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Original research

# Implementation of second round of HPV-based screening for cervical cancer in programmatic contexts in Argentina

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**ABSTRACT**

**Objectives.** To evaluate implementation of the second round of human papillomavirus (HPV)-based cervical screening, introduced in Argentina in 2012–2014 through the Jujuy Demonstration Project for women 30 years and older, and describe the characteristics of women who adhere to the recommended five-year rescreening interval.

**Methods.** A retrospective cohort study was conducted based on the data of two rounds of screening. All women aged 30 years or older who had been HPV-tested during the Jujuy Demonstration Project and had a negative result were included. The Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework was used to evaluate implementation. Multivariable regression was used to examine factors associated with adherence to rescreening.

**Results.** Of 42 307 HPV-negative women, 47.9% (*n* = 20 285) were rescreened in the second round (Reach); 69.2% of health centers provided at least one HPV test at second-round screening (Adoption); and 13.3% (*n* = 5 639) of women were rescreened within the recommended five-year interval. Among the total rescreened, 9.3% (*n* = 1 888) were HPV-positive, of which 95.0% underwent triage Pap and 79.2% of the HPV-positive/abnormal Pap women had colposcopy. Considering women rescreened at five years, the second-round detection rate was 5.3/1 000 screened women. Rescreening at five years was significantly higher among women aged 30–44, with public health insurance, and those living in the provincial capital.

**Conclusions.** Rescreening of HPV-negative women faced challenges linked to its reduced reach, especially if we consider the recommended five-year interval. Our findings suggest that we need to devise specific strategies to increase second-round screening rates.

**Keywords** Uterine cervical neoplasms; human papillomavirus DNA tests; mass screening; implementation science; Argentina.

Cervical cancer screening has shown to reduce the incidence and mortality of cervical cancer (1). However, cervical cancer remains one of the leading causes of cancer death among women from low- and middle-income countries (2).

Nearly all cervical cancers result from a persistent infection by human papillomavirus (HPV) (3). Screening tools based on HPV detection have been developed. There is currently extensive scientific evidence on the effectiveness of the HPV test as a

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detection method of high-grade lesions and cancer (4, 5). HPV testing is more sensitive than cytology for detecting high grade cervical intraepithelial neoplasia (CIN2+) (5, 6), and the World Health Organization (WHO) recommends it as a primary cervical screening method as part of the global strategy to accelerate the elimination of cervical cancer (7).

The HPV test has a high negative predictive value (6), and a negative test provides assurance against the presence of precancerous lesions at least for 5–10 years (1, 5, 8). Therefore, a second round of testing every 5–10 years for HPV-negative women is recommended by WHO as part of a screening program (8, 9). Studies have shown that rescreening of HPV-negative women effectively reduces the risk of cervical intraepithelial neoplasia (CIN) grade 2 or greater (CIN2+) lesions (10) and CIN3+ lesions (6, 11). Thus, rescreening of HPV-negative women is an essential component of an HPV test-based screening program. However, despite the importance of the second round of HPV testing, data about its implementation in low- and middle-income countries are scarce.

Argentina was one of the first countries to implement HPV testing as part of its national cervical cancer screening program, introduced through the Jujuy Demonstration Project (JDP), a four-year population-based study conducted during 2011–2014 (12). The JDP results showed that HPV testing implemented in real-world contexts of middle-income settings increases the detection of CIN2+ lesions and allows for improving programmatic indicators (e.g., lower overscreening, higher adherence to age recommendations). Based on this evidence, the Ministry of Health approved the HPV test as a primary screening test for its nationwide implementation. Argentinean guidelines recommend that HPV-negative women should undergo a second round of screening (or rescreening) at five years (13). In this study, we aimed to evaluate the implementation of the second round of screening after five years among women who tested HPV-negative in the JDP, and describe the characteristics of women who adhered to the recommended five-year rescreening interval.

## METHODS

### Setting

The province of Jujuy was the first in Argentina to implement the HPV test as the primary screening method for cervical cancer prevention (12). The JDP was implemented by the National Program on Cervical Cancer Prevention between 2012 and 2014 to evaluate the introduction of HPV testing (14). Thus, from 1 January 2012, all public health institutions in Jujuy changed the primary screening method from cytology-based screening to HPV testing.

The Jujuy setting has been extensively described elsewhere (14). Briefly, Jujuy province is located in northwest Argentina and has around 798 000 inhabitants; 85% of the population live in urban areas, and 32% of the households are poor (15, 16). Its public health system has more than 280 primary health care centers where HPV testing is offered, one HPV laboratory where samples are processed, two cytology laboratories, nine diagnostic services, and five treatment services. Screening, diagnosis, and treatment are available free of charge for the population that does not have social security or private health insurance. Self-collection was introduced as a programmatic strategy in 2014 (17). The Jujuy primary health care system employs more than 700 full-time community health workers, who visit around 110 000 households (70% of total provincial households) twice a year for health-related tasks including offering of HPV self-collection (14).

