

Contents lists available at ScienceDirect

Preventive Medicine Reports



journal homepage: www.elsevier.com/locate/pmedr

Psycho-social impact of positive human papillomavirus testing in Jujuy, Argentina results from the Psycho-Estampa study

Silvina Arrossi^{a,*}, Maribel Almonte^b, Rolando Herrero^b, Juan Gago^c, Victoria Sánchez Antelo^d, Lucila Szwarc^d, Laura Thouyaret^e, Melisa Paolino^a, Carolina Wiesner^f

^a Centro de Estudios de Estado y Sociedad/Consejo Nacional de Investigaciones Científicas y Técnicas, Sánchez de Bustamante 27, Buenos Aires 1193, Argentina

^b International Agency for Research on Cancer/World Health Organization (IARC-WHO), 150 Cours Albert Thomas, Lyon 69372, France

^c New York University-NYU, School of Medicine, USA

^d Centro de Estudios de Estado y Sociedad, Sánchez de Bustamante 27, Buenos Aires, Argentina

e Programa Nacional de Prevención de Cáncer Cervicouterino /Instituto Nacional del Cáncer (Argentina), Av. Julio A. Roca 781, Buenos Aires, Argentina

^f Instituto Nacional de Cancerología, Calle 1 No.9-85, Bogotá, Colombia

ARTICLE INFO

Keywords: Human Papillomavirus DNA Tests Argentina Latin America Psycho-social impact

ABSTRACT

Human papillomavirus (HPV) testing can have a negative impact on women's lives which might also result in abandoning the follow-up and treatment process. This study measured the psycho-social impact of HPV-positivity among HPV-tested women from Jujuy, Argentina, a middle-low income setting.

In this cross-sectional study (2015–2016), the psycho-social impact of HPV-positivity was measured using the Psycho-Estampa Scale, specifically designed and validated to be used in screening contexts. We measured mean scores for each of the five scale domains, and the Overall Impact score (Values from 1: No impact to 4: Heavy impact). We compared scores according to cytology triage diagnosis using ordinal logistic regression.

A total of 163 HPV-positive women were recruited at the Centro Carlos Alvarado hospital and included in the study sample; of these, 124 (76.1%) had normal triage cytologies. The overall Impact score was between low and moderate (mean:2.56, SD:0.65). The highest psycho-social impact was measured in the Worries about cancer and treatment domain (mean score:3.60, SD:0.60), followed by Sexuality domain (mean:2.50; SD:1.00). The Uncertainty about information provided by health providers domain had the lowest mean score (mean:2.14, SD:0.73). Compared to women with normal cytologies (n = 124), women with abnormal cytologies (n = 39) had a higher likelihood of greater overall Psycho-social Impact (OR: 2.91; p = 0.0036). No statistically significant differences were found in scores of specific domains according to cytology results.

It is important to devise specific counseling interventions to reduce the psycho-social impact of HPV-Testing as primary screening and its potential effect on completion of the diagnosis/ treatment process.

1. Introduction

Worldwide, cervical cancer continues to be a serious public health problem; with more than 500,000 new cases and 250,000 deaths occurring annually, 90% of them in middle-low income countries. (Bray et al., 2018) In recent decades, Human papillomavirus (HPV) testing that detects sexually transmitted infection with oncogenic types of HPV, was developed as an alternative screening method. HPV testing has high sensitivity and negative predictive value, and it has been shown effective to reduce cervical cancer incidence and mortality. (Sankaranarayanan et al., 2009) In addition, HPV testing allows for sample self-collection, which is effective in increasing screening uptake. (Arrossi et al., 2015) At present, the World Health Organization recommends screening with HPV testing in combination with HPV vaccination as the main strategy to accelerate elimination of cervical cancer. (World Health Organization, 2014) Worldwide, more than 15 countries have introduced HPV testing in primary screening; (Cervical Cancer Action, 2017) in the Latin American region, Argentina and Mexico are using it as public health policy for cervical cancer prevention, and in most other countries in the region, pilot or demonstration projects are being implemented in order to move forward towards national implementation. (Jerónimo et al., 2016; Arrossi et al., 2019) High screening coverage as well as high adherence to follow-up recommendations and treatment are necessary in order to achieve a reduction in cervical cancer incidence. (World Health Organization, 2014)

https://doi.org/10.1016/j.pmedr.2020.101070

Received 3 October 2019; Received in revised form 27 February 2020; Accepted 2 March 2020 Available online 05 March 2020

2211-3355/ © 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

^{*} Corresponding author.

E-mail address: silviarrossi@cedes.org (S. Arrossi).

Prevalence of oncogenic HPV infection among women aged 30 and above is relatively high (9% in South America), (Clifford et al., 2005) so a significant proportion of screened women will be diagnosed with HPV infection. HPV testing identifies infection with an oncogenic type of HPV that cannot be treated; triage tests are used to identify HPV positive (HPV +) women who will require diagnosis and treatment: only a portion of HPV + women will have a positive triage indicating a precancerous lesion requiring further evaluation (Wentzensen et al., 2016) (around 70%-88% in studies using cytology triage). (Arrossi et al., 2019; Torres-Ibarra et al., 2019) Due to the HPV-test moderate specificity for detection of cervical precancer, (Koliopoulos et al., 2017) most HPV + women will end up with an HPV + /triage negative result requiring repeat screening in 12/18 months. Thus, infection with an oncogenic type of HPV can be detected, but positivity does not necessarily mean that the infection will cause cervical precancer or cancer or that the woman will require treatment. In most women, HPV infections will resolve naturally.

