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Women's acceptability of and experience with primary human papillomavirus testing for cervix screening: HPV FOCAL trial cross-sectional online survey results

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Objective: To study participant's acceptability of and attitudes towards human papillomavirus (HPV) testing compared to cytology for cervical cancer screening, and what impact having an HPV positive result may have in future acceptability of screening.

Design: Cross-sectional online survey of clinical trial participants.

Setting: Primary care, population-based Cervix Screening Program, British Columbia, Canada.

Participants: A total of 5,532 participants from the HPV FOCAL Trial, in which women received HPV and cytology testing at study exit were included in the analysis. Median age was 54 years. The median time of survey completion was 3 years after trial exit.

Outcome measures: Acceptability of HPV testing for primary cervical cancer screening (primary); attitudes and patient perceptions towards HPV testing and receipt of HPV positive screen results (secondary).

Results: Most respondents (63%) were accepting of HPV testing, with the majority (69%) accepting screening to begin at age 30 with HPV testing. Only half of participants (54%) were accepting of an extended screening interval of 4 to 5 years. In multivariable regression, women who reported HPV testing as acceptable were more likely to have received an HPV positive screen test result during the trial (OR=1.41 95%CI: 1.11,1.80), and were older (OR= 1.01, 95%CI:1.00,1.02).

Conclusions: In this evaluation of acceptability and attitudes regarding HPV testing for cervix screening, most are accepting of HPV testing for screening; however, findings indicate heterogeneity in concerns and experiences surrounding HPV testing and receipt of HPV positive results. These findings provide insights for the development of education, information, and communication strategies during implementation of HPV-based cervical cancer screening.

Trial Registration: ISRCTN79347302 and ClinicalTrials.gov Identifier: NCT00461760

ARTICLE SUMMARY

'Strengths and limitation of this Study'

- Measures of acceptability and patient perceptions of HPV testing within a primary cervix screening program.
- Reports on acceptability of increased screening interval and delayed onset of screening initiation, and impact of a positive HPV test result.
- Recommendations for key health promotion messaging to address potential barriers to HPV testing for primary cervical screening.
- Limitations include that participants were recruited from a large clinical trial on HPV testing for cervical cancer screening and may not be representative of the general screening population.

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INTRODUCTION

It is well established that persistent infection with an oncogenic strain of the human papillomavirus (HPV), the most common sexually transmitted infection around the world, is the causative agent for most cervical cancers [1,2]. There is a robust body of evidence regarding the superior performance of HPV vs. cytology screening in detection of cervical intraepithelial neoplasia (CIN) grade 2 or worse (CIN2+) and greater protection against cervical cancer [3–5]. As such, several countries around the world have implemented primary HPV testing for cervical cancer screening, including Australia, the Netherlands, and the UK, with many other jurisdictions in various planning stages for HPV-based screening implementation. A shift to an HPV-based screening approach results in different program guidelines and, thus, a different experience for the person undergoing screening. The very high negative predictive value of HPV testing permits the interval between screens to be extended to 5 or more years compared to cytology testing, recommended every 2 to 3 years in most jurisdictions [5–7]. Due to high prevalence and regression rates of HPV infection in younger women, HPV-based screening may not be recommended until 25 to 30 years of age [5,6]. In addition, being screened for cervical cancer with a test for a sexually transmitted infection can result in anxiety and concern for those undergoing screening [8,9].

With such a transformative change in what is arguably a well-established screening paradigm, it is crucial to examine women's readiness or acceptance of HPV testing compared to cytology testing for screening, to ensure engagement in screening is not hampered by a change in technology or guidelines. This unintended consequence was illustrated in Australia, prior to the change in the national program from cytology to HPV screening, when a 2017 petition opposing the changes garnered 70,000 signatures [10]. Respondents to the Australian survey indicated concerns about such things as the extended interval and missing cancer cases in younger

women as a result of the program change [10]. Despite enhancements to screening efficacy and safety, a successful change in technology requires acceptance by those who undergo screening. Anticipating women's questions and concerns prior to implementation of program changes can mitigate resistance to change and assist in the design of targeted education strategies.

This analysis is of the 48-month exit survey for the Human Papillomavirus For Cervical Cancer Screening Trial (HPV FOCAL). HPV FOCAL is currently the only North American trial comparing primary HPV testing to cytology (liquid-based) for screening within an organized program, which also provides us with the unique opportunity to assess women's experiences with HPV testing in a population-based program setting. The primary objective of this analysis was to explore participant's acceptability of and attitudes towards HPV testing compared to cytology for cervical cancer screening, and what impact having an HPV positive result may play in future acceptability of screening.