### Study design and participants

We conducted a retrospective cohort study based on the analysis of data corresponding to two rounds of HPV testing in the province of Jujuy. We included all women aged 30 years or older who had been HPV-tested at public health centers during the JPD and had a negative result.

### JDP procedures

HPV testing (Hybrid Capture 2; Germantown, MD, USA) was introduced for primary screening of women aged 30 years and older, irrespective of the previous screening history (14). Women who were HPV-positive were triaged with cytology. Individuals whose samples were classified as Atypical Squamous Cells of Undetermined Significance or worse (ASC-US+) were referred to colposcopy and biopsy if needed. Women with histologically confirmed CIN2+ lesions were referred for excisional treatment. HPV testing and cytology triage were collected simultaneously, but cytology was only read if the woman was HPV-positive. Women who were HPV-positive but had normal cytology were recommended rescreening in 18 months. Women younger than 30 years continued to undergo cytology-based screening. Women who were HPV-positive and used self-collection tests had to attend health centers for cytology triage (17).

Regarding HPV-negative women, the rescreening interval was initially established at three years (14). In 2014, upon review of the national screening guidelines, the rescreening interval was changed to five years (13).

### Data sources

Since 2010, screening, diagnosis, or treatment at Jujuy's public health services have been registered in the National Screening Information System (SITAM, by its Spanish acronym). For this analysis, we extracted data from SITAM of all women screened in the JDP (2012–2014) who had negative HPV results. HPV testing, colposcopies, biopsies, and treatments not registered in SITAM were considered lost to follow-up, including those done in private services without confirmation by the provincial program. The database was de-identified to protect the identity of participants. The Research Ethics Committee of the Ministry of Health of Jujuy approved the study.

### Outcomes

We compared key programmatic indicators using the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework, which allows the evaluation of fundamental dimensions to an intervention's success and scaling up (18, 19).

*Reach* is defined as the proportion of the population that receives the intervention or is affected by a policy or program (18). In this study, we defined reach as the proportion of total rescreening in the target population. For that, we included women with a second HPV test at least 975 days (3 years minus 120 days) after the initial negative test. A second HPV

test performed before 975 days after the initial screening was considered overscreening (more than one screening in the recommended screening interval). The follow-up period finished on 31 December 2021.

In assessing *Effectiveness*, we follow the definition of Rabin and Brownson (20), which is the effect of an intervention that shows its efficacy when implemented in a real-life context. Our effectiveness outcome was the detection rate of CIN2+ lesions, calculated as the proportion of women rescreened at five years with histologically confirmed CIN2+ lesions out of total women rescreened at five years, in line with national screening guidelines. We compared them with the CIN2+ detection rates of the first round of screening (12).

*Adoption* is defined as the intention to employ an evidence-based innovation or practice (19). In this sense, measuring adoption over the long term is an essential indicator for scaling up the strategy throughout the country. We calculated the percentage of health centers that screened at least one HPV-negative woman in the second round out of the total number of health centers in the province.

*Implementation* refers to whether the intervention was implemented as planned (18). In this case, we measured four outcomes: Adherence to the rescreening recommendation seeks to evaluate adherence to the recommended rescreening five-year interval. It was calculated as the proportion of women 30+ who had an HPV test between 1 705 and 1 945 days (i.e., 5 years +/− 120 days) after the initial negative test out of the total HPV-negative women first screened in 2012–2014. In addition, we analyzed the association of women's sociodemographic characteristics with their adherence to the recommended five-year screening interval. For the completion of follow-up we calculated: (1) adherence to triage: proportion of all rescreened HPV-positive women who had a triage procedure (Pap or colposcopy) registered in SITAM; (2) adherence to diagnosis: proportion of all rescreened HPV-positive/Pap ASC-US+ women who had a colposcopy; and (3) adherence to treatment: proportion of rescreened women with CIN2+ lesions who had treatment. Proportions were calculated for each screening modality.

*Maintenance* is the extent to which an intervention or policy becomes part of the usual practices of an organization or service (19). It focuses on the sustainability of the strategy over time. It relates to both the maintenance of individual-level effects of an intervention (i.e., adherence to rescreening) and the maintenance of the intervention at the setting-level (i.e., long-term implementation). In our study, the maintenance of the strategy was measured as the proportion of HPV-negative women screened (after the end of the JDP [2015–2017]) who adhered to the five-year rescreening recommendation (13).