Evidence has shown that as a result of all these characteristics HPV testing can have a negative psycho-social impact on women lives. (Bennett et al., 2019) In effect, as a consequence of the known sexual transmission of the infection, HPV positivity has connotations of promiscuity, stigmatization, impurity, and can result in shame, worries about future sexual relationships and questions about the women's or their partner's sexual behavior. (McCaffery et al., 2006; Kahn et al., 2005; Dominiak-Felden et al., 2013) HPV results can also produce anxiety, fear of death, and disease denial, or women not considering it necessary to continue diagnosis, treatment and follow-up. (Smith et al., 2014; Castro Vásquez, 2014; León-Maldonado et al., 2016).

It has been shown that believing that an abnormal screening test is indicative of cancer and inevitable death, in addition to its association with a sexually transmitted disease can act as barriers for diagnosis and treatment of precancerous lesions. (Flyan, 1998; Sharpe et al., 2005; Liebermann, 2018) Thus, HPV positivity can have a negative psychosocial impact on women lives which not only might result in poor quality of life but also reduce womeńs ability to complete diagnosis, treatment and follow-up.

However, in spite of the evidence about potential negative psychosocial impact of HPV testing as primary screening, no study from Latin America has quantitatively measured it using a validated scale specifically devised to measure it. We carried out the Psycho-Estampa study in Colombia and Argentina, aimed at developing a scale and measuring the psycho-social impact of HPV positivity in the context of cervical cancer prevention programs using HPV-testing as primary screening in Latin America. The Psycho-Estampa study is part of ESTAMPA, a multicentric study led by IARC-WHO aiming to evaluate different cervical screening and triage techniques using HPV (NTC 01881659). In this paper we present results of the psycho-social impact of HPV positivity of women HPV-tested in Jujuy, Argentina.

To our knowledge, this is the first evaluation of the psycho-social impact of HPV testing in the region using a validated scale specifically designed for Latin American women. Therefore, it constitutes key evidence for the design of strategies aimed at reducing impact and improving women's quality of life and increasing their ability to continue follow-up care.

2. Methods

2.1. The setting

The study was carried out in the province of Jujuy, where HPVtesting has been the primary screening method since 2012, (Arrossi et al., 2019) targeting women aged 30 years and older attending the public health system. HPV samples are collected by clinical staff at health centers, and since 2014 HPV self-collection was introduced as a programmatic strategy to increase screening coverage. Women are informed of their results at health care centers. The protocol in use in Jujuy has been described elsewhere (Arrossi et al., 2019) but succinctly HPV + women are triaged with cytology; those with samples that include Atypical Cells of Undetermined Significance or more (ASCUS +) are referred to colposcopy and biopsy if needed. Women with histologically confirmed CIN2 + are referred for treatment. HPV-negative (HPV-) women were recommended for rescreening in five years. HPVtesting and cytology-triage are taken simultaneously, but cytology is read only if women are HPV + . Women who are HPV + and have normal cytology, are recommended for rescreening in 18 months

The study population included women screened at the gynecology service at the Centro Sanitario Dr. Carlos Alvarado, a main hospital located in San Salvador de Jujuy, the provincial capital city. Around 6,000 women are HPV-tested annually in this gynecologic service. HPV + women with abnormal cytologies were referred to colposcopy and biopsy, those with cervical intraepithelial neoplasia (CIN) grade 2 or worse (CIN2 +) on biopsy were adequately treated. Exclusion criteria were having cognitive or sensorial challenges.

2.2. Women eligibility

Eligible women were HPV + women, aged 30–65 years old. From April 2015 to March 2016, eligible women were invited to participate in the study during the consultation for receiving the HPV results; those who agreed signed an informed consent and were contacted around 8 days later for a face-to-face or telephone interview by a trained interviewer.

2.3. Outcome measurement

The psycho-social impact of HPV-testing was measured through the Psycho-Estampa scale, an instrument designed to measure the psychosocial impact of HPV tests within the framework of primary screening for cervical cancer. It consists of five domains with 22 items that were generated from a literature review and in-depth interviews with HPV + women and health personnel. (Anhang et al., 2004; Wiesner Ceballos et al., 2009) The 22 items are evaluated with an ordinal system of 4 categories ranging from 1 (not at all) to 4 (much) and organized theoretically in five domains:

- Emotional domain, which measured impact related to women cognitive perceptions and feelings around having a sexually transmitted infection,
- Sexuality domain, which measured impact related to attitudes and practices regarding sexual relationships,
- 3) Domain referred to the Uncertainty about information provided by health providers, which measured impact related to worries around the received messages and those related to the interaction with health professionals,
- Domain referred to Repercussions on the family, which measured impact related to fears about the transmission of the HPV to other members of the family,
- 5) Domain about Worries about HPV, cancer and treatment, which measured impact related to worries about how the infection was acquired, its treatment and its association to cancer.

Higher scores on the scale indicate a higher negative psycho-social impact. The scale was validated for internal consistency, reliability, construct validity, test–retest, sensitivity to change and concurrent validity (See Supplementary File for a detailed description of the scale validation). Its structure and items can be seen in Appendix A.

2.4. Statistical analysis

Participating women were asked to score each Psycho-Estampa scale item to a 4-point discrete scale (1 = Not at all, 2 = A little, 3 = Some, 4 = Much). Women with no sexual partner at the time of the

interview, were not asked the question regarding impact on sexual life. Women with no children at the time of the interview, were not asked the question regarding fear about transmission to children. The scores for each domain of the scale were computed as the average of the scores of the questions answered for that domain, not taking into account unanswered items (excluding missing values). To create the overall Psycho-Estampa score, the mean was computed as the sum of all the items over the number of items answered on all scale domains.

