-0.68)	5 (0.22)	(0.03-0.41)	3 (0.18)	(0.0-0.39)
12OT only	1897 (8.90-9.70)	466 (16.45)	(15.08-17.81)	298 (11.68)	(10.43-12.92)	296 (11.17)	(8.99-11.17)	231 (8.19)	(7.17-9.20)	197 (7.14)	(6.17-8.10)	173 (6.75)	(5.78-7.72)	156 (6.87)	(5.83-7.91)	80 (4.83)	(3.79-5.86)
HPV16 & 18	12 (0.06)	6 (0.21)	(0.04-0.38)	1 (0.04)	(0.0-0.12)	1 (0.03)	(0.0-0.10)	1 (0.04)	(0.0-0.10)	0 (0.00)	(0.0-0.19)	2 (0.08)	(0.0-0.13)	1 (0.04)	(0.0-0.13)	0 (0.00)	(0.0-0.0)
HPV16 & 12OT	191 (0.94)	56 (1.98)	(1.46-2.49)	36 (1.41)	(0.95-1.87)	23 (0.78)	(0.46-1.10)	23 (0.82)	(0.48-1.15)	23 (0.83)	(0.49-1.17)	9 (0.35)	(0.12-0.58)	15 (0.66)	(0.33-0.99)	6 (0.36)	(0.07-0.65)
HPV18 & 12OT	77 (0.38)	16 (0.56)	(0.29-0.84)	18 (0.71)	(0.38-1.03)	8 (0.27)	(0.08-0.46)	9 (0.32)	(0.11-0.53)	11 (0.40)	(0.16-0.63)	7 (0.27)	(0.07-0.48)	4 (0.18)	(0.01-0.35)	4 (0.24)	(0.01-0.48)
HPV16 & 18 & 12OT	21 (0.10)	6 (0.21)	(0.04-0.38)	3 (0.12)	(0.0-0.25)	5 (0.17)	(0.02-0.32)	4 (0.14)	(0.0-0.28)	2 (0.07)	(0.0-0.17)	0 (0.00)	(0.0-0.0)	1 (0.04)	(0.0-0.13)	0 (0.00)	(0.0-0.0)
Total#	2603 (12.30-13.22)	662 (23.37)	(21.81-24.93)	423 (16.58)	(15.13-18.02)	401 (13.65)	(12.41-14.90)	324 (11.48)	(10.30-12.66)	268 (9.71)	(8.60-10.81)	220 (8.58)	(7.50-9.67)	195 (8.58)	(7.43-9.73)	110 (6.63)	(5.44-7.83)
HPV16 any*	536 (2.63)	156 (5.51)	(4.67-6.35)	91 (3.57)	(2.85-4.29)	78 (2.66)	(2.07-3.24)	73 (2.59)	(2.07-3.24)	53 (1.92)	(1.13)	29 (1.13)	30 (1.32)	30 (1.32)	23 (1.39)	(-)	(-)
HPV18 any*	206 (1.01)	52 (1.84)	(1.31-2.33)	38 (1.49)	(1.02-1.96)	33 (1.12)	(0.74-1.50)	25 (0.89)	(0.54-1.23)	20 (0.72)	(0.41-1.04)	20 (0.78)	11 (0.48)	11 (0.48)	7 (0.42)	7 (0.42)	7 (0.42)
12OT any*	2186 (10.72)	544 (19.20)	(17.75-20.65)	355 (13.91)	(12.57-15.25)	332 (11.30)	(10.16-12.45)	267 (9.46)	(8.38-10.54)	233 (8.44)	(7.40-9.48)	189 (7.37)	176 (7.75)	176 (7.75)	90 (5.43)	90 (5.43)	90 (5.43)
(95% CI)	(10.29-11.14)	(17.75-20.65)	(12.57-15.25)	(12.57-15.25)	(10.16-12.45)	(10.16-12.45)	(8.38-10.54)	(8.38-10.54)	(6.36-8.39)	(6.65-8.85)	(4.34-6.52)	(6.65-8.85)	(4.34-6.52)	(6.65-8.85)	(4.34-6.52)	(4.34-6.52)	(4.34-6.52)

**Table 1.** Single and multiple high-risk HPV type detections in screening stratified by age group in 20,398 women. #Linear trend test coefficient for any high-risk HPV detection: -0.41% per year of age ( $p = 0.0009$ ). \*Any detection: Includes coinfection; each HPV genotype was counted separately. Note: The HPV DNA test genotypes HPV16 and HPV18 individually and detect a pooled group of 12 other high-risk HPV genotypes (12OT: types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). Prev: Prevalence, expressed as the proportion of women with a positive HPV test within each age group.