## Analysis

For the description of *Reach, Adoption, Implementation,* and *Maintenance*, we report percentages with their corresponding 95% confidence intervals (CI). For the evaluation of *Effectiveness*, second-round CIN2+ detection rates were calculated. The rates obtained in the second round were compared with the rates of the first round of screening (12), using Fisher's exact test as a test of statistical significance.

We also compared sociodemographic characteristics of women who adhered to the five-year rescreening recommendation with those who did not. This analysis included age at screening, health insurance (public/social security), and place of

**TABLE 1. Characteristics of the women included in the study, Jujuy province, Argentina**

| | Total of women screened in 2012–2014 | | Women rescreened | | Women without rescreen test | |
|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % |
| **Total** | 42 307 | 100 | 20 285 | 100 | 22 022 | 100 |
| **Age** | | | | | | |
| 30–44 | 23 762 | 56.2 | 12 671 | 62.5 | 11 091 | 50.4 |
| 45–64 | 16 569 | 39.2 | 7 396 | 36.5 | 9 173 | 41.7 |
| 65 and over | 1 976 | 4.7 | 218 | 1.1 | 1 758 | 8.0 |
| **Health Insurance** | | | | | | |
| Public | 23 107 | 55.4 | 11 908 | 59.6 | 11 199 | 51.5 |
| Social security | 18 632 | 44.6 | 8 071 | 40.4 | 10 561 | 48.5 |
| Missing data | 568 | | 306 | | 262 | |
| **Residence** | | | | | | |
| San Salvador de Jujuy | 14 400 | 35.0 | 7 966 | 39.8 | 6 434 | 30.5 |
| Other | 26 714 | 65.0 | 12 057 | 60.2 | 14 657 | 69.5 |
| Missing data | 1 193 | | 262 | | 931 | |
| **Year of first HPV test** | | | | | | |
| 2012 | 19 382 | 45.8 | 11 856 | 58.4 | 7 526 | 34.2 |
| 2013 | 12 039 | 28.5 | 5 633 | 27.8 | 6 406 | 29.1 |
| 2014 | 10 886 | 25.7 | 2 796 | 13.8 | 8 090 | 36.7 |
| **Sample method of first HPV test** | | | | | | |
| Self-collected | 4 205 | 9.9 | 869 | 4.3 | 3 336 | 15.1 |
| Clinician-collected | 38 102 | 90.1 | 19 416 | 95.7 | 18 686 | 84.9 |

***Source:*** Prepared by the authors based on the study data.

residence at the time of screening. The association between each variable and adherence to the recommended screening interval was evaluated using the Chi-squared test. Subsequently, a multivariate analysis was performed using logistic regression. Odds ratios (OR) and 95% CI were calculated. R statistical software (version 4.0.2) was used for data analysis.

## RESULTS

The study population included 42 307 women screened in 2012–2014 during the JPD with a negative HPV test result; 45.8%, 28.5%, and 25.7% were screened in 2012, 2013, and 2014, respectively; 56.2% of the women were 30–44 years old, 55.4% attended the public health system, and 35% lived in San Salvador de Jujuy, the province's capital city (Table 1).

### RE-AIM programmatic indicators

Key programmatic indicators assessed using the RE-AIM framework are shown in Table 2.

*Reach:* 47.9% ($n$ = 20 285) of women with a negative HPV result in 2012–2014 with a registered rescreening between 2015 and 2021 (95% CI [47.5, 48.4]).

*Effectiveness*: Among women who were rescreened at five years ($n$ = 5 639), 30 CIN2+ lesions were diagnosed, with a detection rate of 5.3 CIN2+ lesions/1 000 rescreened women (no cancer diagnosed). This detection rate is 57% lower than that obtained in the first round (12.3 CIN2+ lesions/1 000 screened women) (12), and this difference is statistically significant ($p$ = 0.0001).

*Adoption*: 69.2% of the health centers in the province performed at least one rescreening test at five years. This percentage rises to 86.1% when the rescreening interval is broadened to three years or more after the initial round of screening (Table 2).

*Implementation:* We observed that 13.3% of the women with a negative result in 2012–2014 underwent rescreening at five years (95% CI [13.0, 13.7]). Out of the total number of women rescreened in the second round, 1 888 (9.3%) had a positive HPV result: 1 349 with a clinician-collected sample and 539 with a self-collected sample (Figure 1).