A mean total Psycho-Estampa score of 2 or below was interpreted as a domain with a tendency to be answered as little to no impact; a score of 3 was considered a trend to women answering moderate impact and a score of 4 was taken as indicative of heavy psycho-social impact.

Basic descriptive statistics and frequency calculations were performed on socio-demographic variables (age, number of sexual partners, education level) and cytology diagnosis. We also compared scores in each domain and the total score according to cytology-results. First, we grouped both abnormal categories of cytological diagnosis (Low grade squamous intraepithelial lesions -LSIL and high grade squamous intraepithelial lesions -HSIL), as in the Argentinean protocol all HPV + women with abnormal cytologies are referred for colposcopy and biopsy if needed. Secondly, differences between the groups were analyzed using ordinal logistic regression, obtaining odds ratios for having a high, moderate or low score for those with normal cytology when compared to those with abnormal cytology after controlling for age, ever having a partner, and education level.

We used R statistical software (version 3.5.0) for all analysis.

2.5. Ethical Committee approval

This study was approved by the Ethical Research Committee of the Jujuy Ministry of Health, Argentina (Approval 04/22/2015); written consent was obtained from all women participating in the study.

3. Results

3.1. Women socio-demographic characteristics

A total of 163 HPV + women were invited to participate in the study, all of them accepted and were included in the study sample. Of these, 118 had a current sexual partner and answered items referred to the impact on Sexuality, and 109 had children and answered items regarding regarding impact on their attitudes towards their children (Table 1). Mean age was 38 years (SD = 8 years) and mean number of sexual partners was 1.82. Most women had higher (53.4%) or secondary (36.8%) level of education. Regarding cytology triage, most patients (n = 124; 76.1%) had normal cytologies.

Table 1

Women	socio-demographic	characteristics	and	cytological	result	(normal/ab
normal)	. Jujuy, 2015-2016					

Age	Mean SD Median	38 8 35
Age by groups	30–34	76 (46.6%)
	35–45	61 (37.4%)
	46–54	17 (10.4%)
	55–65	9 (5.5%)
Educational Level	Primary school	16 (9.8%)
	Secondary school	60 (36.8%)
	College/university	87 (53.4%)
Number of sexual partners (In life)	1	30 (18.4%)
	2–3	133 (81.6%)
Cytological Result	Normal	124 (76.1%)
	Abnormal	39 (23.9%)

3.2. Psycho-social impact by domain

The measurement of the psycho-social impact of HPV testing in this group of women showed that the mean overall impact score was 2.56, SD: 0.65: median: 2.57. Results for each domain can be seen in Tables 2 and 3. The domain with the highest score was "Worries about cancer and treatment" (mean score: 3.6, SD:0.60, median: 4). Within this domain, the item with the highest score was PSE22: "I am worried about having cervical cancer" (mean 3.81, SD:0.61, median: 4.00). The Sexuality domain showed the second highest mean score (2.50; SD:1, median: 2.33). Within this domain the item with the highest score was PSE11: "After receiving my HPV test results. I worry about infecting my partner during sex" (mean score 2.76, SD:1.23, median: 2.82). The "Uncertainty about information provided by health providers" Domain had the lowest mean score: 2.14, SD: 0.73, median: 2.25. Within this domain, PSE16: "When I received my HPV exam results, I didnt feel comfortable with the way the health workers treated me" had the lowest mean score (1.44, SD:0.92, median: 1.00), which also represented the lowest score among all items of the psycho-social impact scale. The Repercussions on the family (mean score 2.27, SD: 1.24, median: 2.00), and Emotional symptoms (mean score 2.30; SD:0.82, median: 2.31) domains also had relatively low scores. However, in this latter domain, median scores in 3 items was 3 (PSE5: "When I think about my HPV exam results, I feel sad"; PS2: "When I think about my HPV exam results, I don't feel good about my body", and PS4: "When I think about my HPV exam results, I get nervous"), indicating that half of the women had moderate or high psycho-social impact

3.3. Psycho-social impact according to Women characteristics

Table 3 shows scores for the five psycho-social domains and Overall impact according to socio-demographic characteristics of women and cytology diagnosis: Women aged 35–45 had higher scores in most domains, as well as women with abnormal cytology. Higher scores on the Sexuality domain were observed in women with primary school level of education and in those reporting having had only one sexual partner.

Results from the ordinal logistic regression showed a significant association between the odds of having higher negative psycho-social impact and having an abnormal triage cytology and a less strong association with age. The odds of having higher negative psycho-social impact among women with abnormal cytologies was 2.9 (OR: 2.9, 95%CI:1.43–6.07) compared to those with normal cytologies (Table 4). Also, one unit decrease in age (year) was associated with a reduced likelihood of having a higher total psycho-social impact (OR:0.95; p = 0.036, CI = 0.92–0.99).

No statistically significant associations were found between the scores measured for each specific domain and cytology diagnosis (Appendix B).

4. Discussion

While several studies have suggested that women can be psychosocially burdened by a positive HPV test, (Maissi et al., 2004; McBride et al., 2019; Kitchener et al., 2008) to our knowledge, our study is the first to have quantitatively measured it in a middle-low income setting in the context of population-based HPV-screening: in Jujuy programmatic HPV testing was introduced as the primary screening test in 2012 and has since been the standard of care. (Arrossi et al., 2019) In Argentina, HPV testing and cytologies are taken in the same screening visit and sent together to the central Cytology/Histology/HPV Laboratory for analysis, so if HPV +, women receive results of HPV testing together with results from cytologies. This has allowed us to measure the impact among women according to their HPV testing and triage (cytology) result.