Lesion detected	Population screened by age group and prevalence of high-risk HPV detection								
	Total	25-29y	30-34y	35-39y	40-44y	45-49y	50-54y	55-59y	60-64y
	(N=20398)	(n=2833)	(n=2552)	(n=2937)	(n=2822)	(n=2761)	(n=2563)	(n=2272)	(n=1658)
	(HPV += 2603)	(HPV += 662)	(HPV += 423)	(HPV += 401)	(HPV += 324)	(HPV += 268)	(HPV += 220)	(HPV += 195)	(HPV += 110)
CIN2 (n)	154	36	31	26	21	18	8	8	6
Prevalence (%)	0.75	1.27	1.21	0.89	0.74	0.65	0.31	0.35	0.36
(95% CI)	(0.63-0.87)	(0.86-1.68)	(0.79-1.63)	(0.55-1.23)	(0.42-1.06)	(0.35-0.95)	(0.09-0.53)	(0.11-0.59)	(0.07-0.65)
Rate on HPV+ (%)	5.92	5.44	7.33	6.48	6.48	6.72	3.64	4.10	5.45
CIN3* (n)	141	35	37	29	18	7	6	7	2
Prevalence (%)	0.69	1.24	1.45	0.99	0.64	0.25	0.23	0.31	0.12
(95% CI)	(0.58-0.80)	(0.83-1.65)	(0.99-1.91)	(0.63-1.35)	(0.35-0.93)	(0.06-0.44)	(0.04-0.42)	(0.08-0.54)	(0.0-0.29)
Rate on HPV+ (%)	5.42	5.29	8.75	7.23	5.56	2.61	2.73	3.59	1.82
Cancer (n)	29	2	3	5	8	7	3	1	0
Prevalence (%)	0.14	0.07	0.12	0.17	0.28	0.25	0.12	0.04	0.00
(95% CI)	(0.09-0.19)	(0.0-0.17)	(0.0-0.25)	(0.02-0.32)	(0.09-0.47)	(0.06-0.44)	(0.0-0.25)	(0.0-0.12)	-
Rate on HPV+ (%)	1.11	0.30	0.71	1.25	2.47	2.61	1.36	0.51	0.00
CIN2 or worse (n)	324	73	71	60	47	32	17	16	8
Prevalence (%)	1.59	2.58	2.78	2.04	1.67	1.16	0.66	0.70	0.48
(95% CI)	(1.42-1.76)	(2.00-3.16)	(2.14-3.42)	(-)	(-)	(-)	(-)	(-)	(-)
Rate on HPV+ (%)	12.45	11.03	16.78	14.96	14.51	11.94	7.73	8.21	7.27

**Table 2.** – Prevalence of precancerous lesions and cervical cancer by age group in 20,398 women screened by HPV DNA test and the lesions rate among high-risk HPV positive test. \*CIN3 included 4 adenocarcinomas in situ (AIS: ages 27, 29, 35 and 42). Linear trend test coefficient: decreasing % per year of age (and p-value): CIN2 = 0.07% ( $p < 0.0001$ ); CIN3 = 0.04% ( $p = 0.0002$ ); Cancer = 0.002% ( $p = 0.46$ ). Notes: Prevalence: Expressed as the proportion of women with a positive high-risk HPV DNA test (HPV+) within each age group; Rate among HPV+: Number of lesions detected by age group over HPV+; CIN: Cervical intraepithelial neoplasia; 95% CI: 95% confidence interval.



**Fig. 2.** HSIL (orange) and cervical cancer (purple) distribution by 3-year age group among 2603 women testing HPV DNA positive. Lines are rates of lesions and bars are number of cases. HSIL showed the highest rates (~13%) between 30 and 38 years of age, then progressively decreased until reaching a second, lower and late peak (8.2%) at age 61. Cervical cancer rate peaked around age 45–46 and was truncated after age 55 due to high proportion of the HSIL treatment performed in the screening program.