Among women with a clinician-collected sample, 1 341 had a record of a triage method, and among them, 94.7% ($n$ = 1 270/1 341) obtained a triage Pap result, of which 31.3% (397/1 270) registered ASC-US+. Of the women with a positive self-collected sample in the second round, 83.9% ($n$ = 452/539) recorded the triage method; 22.6% ($n$ = 102/452) of these women with self-collected samples recorded Pap ASC-US+. Regarding adherence to diagnosis, out of the total number of women with ASC-US+ triage ($n$ = 499; 397 with clinician-collected sample and 102 with self-collected sample), 79.2% ($n$ = 395/499) obtained a colposcopy. In addition, 10 women have a record of undergoing a colposcopy as a triage method following a positive HPV test. This study identified 84 women (68 with a clinician-collected sample and 16 with a self-collected sample) with histologically confirmed CIN2+ results. CIN2+ detection rate (considering all women rescreened independently of the timeframe) was 4.1/1 000 rescreened women ($n$ = 84/20 285). By 31 December 2021, 88.1% of these women had received treatment.

*Maintenance*: 3.6% of HPV-negative women screened in 2015–2017 underwent rescreening at five years (95% CI [3.4, 3.8]) (Table 2). This percentage rises to 13.7% if we consider a broader rescreening interval of five years and over (95% CI [13.3, 14.1]).

### Sociodemographic analysis of adherence to the national recommendation

Table 3 presents the sociodemographic characteristics of women according to their adherence to the five-year rescreening recommendation. Some 62.2% of adherent women were 30–44 years old (vs. 55.2% among nonadherent), 60.2% had public health insurance (vs. 54.6%), and 60.6% resided outside of the capital city (vs. 65.7%); 89.3% had a clinician-collected test as a screening method in the first round (vs. 90.2%).

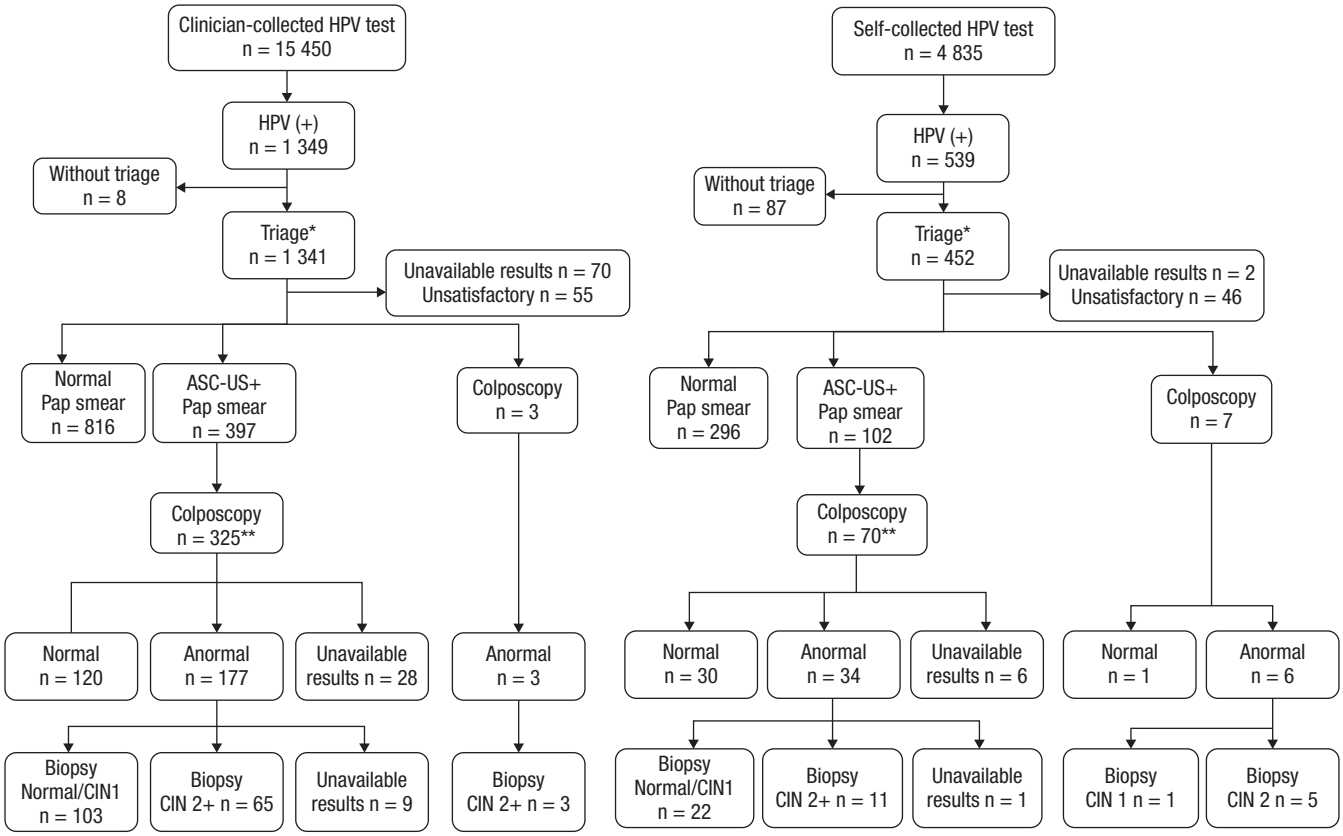
Table 4 presents a multivariate analysis to measure the probability of adherence controlled by sociodemographic characteristics. All variables included in the analysis showed significant association with adherence. Women aged 45–64 (OR: 0.852; 95% CI [0.802, 0.905], $p < 0.001$) and 65 and over (OR: 0.174; 95% CI