The highest measure of impact was observed on the "Women worries about cancer and treatment" domain. Several qualitative studies

Table 2

Psycho-Estampa scale domains and items (mean. SD. Median). Jujuy, 2015-2016.

		Mean	SD	Median
Domain	1: Emotional Symptoms	2.3	0.82	2.31
PSE1	"When I think about the results of my HPV exam, I feel sick."	2.2	1.07	2.00
PSE2	"When I think about my HPV exam results, I don't feel good about my body."	2.45	1.16	3.00
PSE3	"When I think about my HPV exam results, I feel ashamed."	2.4	1.22	2.00
PSE4	"When I think about my HPV exam results, I get nervous."	2.66	1.17	3.00
PSE5	"When I think about my HPV exam results, I feel sad."	2.72	1.20	3.00
PSE6	"After receiving my HPV exam results, it has been harder for me to concentrate on my daily routine."	2.13	1.20	2.00
PSE7	"After learning about my results, I dont sleep as well as before."	1.87	1.11	1.00
PSE8	"After receiving my HPV test results, İm afraid that my partner will reject me."	2.01	1.22	1.00
Domain	2: Sexuality	2.5	1.00	2.33
PSE9	"After receiving my HPV test results, I don't feel like having sex."	2.32	1.21	2.00
PSE10	"After receiving my HPV test results, I have sex less frequently."	2.42	1.29	2.00
PSE11	"After receiving my HPV test results, I worry about infecting my partner during sex."	2.76	1.23	3.00
Domain	3: Uncertainty about information provided by health care workers	2.14	0.73	2.25
PSE12	"When I think about my HPV exam results, I get angry."	2.52	1.29	3.00
PSE13	"As a consequence of my HPV results, Im worried that I wont be able to get pregnant."	2.53	1.32	3.00
PSE14	"After receiving my HPV results, I feel uncomfortable asking health workers any questions."	2.00	1.25	1.00
PSE15	"I thought that the information about HPV that the health workers gave me was confusing."	2.07	1.18	2.00
PSE16	"When I received my HPV, exam results, I didnt feel comfortable with the way the health workers treated me."	1.44	0.92	1.00
Domain	4: Repercussions on the family	2.27	1.24	2.00
PSE17	"After receiving my HPV results, Îm afraid that I could infect my children."	2.08	1.34	1.00
PSE18	"After receiving my positive HPV test results, İm afraid that at home I might infect other people [women] who use the same bathroom that I do."	2.40	1.35	3.00
Domain	5: Worries about cancer and its treatment	3.60	0.60	4.00
PSE19	"After receiving my HPV test results, I want to know how I got infected."	3.68	0.73	4.00
PSE20	"It worries me to know the Human papillomavirus cannot be cured."	3.61	0.80	4.00
PSE21	"It worries me to know that even though I am infected with the Human papillomavirus. Íve been told that I doát need to be treated for it."	3.30	1.07	4.00
PSE22	"Ím worried that I might have cervical cancer."	3.81	0.61	4.00

Table 3

Psycho-Estampa scale domains and Total Impact score by socio-demographic variables and cytological Results (mean. SD). Jujuy, 2015-2016.

		Age			Educational Level			Number of partners (in		Cytological result						
		30–34	35–45	46–54	55–65	Total	Primary school	Secondary school	Tertiary/ university	Total	One	More than one	Total	Abnormal	Normal	Total
Domain 1. Emotional	Mean	2.30	2.48	2.07	1.80	2.32	2.19	2.30	2.35	2.32	2.29	2.32	2.32	2.62	2.22	2.32
Symptoms	SD	0.78	0.90	0.91	0.78	0.82	0.93	0.82	0.86	0.82	0.89	0.85	0.82	0.84	0.84	0.85
	Valid n	76	61	17	9	163	16	60	87	163	30	133	163	39	124	163
Domain 2. Sexuality	Mean	2.36	2.72	2.53	2.28	2.50	2.74	2.42	2.50	2.50	2.67	2.46	2.50	2.76	2.42	2.50
	SD	0.93	1.09	0.99	1.12	1.00	1.11	0.96	1.02	1.00	1.11	0.98	1.00	1.00	0.99	1.00
	Valid n	56	39	17	6	118	13	44	61	118	21	97	118	28	90	118
Domain 3. Uncertainty	Mean	2.21	2.10	1.88	1.78	2.14	2.18	2.05	2.14	2.14	2.18	2.09	2.14	2.11	2.11	2.11
about information	SD	0.75	0.63	0.83	0.90	0.73	0.90	0.72	0.71	0.73	0.76	0.73	0.73	0.76	0.73	0.73
provided by HCW	Valid n	76	61	17	9	163	16	60	87	163	30	133	163	39	124	163
Domain 4.	Mean	2.32	2.31	2.12	2.00	2.27	2.41	2.13	2.35	2.27	2.28	2.27	2.28	2.27	2.27	2.28
Repercussions on	SD	1.23	1.27	1.33	1.12	1.24	1.25	1.17	1.29	1.24	1.22	1.25	1.24	1.29	1.23	1.24
the family	Valid n	76	61	17	9	163	16	60	87	163	30	133	163	39	124	163
Domain 5. Worries	Mean	3.54	3.66	3.59	3.72	3.60	3.66	3.68	3.53	3.60	3.56	3.61	3.60	3.67	3.58	3.60
about cancer and its	SD	0.64	0.56	0.67	0.40	0.60	0.54	0.48	0.68	0.60	0.62	0.60	0.60	0.51	0.63	0.60
treatment	Valid n	76	61	17	9	163	16	60	87	163	30	133	163	39	124	163
Score global	Mean	2.41	2.48	2.41	2.16	2.56	2.49	2.41	2.42	2.56	2.43	2.42	2.56	2.57	2.38	2.56
	SD	0.63	0.65	0.72	0.71	0.65	0.67	0.59	0.69	0.65	0.69	0.64	0.65	0.63	0.65	0.65
	Valid n	76	61	17	9	163	16	60	87	163	30	133	163	39	124	163