## Methods

We conducted a population-based observational study using data from the first screening round (October, 2017 to September, 2022) of the PREVENTIVO program, implemented in Indaiatuba, Sao Paulo, Brazil, for women aged 25–64 years attending the public healthcare system. The program is managed through a centralized informatics platform, and each woman can be screened only once per screening round. Cervical samples were collected by clinicians using a Cervex-Brush (Rovers Medical Devices, BV, Lekstraat, the Netherlands) and preserved in PreservCyt solution (Hologic Inc., Marlborough, MA, US). High-risk HPV DNA testing was performed using the Cobas assay (Roche Molecular Systems, Pleasanton, CA, USA), which individually detects HPV16 and HPV18 and provides a pooled result for the 12 other hr-HPV genotypes (types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68), “12OT”. Screening is conducted at five-year intervals. Women testing positive for HPV16 and/or HPV18 were referred for colposcopy and biopsy when indicated. Those positive only for 12OT underwent reflex cytology from the same sample, and any cytological abnormality prompted colposcopy; if cytology was negative, repeat hr-HPV testing after 12 months was recommended. Histological diagnoses were confirmed with p16(INK4a) immunohistochemistry (Ventana Medical Systems Inc., Tucson, AZ, USA) and classified according to the Lower Anogenital Squamous Terminology (LAST)<sup>32</sup>. The final diagnosis was considered the highest-grade lesion identified across all histological assessments, including biopsies and excisional procedures.

For this study, we used an anonymized program database that included hr-HPV test results, histopathological diagnoses of HSIL (cervical intraepithelial neoplasia [CIN] grade 2 or 3, and adenocarcinoma in situ), cervical carcinoma, and age, grouped in two to five-year intervals. Prevalence rates with 95% confidence intervals (CI) were calculated for hr-HPV detection and lesions diagnoses for each five-year age group. Linear regression was used to assess trends in hr-HPV prevalence, HSIL, and cervical cancer across age groups, and angular coefficients (slope) were obtained. Curves were generated to illustrate prevalences and lesion rates. The rates of CIN2, CIN3 and cancer among hr-HPV-positive women were also calculate for each five-year group. Statistical analyses were performed using StatsDirect version 3.3 (England, [www.statsdirect.com](http://www.statsdirect.com)), with significance set at  $p < 0.05$ .

## Data availability

The dataset from this study will be safely stored following the principles of research ethics. Upon completion of the study, data may be made available by the corresponding author ([juliotex@unicamp.br](mailto:juliotex@unicamp.br)) upon request with justification.