**TABLE 2. Reach, effectiveness, adoption, implementation, and maintenance of the HPV testing screening strategy for the second round of screening, Jujuy province, Argentina**

| RE-AIM dimension | Outcome |
|---|---|
| **REACH** | |
| Total women with a negative HPV result in 2012–2014 with a registered rescreening between 2015–2021 | 47.9%<br>95% CI (47.5, 48.4)<br>($n$ = 20 285/42 307) |
| **EFFECTIVENESS** | |
| CIN2+ detection rate in women rescreened at 5 years per 1 000 screened women | 5.3<br>($n$ = 30/5 639) |
| **ADOPTION** | |
| Health centers that perform rescreening at 5 years | 69.2%<br>($n$ = 200/289) |
| Health centers that perform rescreening at 3 years and over | 86.1%<br>($n$ = 249/289) |
| **IMPLEMENTATION** | |
| **Adherence to the rescreening recommendation** | |
| Rescreening at 5 years | 13.3%<br>95% CI (13.0, 13.7)<br>($n$ = 5 639/42 307) |
| **Total adherence to triage, diagnosis, and treatment** | |
| Triage Pap tests performed | Total: 95.0%<br>Clinician-collected: 99.4% ($n$ = 1 341/1 349)<br>Self-collected: 83.9% ($n$ = 452/539) |
| Colposcopy (ASC-US+ women with colposcopy record) | Total: 79.2%<br>Clinician-collected: 81.9% ($n$ = 325/397)<br>Self-collected: 68.6% ($n$ = 70/102) |
| Treatment (CIN2+ with treatment record) | 88.1%<br>($n$ = 74/84) |
| **MAINTENANCE** | |
| **Adherence to HPV rescreening recommendations among women with negative HPV tests (2015–2017)** | |
| Rescreening at 5 years | 3.6%<br>95% CI (3.4, 3.8)<br>($n$ = 1 047/28 977). |

ASC-US+, atypical squamous cells of undetermined significance or worse; CIN, cervical intraepithelial neoplasia.
***Source:*** Prepared by the authors based on the study data.

**FIGURE 1. Follow-up of HPV-positive women using clinician-collected and self-collected samples for rescreening**




***Notes*:** ASC-US+, atypical squamous cells of undetermined significance or worse; CIN, cervical intraepithelial neoplasia.
* Triage included Pap smear or colposcopy.
** For 72 records involving clinician-collected HPV tests, and 32 records involving self-collected HPV tests, colposcopy examination data were missing.
***Source*:** Prepared by the authors based on the study data.

[0.129, 0.228], $p < 0.001$) were less likely to be rescreened at the recommended timeframe of five years compared to those aged 30–44. Moreover, those women who resided outside of San Salvador de Jujuy were also 0.811 (95% CI [0.764, 0.860], $p < 0.001$) times less likely to be rescreened when compared to those who lived in the provincial capital city. Women with public health insurance were 1.136 (95% CI [1.070, 1.205], $p < 0.001$) times more likely to be rescreened than women with social security. Finally, women who had a clinician-collected test as a method of screening in the first round were less likely to be rescreening, having 0.863 odds of being rescreened, than women who had a self-collected test (95% CI [0.786, 0.948], $p < 0.005$).

## DISCUSSION

Our study presents an evaluation of a second round of HPV screening implemented within a population-based cervical cancer screening strategy in a middle-income setting. Our findings regarding adherence to the recommended five-year rescreening interval, detection rates for CIN2+, and the overall program sustainability highlight the challenges and potential benefits of implementing HPV-based rescreening programs in such settings. In the context of WHO's global call to accelerate the elimination of cervical cancer (7), this study provides real-world evidence to inform the implementation of HPV testing-based screening strategies in low- and middle-income countries, aligning with the ongoing national and global paradigm shift toward HPV testing in cervical cancer screening.