carried out in Latin America have reported results in the same direction. (Smith et al., 2014; Castro Vásquez, 2014; León-Maldonado et al., 2016) In a study carried out in Mexico by Leon Maldonado et al., 2016) women assumed that HPV was an inevitably serious disease that might be analogous to HIV or necessarily cause cancer. For the authors, misunderstandings about HPV and confusion regarding the testing process itself exacerbated the fears and negative emotions that women often experience when they learn about the sexually transmitted nature of HPV and cervical cancer etiology. In our study, a high impact on this domain was measured even among women who had not been diagnosed with cervical lesions. In line with this finding, a qualitative study that analyzed concerns about HPV among ethnically diverse, low-income women from the United States found that knowing that HPV does not always progress into cervical cancer

does not modify the overall sensations of worry and fear. (Anhang et al., 2004) In contrast with our finding, a study carried out in the UK (Kitchener et al., 2008) found that HPV testing did not add significant psychologic distress to women with normal cytologies; however, in that study scales used to measure distress were not HPV-specific, therefore their results might not be entirely comparable with ours.

HPV + women with normal cytologies are recommended rescreening in 12/18 months, (World Health Organization, 2014) this means that they will not have a more conclusive diagnosis until a considerable amount of time has gone by. This waiting might result in increased psycho-social impact, and decreased adherence to rescreening. In Jujuy, it has been shown that only 26% of HPV + women with normal cytologies adhere to repeat screening in the recommended time frame (18 months). (Gago et al., 2019) Subjective reasons

Table 4

Ordinal logistic regression to measure association between demographic factors and cytology diagnosis, and Total Impact Score. Jujuy, 2015–2016.

Factors	Value	Std. Error	OR	CI	p value
Education level					
Primary level			Ref		
Secondary level	-0.58	0.60	0.56	0.17-1.83	0.3397
Tertiary/University	-0.72	0.59	0.49	0.15-1.56	0.2291
Number of partners					
One			Ref		
Two or more	0.04	0.38	1.04	0.48 - 2.24	0.9121
Cytology result					
Normal			Ref		
Abnormal	1.07	0.37	2.92	1.42-6.07	0.0036
Age	-0.04	0.02	0.95	0.92-0.99	0.0363
Intercept					
[Not at all.little] (Little.Some]	-3.09	1.14	0.05		0.0069
(Little.Some] (Some.Much]	-0.77	1.11	0.46		0.4916

including fear, and disease denial (Paolino and Arrossi, 2012) have been mentioned as the main explanation for abandoning the follow-up and treatment process in cytology-based screening contexts. Given that a significant proportion of these women will be diagnosed with CIN2 + lesions at repeat screening, (Arrossi et al., 2019) it is very important to devise specific interventions to provide HPV + women with normal cytologies with counseling support aimed at decreasing the psycho-social impact and increasing their capacity to adhere to repeat screening at 18 months.

In our study, in the Sexuality and Emotional Domains the level of the psycho-social impact was between low and moderate (scores between 2 and 3). Evidence has shown that the kind and quality of information that women receive before obtaining the test results have an influence on the psycho-social impact of HPV positivity. (Wiesner Ceballos et al., 2009; Wiesner et al., 2012) The above mentioned study carried out in the United States (Anhang et al., 2004) found that when women previously know that HPV is a high prevalent infection among young population, they showed significantly lower levels of anxiety than those who did not know. In our study we did not evaluate the quality of the information received during the screening visit and/or consultation to receive the HPV test results, but we ensured that health providers informing women had previously participated in training organized by the National Program on Cervical Cancer Prevention on how to communicate HPV results. Also, specific communication materials were produced both for women and providers, highlighting the key message that HPV was a highly prevalent infection which could have been contracted many years ago. (Arrossi et al., 2016) A qualitative study among women HPV + or diagnosed with CIN (Castro Vásquez, 2014) showed that feelings of fear and anguish were related to how they were treated during the consultation and the information provided or omitted by doctors. Other studies carried out in contexts of cytologybased screening also showed that insufficient interaction with health professionals can result in women's higher stress and anxiety. (Schoenberg et al., 2010; Flyan, 1998; Sharpe et al., 2005) It is possible that the information provided by the gynecology service at the hospital, and the quality of the interaction with health professionals in charge of providing results in our study had contributed to reduce the impact on these domains. This is supported by the fact that the item measuring impact related to the "Information received during the consultation" was the one with the lower score in the whole scale. The low score on this information-related item also suggests that even in cases when women consider that they receive clear information, this might not be enough to reduce the level of impact regarding the Fear of cancer and treatment domain, which might need specific counseling strategies for its reduction.

The level of overall impact found in our study was moderate and was influenced by particularly low scores in the Uncertainty about information provided by health providers domain. The interdependence between uncertainty about the information provided by health providers and the overall psycho-social impact could imply that among women screened at other services and by other health professionals, the psycho-social impact might be higher.