Received: 17 August 2025; Accepted: 29 December 2025

Published online: 07 January 2026

## References

1. Tewari, K. S. Cervical cancer *NEJM* **392**, 56–71 (2025).
2. Wu, J. et al. Global burden of cervical cancer: current estimates, Temporal trend and future projections based on the GLOBOCAN 2022. *J. Natl. Cancer Cent.* **5**, 322–329 (2025).
3. Ferlay, J. et al. *Global Cancer Observatory: Cancer Today* (International Agency for Research on Cancer, 2024). <https://gco.iarc.who.int/today>
4. National Cancer Institute. Cancer incidence in Brazil. Estimate (2023). <https://www.inca.gov.br/sites/ufu.sti.inca.local/files/mediadocument/estimativa-2023.pdf> (2023).
5. Schiffman, M. & Wentzensen, N. Human papillomavirus infection and the multistage carcinogenesis of cervical cancer. *Cancer Epidemiol. Biomarkers Prev.* **22**, 553–560 (2013).
6. Gilham, C., Sargent, A., Crosbie, E. J. & Peto, J. Long-term risks of invasive cervical cancer following HPV infection: follow-up of two screening cohorts in Manchester. *Br. J. Cancer.* **128**, 1933–1940 (2023).
7. World Health Organization. Human papillomavirus vaccines: WHO position paper. *Weekly Epidemiological Record* **50**, 645–672. December (2022). <https://iris.who.int/bitstream/handle/10665/365350/WER9750-eng-fre.pdf?sequence=1> (2022).
8. World Health Organization editor. *WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention* (World Health Organization, 2013).
9. Clifford, G. M. et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the international agency for research on cancer HPV prevalence surveys: a pooled analysis. *Lancet* **366**, 991–998 (2005).
10. Kyrgiou, M. et al. Cervical screening: ESGO-EFC position paper of the European society of gynaecologic oncology (ESGO) and the European federation of colposcopy (EFC). *Br. J. Cancer.* **123**, 510–517 (2020).
11. Carvalho, C. F. et al. Cervical cancer screening with HPV testing: updates on the recommendation. *Rev. Bras. Ginecol. Obstet.* **44**, 264–271 (2022).
12. Bruni, L. et al. Cervical human papillomavirus prevalence in 5 continents: Meta-Analysis of 1 million women with normal cytological findings. *J. Infect. Dis.* **202**, 1789–1799 (2010).
13. Checchi, M. et al. The impact of over ten years of HPV vaccination in England: surveillance of type-specific HPV in young sexually active females. *Vaccine* **41**, 6734–6744 (2023).
14. Machalek, D. A. et al. Very low prevalence of vaccine human papillomavirus types among 18- to 35-year old Australian women 9 years following implementation of vaccination. *J. Infect. Dis.* **217**, 1590–1600 (2018).
15. Gravitt, P. E. et al. A cohort effect of the sexual revolution May be masking an increase in human papillomavirus detection at menopause in the United States. *J. Infect. Dis.* **207**, 272–280 (2013).
16. Roteli-Martins, C. M. et al. Prevalence of human papillomavirus infection and associated risk factors in young women in Brazil, Canada, and the United States: a multicenter cross-sectional study. *Int. J. Gynecol. Pathol.* **30**, 173–184 (2011).
17. Colpani, V. et al. Prevalence of human papillomavirus (HPV) in Brazil: A systematic review and meta-analysis. *Plos One.* **15**, e0229154. <https://doi.org/10.1371/journal.pone.0229154> (2020).
18. Wendland, E. M. et al. Prevalence of HPV infection among sexually active adolescents and young adults in Brazil: the POP-Brazil study. *Sci. Rep.* **10** <https://doi.org/10.1038/s41598-020-61582-2> (2020).
19. Teixeira, J. C., Maestri, C. A., Machado, H. D. C., Zeferino, L. C. & Carvalho, N. S. Cervical cancer registered in two developed regions from Brazil: upper limit of reachable results from opportunistic screening. *Rev. Bras. Ginecol. Obstet.* **40**, 347–353 (2018).
20. Teixeira, J. C. et al. Cervical cancer screening program based on primary DNA-HPV testing in a Brazilian city: a cost-effectiveness study protocol. *BMC Public Health.* **20**, 576. <https://doi.org/10.1186/s12889-020-08688-4> (2020).
21. Vale, D. B. et al. Is the HPV-test more cost-effective than cytology in cervical cancer screening? An economic analysis from a middle-income country. *PLoS One.* **16**, e0251688. <https://doi.org/10.1371/journal.pone.0251688> (2021).