High rescreening coverage in subsequent rounds is crucial for the long-term effectiveness of the HPV testing strategy. Overall, our study shows low adherence to rescreening among HPV-negative women. While the analyses showed an increase in second round participation rates over time (reaching a cumulative participation in rescreening of approximately 48%), adherence to a more precise five-year rescreening interval remains below 14%. Other studies using real-world screening program data have reported higher participation rates in the second round, ranging from 40% to 88% (11, 21, 22). However, those studies were conducted in organized screening programs from high-income countries. These programs regularly invite the target population through letters, emails, or phone calls (22, 23). Low levels of screening coverage have been observed in lower-middle-income countries (24). In these settings, alternative invitation or reminder strategies are needed. In Argentina, the ATICA study showed that sending SMS messages effectively increased adherence to triage among women with HPV-positive self-collection (25). The ATICA strategy could be adapted to other steps in the screening process and can contribute to increasing adherence to rescreening in the second round.

Our results showed a decreasing probability of adherence to rescreening at five years with increasing age. This finding aligns with observations from other studies (28, 30, 31). For

**TABLE 3. Sociodemographic characteristics of women screened during 2012–2014 according to rescreening at 5 years, Jujuy province, Argentina**

| | Total women screened 2012–2014 | | Rescreening at 5 years | | | | *p* value |
|---|---|---|---|---|---|---|---|
| | | | No | | Yes | | |
| | *n* | % | *n* | % | *n* | % | |
| **Total** | 42 307 | 100 | 36 668 | 100 | 5 639 | 100 | |
| **Age** | | | | | | | <0.001 |
| 30–44 | 23 762 | 56.2 | 20 252 | 55.2 | 3 510 | 62.2 | |
| 45–64 | 16 569 | 39.2 | 14 493 | 39.5 | 2 076 | 36.8 | |
| 65 and over | 1 976 | 4.7 | 1 923 | 5.2 | 53 | 0.9 | |
| **Health insurance**[a] | | | | | | | <0.001 |
| Public | 23 107 | 55.4 | 19 763 | 54.6 | 3 344 | 60.2 | |
| Social security | 18 632 | 44.6 | 16 421 | 45.4 | 2 211 | 39.8 | |
| **Residence**[b] | | | | | | | <0.001 |
| Other | 26 714 | 65.0 | 23 343 | 65.7 | 3 371 | 60.6 | |
| San Salvador de Jujuy | 14 400 | 35.0 | 12 204 | 34.3 | 2 196 | 39.4 | |
| **Sample method of first HPV test** | | | | | | | 0.03 |
| Self-collected | 4 205 | 9.9 | 3 599 | 9.8 | 606 | 10.7 | |
| Clinician-collected | 38 102 | 90.1 | 33 069 | 90.2 | 5 033 | 89.3 | |

***Notes:*** [a] 568 missing.
[b] 1 193 missing.
***Source:*** Prepared by the authors based on the study data.

**TABLE 4. Multivariate logistic regression, variables associated with adherence to rescreening, Jujuy province, Argentina**

| | Adherence | Multivariate analysis | | |
|---|---|---|---|---|
| | (%) | OR | 95% CI | *p* value |
| **Total** | 13.3 | | | |
| **Age** | | | | |
| 30–44 | 14.8 | 1 | | |
| 45–64 | 12.5 | 0.852 | (0.802, 0.905) | <0.001 |
| 65 and over | 2.7 | 0.174 | (0.129, 0.228) | <0.001 |
| **Health insurance** | | | | |
| Social security | 11.9 | 1 | | |
| Public | 14.5 | 1.136 | (1.070, 1.205) | <0.001 |
| **Residence** | | | | |
| San Salvador de Jujuy | 15.2 | 1 | | |
| Other | 12.6 | 0.811 | (0.764, 0.860) | <0.001 |
| **Sample method of first HPV test** | | | | |
| Self-collected | 14.4 | 1 | | |
| Clinician-collected | 13.2 | 0.863 | (0.786, 0.948) | 0.002 |

***Source:*** Prepared by the authors based on the study data.

example, in Jujuy, a study showed that among a population of HPV-positive/cytology-negative women, those aged 65 and over were less likely to be retested when compared to those aged 30–34 (31). In addition, women outside the reproductive age group tend to be less frequent users of health services. Women in older age groups have a higher incidence of cervical cancer (29). Thus, a customized approach should be considered to increase retention in the screening process for this population group at increased risk of cervical cancer.

Prior studies reported lower adherence among uninsured women (32). In contrast, our findings suggest that women with public health insurance have a higher adherence probability than those with social security. These data, however, should be interpreted with care, as HPV testing is only available within the public health system. Women screened in the first round may have continued their healthcare routine within the social security system. These findings are consistent with those of previous studies conducted in Argentina (33).

Adherence to both colposcopy (79%) and treatment (88%) was higher than adherence to the rescreening recommendation. In the first round of screening, the province of Jujuy exhibited similar adherence rates for diagnosis (70%) and treatment (81%) (12). Since 2012, a patient navigation program has been implemented in Jujuy. Two navigators utilize SITAM to identify nonadherent women. They subsequently contact these women via telephone calls or home visits to provide specific support and facilitate connections with healthcare providers responsible for follow-up care and treatment (34). The sustained implementation of this strategy is crucial in reducing cervical cancer incidence and mortality.