A study carried out in Korea (Lee et al., 2019) to measure the psycho-social impact of HPV related diseases also found a moderate overall impact. However, the Korean study used the HPV Impact Profile (HIP) scale, developed by ROCHE to measure the impact on HPVrelated disease, (Mast et al., 2009) which is not specific to the impact of HPV screening positivity. For example, the HIP includes questions regarding genital warts and therefore, its final score is not entirely comparable with scores obtained with the Psycho-Estampa scale. Andreassen et al, (Andreassen et al., 2019) who carried out a study in the context of population-based HPV-testing found no negative impact among HPV + women; however they used the Patient Health Questionnaire-4 (PHQ-4), a 4-item scale whose main objective is to provide a brief measurement of depression and anxiety; therefore, no item in that scale is worded as to detect the psycho-social impact of HPV-testing. Also, they measured impact 4-24 months after women had been informed about their last screening test result, so there might be a time effect that should also be considered.

The overall level of psycho-social impact was associated to the cytology diagnosis, being women with abnormal triage cytolologies those with an increased probability of having a higher psycho-social impact. A study carried in the UK that used the HIP scale (Mast et al., 2009) to measure impact among women with abnormal cytologies also found a significant reduced impact among women with normal cytologies, but women in that study had not been HPV tested and their HPV status was unknown. (Dominiak-Felden et al., 2013) A qualitative study carried out in Dublin by ÓConnor et al., (O'Connor et al., 2015) found that factors that influenced whether women experienced negative emotional responses regarding HPV-infections were mainly dominated by concerns over abnormal cytology or diagnosis of CIN. However, in the sample included in the study by ÓConnor et al only six women were HPV + while 11 women were HPV negative; in addition, women had been HPV-tested up to 6 months ago; therefore, their responses might have been affected by time elapsed since diagnosis. Our study measured the impact one week after having received the results, so we think that we were able to measure the immediate psycho-social impact of a positive HPV result received as part of a routine, programmatic HPVbased screening.

We used a measurement instrument (The Psycho-Estampa scale) specifically designed and validated to measure the impact of HPVtesting among Latin American women. This is the first time that data on the impact of HPV-testing is measured using the Psycho-Estampa scale. Other studies (Lee et al., 2019) have used the HIP scale and the PHQ-4 scale. (Mast et al., 2009) As above-mentioned, the HIP scale has been developed to measure impact of various HPV-related diseases. Also, many items in the HIP scale are worded in a way that answers given by women might be referring to the impact of the gynecologic consultation experience rather than to of the impact derived from the result of the test in itself. Regarding the study that used the PHQ-4 scale (Andreassen et al., 2019) women were interviewed 4-24 months after they had been informed about their last screening test result, so a time effect might also affect comparability of results. Also, as mentioned above, no item in that scale is worded as to detect the psycho-social impact of HPVtesting.

Our study is the first to use the Psycho-estampa scale, a measurement tool specifically designed to measure the psycho-social impact of HPV-positivity among subjects who are screened with HPV-testing provided as primary screening.

Our study has a main limitation, which is that we measured impact on a sample of women attending a main hospital in San Salvador de Jujuy, the provincial capital city. Therefore, impact measured in our sample may not be representative of the impact experienced by women receiving results in other health centers, and in other areas, i.e. rural areas. Also, the majority of women were highly educated, whereas at population level 42% of women living in Jujuy province have up to primary level of education. (INDEC, 2001) It was certainly a population screened in the context of routine screening, so the impact women experienced happened with HPV testing provided in real world, programmatic conditions. Further research expanding these findings to other groups of HPV-tested women will help clarify these issues.

Our results suggest that there is a need for interventions aimed at reducing the psycho-social impact of HPV-testing. WHO recommends counseling as a strategy for inter-personal communication between the health provider and the woman, as it will allow women to become more informed and knowledgeable about HPV and cervical cancer prevention, will allow them to discuss sensitive topics, such as sexuality, disease, and death, and will encourage them to adopt preventive practices. (Pan American Health Organization, 2016) Therefore, it is important to develop strategies that include counseling for providing HPV-results so they can be implemented and evaluated as a tool to reduce the psychosocial impact of HPV-testing.

5. Conclusions

HPV testing is the current recommended standard of care for cervical cancer screening, but its reduced specificity not only affects the diagnosis workload at colposcopy centers but might have a negative social and psychological impact on women lives. This is the first study to quantitatively measure the psycho-social impact of HPV positivity among women screened with HPV testing in Latin America. We found that the psycho-social impact was particularly high in the Fear of Cancer and Treatment Domain. The overall psycho-social impact was moderate, but it was increased among women with abnormal triage cytologies. As the psycho-social impact of HPV positivity can not only result in psychological distress but it can also influence women adherence to follow-up recommendations and treatment, specific counseling interventions to reduce it are needed.

CRediT authorship contribution statement

Silvina Arrossi: Conceptualization, Methodology, Writing - original draft, Writing - review & editing, Supervision, Funding acquisition. Maribel Almonte: Conceptualization, Methodology, Writing - review & editing, Formal analysis. Rolando Herrero: Conceptualization, Methodology, Writing - review & editing, Funding acquisition. Juan Gago: Writing - review & editing, Formal analysis, Data curation. Victoria Sánchez Antelo: Writing - review & editing, Visualization. Lucila Szwarc: Writing - review & editing, Investigation. Laura Thouyaret: Writing - review & editing, Investigation, Project administration. Melisa Paolino: Writing - review & editing, Investigation, Data curation. Carolina Wiesner: Conceptualization, Writing - review & editing, Methodology, Formal analysis.

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.

Acknowledgments

Paula Barletta and Julieta Zalacain Colombo from the National Cancer Institute (Argentina), Dr. Elsa Figueroa and authorities of the Hospital Centro Sanitario Carlos Alvarado, Jujuy province, Argentina; and Ángela Góngora from Instituto Nacional de Cancerología (Colombia).

Financial support

This project received support from IARC, the Argentinian National Cancer Institute and CONICET. The funders had no role in study design, data collection, analysis, or writing of the report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2020.101070.