22. Teixeira, J. C. et al. Transition from opportunistic cytological to organized screening program with DNA-HPV testing detected prevalent cervical cancers 10 years in advance. *Sci. Rep.* **14**, 20761. <https://doi.org/10.1038/s41598-024-71735-2> (2024).
23. Minister of Health. Brazil. Cervical Cancer Screening (Brazilian Guideline). (2025). Available at <https://www.gov.br/saude/pt-br/a-suntos/pcdt/r/rastreamento-cancer-do-colo-do-utero/view>
24. Smith, J. S., Melendy, A., Rana, R. K. & Pimenta, J. M. Age-specific prevalence of infection with human papillomavirus in females: a global review. *J. Adolesc. Health.* **43**, 1–41. <https://doi.org/10.1016/j.jadohealth.2008.07.009> (2008). (4 Suppl), S5–25, S25.e.
25. Ke, Q. et al. Multicenter study on the distribution and prevalence of human papillomavirus types in Hangzhou, Zhejiang from 2017 to 2023. *Sci. Rep.* **15**, 9374. <https://doi.org/10.1038/s41598-025-92102-9> (2025).
26. Teixeira, J. C., Maestri, C. A., Machado, H. D. C., Zeferino, L. C. & Carvalho, N. S. Incidence rates and Temporal trends of cervical cancer relating to opportunistic screening in two developed metropolitan regions of Brazil: a population-based cohort study. *Sao Paulo Med. J.* **137**, 322–328 (2019).
27. Dilley, S., Huh, W., Blechter, B. & Rositch, A. F. It's time to re-evaluate cervical cancer screening after age 65. *Gynecol. Oncol.* **162**, 200–202 (2021).
28. Tranberg, M. et al. Value of a catch-up HPV test in women aged 65 and above: A Danish population-based nonrandomized intervention study. *PLoS Med.* **20**, e1004253. <https://doi.org/10.1371/journal.pmed.1004253> (2023).
29. Davies, J. C. et al. Urine high-risk human papillomavirus testing as an alternative to routine cervical screening: A comparative diagnostic accuracy study of two urine collection devices using a randomised study design trial. *BJOG* **131**, 1456–1464 (2024).
30. Tranberg, M. et al. High-risk human papillomavirus testing in first-void urine as a novel and non-invasive cervical cancer screening modality—a Danish diagnostic test accuracy study. *BMC Med.* **23**, 327. <https://doi.org/10.1186/s12916-025-04149-0> (2025).
31. Gilham, C., Crosbie, E., Nedjai, B., Macleod, U. & Davies-Oliveira, J. Catch-up screen: offering an at-home urine HPV test to women aged > 65 in the UK. EUROGIN 2024, Stockholm, Sweden, March 13–16, Abstract 6957, page 9. (2004). [https://www.eurogin.com/content/dam/markets/aest/eurogin/pdfs/2024/EUROGIN2024\\_Abstracts\\_FC.pdf](https://www.eurogin.com/content/dam/markets/aest/eurogin/pdfs/2024/EUROGIN2024_Abstracts_FC.pdf)
32. Darragh, T. M. et al. The lower anogenital squamous terminology (LAST) standardization project for HPV-Associated lesions: background and consensus recommendations from the college of American pathologists and the American society for colposcopy and cervical pathology. *Arch. Pathol. Lab. Med.* **136**, 1266–1297 (2012).

## Acknowledgements

The authors gratefully acknowledge the São Paulo Research Foundation (FAPESP) for the scientific initiation scholarship awarded to L. Vasconcelos (Grant #2023/07383-4), and to H.C.L. Lima (Grant #2022/16607-0), and the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES) for the master's scholarship awarded to Rafaella M. Rego (Grant #88887.951200/2024-00).

## Author contributions

J.T., D.V., C.C., and L.Z. developed the research protocol. J.T., C.C., R.R., E.C., L.V. H.L., and M.D. working to collect the data. J.T., D.V., R.R., M.D., and L.Z. coordinated the analysis and the development of this manuscript. All authors reviewed the manuscript.

## Funding

This project was funded by the University of Campinas (Women's Hospital), Indaiatuba City (SUS), and Roche Diagnostics, as detailed below: The study (screening program implementation and cost-effectiveness analysis) was designed by researchers from the University of Campinas and introduced by the Indaiatuba City Hall. Both the University of Campinas and the municipality used the existing and functioning structure to implement the new screening program and carry out the study at no additional cost. The supplies and equipment required to perform HPV testing were provided and/or supported by Roche Diagnostics. No compensation or cash transfers were provided to any institution or researchers named in the cooperation agreement between the parties. The authors executed all of the research, including manuscript writing and the decision to publish.

## Declarations

## Competing interests

The authors declare no competing interests.

## Ethical approval

This study is part of a larger research project that developed and implemented the PREVENTIVO program. The Research Ethics Committee of the University of Campinas approved this study (number 1045580; dated May 1, 2015). The Committee waived the need for informed consent. All study procedures were carried out in accordance with the approved research protocol and followed the regulatory standards of the National Health Council of Brazil. In 2017, the mayor of Indaiatuba sanctioned a law instituting the DNA-HPV test as the standard for screening, replacing conventional cytology in all public health systems. The research group had no contact with participants and accessed electronic database to generate a secondary spreadsheet for statistical analyses, without identifying subjects.

## Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-34501-6>.

**Correspondence** and requests for materials should be addressed to J.C.T.

**Reprints and permissions information** is available at [www.nature.com/reprints](http://www.nature.com/reprints).

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

**Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, 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 you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. 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-nc-nd/4.0/>.

© The Author(s) 2026