A central question surrounding the implementation of long-term HPV testing strategies concerns its effectiveness in detecting CIN2+ lesions and the optimal interval between negative screening tests. The effectiveness of the HPV test in detecting cervical abnormalities has been widely documented in controlled trials (1, 4, 35). However, to formulate evidence-based recommendations regarding the optimal screening interval, effectiveness and implementation must be

rigorously evaluated within low- and middle-income settings and programmatic contexts. Our study findings revealed a CIN2+ detection rate of 5.3 per 1 000 women rescreened at five years. As anticipated, this rate is lower than observed in the first round. These results align with observations reported in other investigations of long-term HPV testing strategies (11, 22). In our study, effectiveness reflects the CIN2+ detection rate based on adherence to the five-year rescreening interval, as well as triage and colposcopy/biopsy. Thus, although it does not necessarily represent the CIN2+ detection rate of the second round of HPV testing that could have been achieved if a higher proportion of HPV-negative women had been rescreened, it reflects what can realistically be achieved under programmatic real-world conditions. Therefore, considering this finding within the broader context of the study, a recommendation for a five-year screening interval remains appropriate. Furthermore, lesions detected were CIN2 and CIN3, with no cancer diagnosis. This finding highlights the effectiveness of the first screening round in identifying precancerous lesions amenable to treatment, thereby preventing cervical cancer development. Therefore, the implementation of an HPV-based screening strategy is likely to contribute to a reduction in both the incidence and mortality rates of cervical cancer.

Regarding maintenance of the strategy, our study shows that although rescreening at five years was maintained as a public health strategy, the women's adherence was very low. The fact that rescreening at five years which was due in 2020–2021 fell during the COVID-19 pandemic certainly affected the level of rescreening adherence: only 13% of women who received a negative HPV test in 2015–2017 underwent rescreening at five years or later, and a mere 3.6% adhered to the five-year recommendation. As documented in various studies, maintaining preventive healthcare practices became especially challenging during the COVID-19 pandemic (26). Specifically, in the province of Jujuy, a decrease in cervical cancer screening and management after diagnosis was observed during the year 2020 (27).

The study is not without limitations that should be considered when interpreting the findings. First, our analysis was restricted to variables routinely captured within the screening information system SITAM. Unrecorded variables may have further influenced adherence to rescreening. Second, the study's observational nature limits our ability to establish causal relationships between the analyzed variables and adherence to rescreening. Finally, adherence to rescreening, diagnosis, and treatment rates may be underestimated due to the absence of data from private healthcare providers and the social security subsystem.

## Conclusion

In conclusion, our study in a middle-income setting aligns with existing expectations by demonstrating a decline in detection rates during the second round of HPV testing (9, 22, 35). However, we also observed limitations in sustaining rescreening participation at the recommended five-year interval. These findings support the current recommendation for the screening intervals and underscore the need to develop strategies to enhance long-term adherence. These findings provide crucial data to inform the development and optimization of HPV screening programs in similar contexts.

**Author contributions.** PBB: writing – original draft, visualization. MP: writing – original draft, data curation, methodology. FB: methodology, data curation, formal analysis. MA: writing – review and editing. AB: writing – review and editing. JDM: visualization. SA: funding acquisition, conceptualization, data curation, methodology, writing – review and editing.

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**Data availability.** The datasets used in this study are available from the corresponding author on reasonable request. De-identified individual participant data on which summary statistics and tables are based will be made available up to five years after the acceptance for publication of the main findings. These data can be requested to the principal investigator (Dr. Silvina Arrossi) and only under a data-sharing agreement.

**Disclaimer.** Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the *RPSP/PAJPH* and/or the Pan American Health Organization, World Health Organization, or International Agency for Research on Cancer.

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# Segunda ronda de tamizaje del cáncer cervicouterino mediante la prueba del VPH en contextos programáticos en Argentina

**RESUMEN**

**Objetivos.** Evaluar la ejecución de la segunda ronda de tamizaje del cáncer cervicouterino mediante la detección del virus del papiloma humano (VPH), que se introdujo en 2012-2014 en la provincia argentina de Jujuy con un proyecto piloto para mujeres de edad igual o superior a 30 años; y describir las características de las mujeres que acuden, tal como se recomienda, a una repetición del tamizaje al cabo de cinco años.