References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68(6):394-424. Available from: https://doi. org/10.3322/caac.21492.
- Sankaranarayanan, R., Nene, B.M., Shastri, S.S., Jayant, K., Muwonge, R., Budukh, A.M., et al., 2009. HPV screening for cervical cancer in rural India. N Engl J Med. 360, 1385–1394. https://doi.org/10.1056/NEJMoa0808516.
- Arrossi S, Thouyaret L, Herrero R, Campanera A, Magdaleno A, Cuberli M, et al. Effect of self-collection of HPV DNA offered by community health workers at home visits on uptake of screening for cervical cancer (the EMA study): a population-based clusterrandomised trial. Lancet Glob Health. 2015 Feb; 3(2):e85-94. Available from: http:// dx.doi.org/10.1016/S2214-109X(14)70354-7.
- World Health Organization, 2014. Comprehensive cervical cancer control: a guide to essential practice. WHO, Geneva.
- Cervical Cancer Action. Global Progress of HPV DNA Testing for Cervical Cancer Screening, June 2017. Available at: http://www.cervicalcanceraction.org/comments/comments2.php; last acceded 23/12/2019.
- Jerónimo J, Holme F, Slavkovsky R, Camel C. Implementation of HPV testing in Latin America. J Clin Virol. 2016 Mar; 76(1):S69-S73. Available from: https://doi.org/10. 1016/j.jcv.2015.11.035.
- Arrossi S, Paolino M, Laudi R, Gago J, Campanera A, Marín O, Falcón C, Serra V, Herrero R, Thouyaret L. Programmatic human papillomavirus testing in cervical cancer prevention in the Jujuy Demonstration Project in Argentina: a population-based, beforeand-after retrospective cohort study. Lancet Global Health. 2019; 7:e772–83. Available from: https://doi.org/10.1016/S2214-109X(19)30048-8.
- Clifford GM1, Gallus S, Herrero R, Muñoz N, Snijders PJ, Vaccarella S, 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. 2005 Sep; 17-23;366(9490):991-Available from: https://doi.org/10. 1016/S0140-6736(05)67069-9.
- Wentzensen N, Schiffman M, Palmer T, Arbyn M. Triage of HPV positive women in cervical cancer screening. J Clin Virol. 2016;76 Suppl 1(Suppl 1):S49–S55. doi:10.1016/ j.jcv.2015.11.015.
- Torres-Ibarra, L., Cuzick, J., Lorincz, A.T., et al., 2019. Comparison of HPV-16 and HPV-18 Genotyping and Cytological Testing as Triage Testing Within Human Papillomavirus-Based Screening in Mexico. JAMA Netw Open. 2 (11), e1915781. https://doi.org/10.1001/jamanetworkopen.2019.15781.
- Koliopoulos G, Nyaga VN, Santesso N, Bryant A, Martin-Hirsch PPL, Mustafa RA, et al. M. Cytology versus HPV testing for cervical cancer screening in the general population. Cochrane Database of Syst Rev. 2017 Aug; 10(8):CD008587. Available from: https:// doi.org/10.1002/14651858.CD008587.pub2.
- Bennett, K.F., Waller, J., Ryan, M., Bailey, J.V., Marlow, L.A.V., 2019. The psychosexual impact of testing positive for high-risk cervical human papillomavirus (HPV): A systematic review. Psychooncology 28 (10), 1959–1970. https://doi.org/10.1002/ pon.5198.
- McCaffery K, Waller J, Nazroo J, Wardle J. Social and psychological impact of HPV testing in cervical screening: a qualitative study. Sex Transm Infect. 2006; 82:169-174. Available from: http://dx.doi.org/10.1136/sti.2005.016436.
- Kahn JA, Slap GB, Bernstein DI, Kollar LM, Tissot AM, et al. Psychological, behavioral, and interpersonal impact of human papillomavirus and Pap test results. J Womens Health (Larchmt). 2005 Sept; 14:650-659. Available from: https://doi.org/10.1089/ iwh.2005.14.650.
- Dominiak-Felden G, Cohet C, Atrux-Tallau S, Gilet H, Tristram A, et al. Impact of human papillomavirus-related genital diseases on quality of life and psycho-social wellbeing: results of an observational, health-related quality of life study in the UK. BMC Public Health. 2013 Nov; 13:1065. Available from: https://doi.org/10.1186/1471-2458-13-1065.
- Smith RA, Hernandez R. Catona, D. Investigating Initial Disclosures and Reactions to Unexpected, Positive HPV Diagnosis. West J Commun. 2014 Jul; 78(4):426-440. Available from: https://doi.org/10.1080/10570314.2013.786120.
- Castro Vásquez, M.C., 2014. Arellano Gálvez MC. Redes sociales de apoyo y género: vivencia de mujeres con VPH, displasias y cáncer cervicouterino. La ventana. Revista de estudios de género. 5 (39), 208–240.
- León-Maldonado L, Wentzell E, Brown B, Allen-Leigh B, Torres-Ibarra L, Salmerón J, Lazcano-Ponce E. Perceptions and Experiences of Human Papillomavirus (HPV) Infection and Testing among Low-Income Mexican Women. PLoS One. 2016 May; 11(5):e0153367. Available from: https://doi.org/10.1371/journal.pone.0153367.
- Flyan, F., 1998. Screening for cervical cancer: a rewiew of womeńs attitudes, knowledge, and behaviour. Br J Gen Pract. 48 (433), 1509–1514.