**Método.** Se llevó a cabo un estudio de cohorte retrospectivo con los datos de dos rondas de tamizaje. Se incluyeron todas las mujeres de edad igual o superior a 30 años a las que se había realizado la prueba del VPH con resultado negativo en el proyecto piloto en Jujuy. Para evaluar la ejecución de la ronda, se aplicó el marco de cobertura, eficacia, adopción, ejecución y mantenimiento (RE-AIM, por su sigla en inglés). Se utilizó una regresión multivariable para examinar los factores asociados a la adhesión a la repetición del tamizaje.

**Resultados.** De las 42 307 mujeres que habían presentado un resultado negativo en la prueba del VPH, en el 47,9% (n = 20 285) se realizó el nuevo tamizaje en la segunda ronda (cobertura); el 69,2% de los establecimientos de salud realizaron al menos una prueba del VPH en la segunda ronda (adopción); y en el 13,3% de las mujeres (n = 5639) se llevó a cabo el segundo tamizaje dentro del margen recomendado de cinco años. Del total de mujeres en las que se repitió el tamizaje, el 9,3% (n = 1888) presentó un resultado positivo para el VPH, y en el 95,0% de estas mujeres se llevó a cabo una citología cervicouterina (prueba de Papanicolaou) con fines de triaje; a su vez, en el 79,2% de las mujeres que presentaron un resultado positivo para el VPH y anomalías citológicas se realizó una colposcopia. Por lo que respecta a las mujeres en las que se repitió el tamizaje a los cinco años, la tasa de detección en la segunda ronda fue de 5,3/1000 mujeres. El porcentaje de mujeres que acudieron al segundo tamizaje a los cinco años fue significativamente mayor en la franja etaria de 30-44 años, así como en las mujeres que disponían de seguro de salud público y en las residentes de la capital de la provincia.

**Conclusiones.** El segundo tamizaje para las mujeres con un resultado negativo en la primera ronda se enfrenta a desafíos relacionados con la reducción de su cobertura, especialmente si tenemos en cuenta el lapso recomendado de cinco años. A tenor de nuestros resultados, es preciso diseñar estrategias específicas para aumentar las tasas de tamizaje en segunda ronda.

**Palabras clave** Neoplasias del cuello uterino; pruebas de ADN del papillomavirus humano; tamizaje masivo; ciencia de la implementación; Argentina.

# Implementação da segunda rodada de rastreamento do câncer do colo do útero com base na pesquisa de HPV em contextos programáticos na Argentina

**RESUMO**

**Objetivos.** Avaliar a implementação da segunda rodada do rastreamento cervical do papilomavírus humano (HPV), introduzido na Argentina em 2012–2014 por meio de um projeto-piloto em Jujuy para mulheres de 30 anos ou mais, e descrever as características das mulheres que seguem o intervalo recomendado de cinco anos entre os exames de rastreamento.

**Métodos.** Foi realizado um estudo de coorte retrospectivo com base nos dados de duas rodadas de rastreamento. O estudo incluiu todas as mulheres com 30 anos de idade ou mais que fizeram o teste de HPV durante o projeto-piloto de Jujuy e tiveram um resultado negativo. Para avaliar a implementação, foi utilizada a estrutura de avaliação RE-AIM (sigla em inglês para alcance, efetividade, adoção, implementação e manutenção). Também foi usada uma regressão multivariada para examinar os fatores associados à adesão à repetição do rastreamento.

**Resultados.** Das 42 307 mulheres com resultado negativo para HPV, 47,9% (n = 20 285) fizeram um novo rastreamento na segunda rodada (alcance); 69,2% dos centros de saúde realizaram pelo menos um teste de HPV na segunda rodada (adoção); e 13,3% (n = 5 639) das mulheres fizeram um novo rastreamento dentro do intervalo recomendado de cinco anos. Das mulheres que repetiram o rastreamento, 9,3% (n = 1 888) tiveram um resultado positivo para HPV, das quais 95,0% fizeram o exame de Papanicolau. Além disso, 79,2% das mulheres com resultado positivo para HPV ou com Papanicolau alterado foram submetidas à colposcopia. Considerando as mulheres que realizaram um novo rastreamento em cinco anos, a taxa de detecção na segunda rodada foi de 5,3 por 1000 mulheres testadas. A repetição do rastreamento em cinco anos foi significativamente maior em mulheres de 30 a 44 anos, que tinham seguro de saúde público e que moravam na capital da província.

**Conclusões.** A repetição do rastreamento de mulheres com resultado negativo para HPV envolveu desafios relacionados a limitações do alcance, especialmente quando se considera o intervalo recomendado de cinco anos. Os achados sugerem que é preciso desenvolver estratégias específicas para aumentar as taxas de realização do rastreamento na segunda rodada.

**Palavras-chave** Neoplasias do colo do útero; testes de DNA para papilomavírus humano; programas de rastreamento; ciência da implementação; Argentina.