- Sharpe P, Brandt H, Mccree D. Knowledge and beliefs about abnormal Pap test results and HPV among women with high-risk HPV: Results from in-depth interviews. Women Health. 2005; 42(2):107-133. Available from: https://doi.org/10.1300/ J013v42n02_07.
- Liebermann, VanDevanter, 2018. Hammer, Fu, Social and Cultural Barriers to Women's Participation in Pap Smear Screening Programs in Low- and Middle-Income Latin American and Caribbean Countries: An Integrative Review. Journal of Transcultural Nursing 29 (6), 591–602.
- Anhang R, Wright TC Jr, Smock L, Goldie SJ. Women's desired information about human papillomavirus. Cancer. 2004 Jan; 100(2): 315-320. Available from: https://doi.org/ 10.1002/cncr.20007.
- Wiesner Ceballos C, Acosta Peñaloza J, Díaz del Castillo A, Tovar Murillo S, Salcedo Fidalgo H. Efectos psicológicos y sociales que genera la prueba del virus del papilloma. 2009; 13(3):145-156. Available from: https://doi.org/10.1016/S0123-9015(09)70133-7.
- Maissi, E., Marteau, T.M., Hankins, M., Moss, S., Legood, R., Gray, A., 2004. Psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: cross sectional questionnaire study. BMJ. 328 (7451), 1293. https://doi.org/10.1136/bmj.328.7451.1293.
- McBride, E., Marlow, L.A., Forster, A.S., Ridout, D., Kitchener, H., Patnick, J. and Waller, J. (2019), Anxiety and distress following receipt of results from routine HPV primary testing in cervical screening: The psychological impact of primary screening (PIPS) study. Int. J. Cancer. doi:10.1002/ijc.32540.
- Kitchener HC, Fletcher I, Roberts C, Wheeler P, Almonte M, Maguire P. The psychosocial impact of human papillomavirus testing in primary cervical screening-a study within a randomized trial. Int J Gynecol Cancer. 2008 Jul-Aug; 18(4):743-8. Available from: https://doi.org/10.1111/j.1525-1438.2007.01113.x.
- Gago J, Paolino M, Arrossi S. Factors associated with low adherence to cervical cancer follow-up retest among HPV+/ cytology negative women: a study in programmatic context in a low-income population in Argentina. BMC Cancer. 2019 Apr; 19(1):367. Available from: https://doi.org/10.1186/s12885-019-5583-7.
- Paolino M, Arrossi S. Analysis of the reasons for abandoning the follow-up and treatment process in women with pre-cancerous cervical lesions in the province of Jujuy: implications for health management. Salud Colect. 2012; 8(3):247–61. Available from: https://doi.org/10.1590/S1851-82652012000400003.

Wiesner Ceballos C, Acosta Peñaloza J, Díaz del Castillo A, Tovar Murillo S, Salcedo

Fidalgo H. Efectos psicológicos y sociales que genera la prueba del virus del papiloma humano: un estudio exploratorio. Revista Colombiana de Cancerología. 2009; 13:145-156. Available from: https://doi.org/10.1016/S0123-9015(09)70133-7.

- Wiesner C, Acosta J, Diaz Del Castillo A, Tovar S. Social representations of human papillomavirus in Bogota, Colombia. Med Anthropol. 2012; 31: 77-92. Available from: https://doi.org/10.1080/01459740.2011.633947.
- Arrossi, S., Curotto, M., Thouyaret, L., Paolino, M., Cuberli, M., Laudi, R., 2016. Manual para la implementación del Test de VPH en contexto programático. Ministerio de Salud de la Nación, Buenos Aires.
- Schoenberg N, Baltisberger J, Bardach S, Dignan M. Perspectives on Pap test follow-up care among rural Appalachian women. Women Health. 2010; 50(6):580-597. Available from: https://doi.org/10.1080/03630242.2010.516702.
- Lee TS, Kothari-Talwar S, Singhal PK, Yee K, Kulkarni A, Lara N, et al. Cross-sectional study estimating the psychosocial impact of genital warts and other anogenital diseases in South Korea. BMJ Open. 2019 Mar; 9(3):e025035. Published 2019 Mar 20. Available from: http://dx.doi.org/10.1136/bmjopen-2018-025035.
- Mast TC, Zhu X, Demuro-Mercon C, Cummings HW, Sings HL, Ferris DG. Development and psychometric properties of the HPV Impact Profile (HIP) to assess the psychosocial burden of HPV. Curr Med Res Opin. 2009 Nov; 25(11):2609–19. Available from: https://doi.org/10.1185/03007990903238786.
- Andreassen, T., Hansen, B.T., Engesaeter, B., et al., 2019. Psychological effect of cervical cancer screening when changing primary screening method from cytology to highrisk human papilloma virus testing. Int J Cancer. 145 (1), 29–39. https://doi.org/10. 1002/ijc.32067.
- O'Connor M, Costello L, Murphy J, Prendiville W, Martin C M, O'Leary JJ, et al. Influences on human papillomavirus (HPV)-related information needs among women having HPV tests for follow-up of abnormal cervical cytology. J Fam Plann Reprod Health Care. 2015 Apr; 41(2):134-141. Available from: http://dx.doi.org/10.1136/jfprhc-2013-100750.
- INDEC, Instituto Nacional de Estadísticas y Censos [Internet]. Sistema Integrado de Estadísticas Sociodemográficas (SESD). Dirección de Estadísticas Sectoriales en base a los Censos Nacionales de Población, Hogares y Viviendas 2001 y 2010 [cited 2019 Sept 17]. Available from: https://www.indec.gob.ar/indec/web/Institucional-Indec-IndicadoresSociodemograficos.
- Pan American Health Organization. Integrating HPV testing in cervical cancer screening program: a manual for program managers. Washington, D.C.: PAHO, 2016.