METHODS

Participants

Survey participants were recruited through the HPV FOCAL trial, a publicly funded randomized control trial comparing primary HPV testing every four years (HPV arm) to liquid-based cytology testing (cytology arm) every two years for cervical cancer screening (ISRCTN79347302). HPV FOCAL recruited women, 25-65 years of age, from two largely metro areas in British Columbia who were due for cervical cancer screening from 2008 through to 2012. Trial design and primary outcome results have been previously described in detail [3,11–14]. Participants were provided with information on HPV, HPV testing and cervical cancer upon enrollment and throughout the trial follow-up period. A total of 9552 women were randomized to the HPV arm and 9457 women to the cytology arm. Women from both the HPV and cytology arms completed trial exit screening between 2012 and 2016, where they received HPV and cytology co-testing at the exit screen. Results were provided to their primary care provider, who then conveyed them to the participants. From August 2017-February 2018 women from both arms who had attended the 48-month exit screen were invited to complete the online exit survey (FIGURE 1).

HPV FOCAL exit survey

The survey included 26 items that asked participants about HPV knowledge and information seeking before and during the study, acceptability of HPV testing, willingness to increase the screening interval, commencement screening age for HPV testing, attitudes and concerns about test positive results and communication needs around screening results, in addition to demographic details (SUPPLEMENTARY FILE). Reponses included 7- and 5-point Likert scales, and survey responses were linked to HPV FOCAL trial screen test results. Survey items were based upon previous HPV FOCAL surveys assessing HPV testing acceptance [15] The survey was distributed and managed using the web-based platform of Fluidsurveys

(www.fluidsurveys.com). The survey was pilot tested and revised for face and content validity with approximately 20 women, aged 30 and above prior to distribution to FOCAL participants.

Patient and public involvement

Patient concerns and questions identified the need for the study. Patients were involved in pilot testing and revision of the survey.

Response rate and inclusion criteria

Participants from the HPV FOCAL trial from both the HPV and cytology arms who had completed their study 48 month exit screen, had indicated consent to be contacted for future research, and for whom email addresses were available were eligible for survey invitation. The invite to complete the survey was sent via email, with one reminder sent a month later for those who had not initiated or completed the survey. Participants were provided with a unique study identifier to access the survey and no personal identifiers were captured during survey completion. Participants were informed they had the option to complete none, some, or all of the survey with completion of survey questions as indication of consent.

Survey completeness was reviewed, and duplicate surveys, where the same woman completed all or some of the survey more than once, were identified. For those with a duplicate entry, the first complete survey was used in the analysis with all other survey attempts discarded. Response rate (%) was the sum of completed surveys plus partial surveys, divided by the number of invitations sent to eligible valid email addresses, as per the American Association for Public Opinion Research guidelines[16]. Non-response included: refusals (clicked the survey link, but did not complete consent or any items), and those assumed eligible with no response received. Email addresses that were undeliverable were considered invalid and not included in the analysis.

Statistical analysis

Survey respondents were compared to HPV FOCAL trial participants on age, study arm, and location of trial recruitment to explore if survey sample was representative of FOCAL trial population.

Our main outcome of HPV testing acceptability was assessed by response to the question "having an HPV test instead of a Pap to screen for cervical cancer is acceptable to me", which was dichotomized from a 5-point Likert scale, with those reporting strongly agree or agree, categorized as 'accepting', and those reporting neutral, don't know, disagree and strongly disagree as 'not accepting' of HPV testing. This categorization was chosen to capture those who were truly accepting and biased towards the null. Only complete surveys were included, with those who were missing or preferred not to answer excluded. Participants were classified as being HPV positive, if they received an HPV positive screening result at any point during their participation in the HPV FOCAL trial, otherwise a participant was classified as HPV negative.

Bivariable analysis explored differences in acceptability of HPV testing based on demographics, HPV screening test result, and length of time since study exit. Factors associated with acceptability, such as HPV screening starting at 30 years of age and increased screening interval, were also examined.

Socio-demographics and attitudes towards HPV testing were explored descriptively with Chi-square and Fisher's exact tests (where applicable) for categorical variables and median score test for continuous variables.

Multivariate logistic regression was used to explore the association of the acceptability of HPV testing with *a priori* identified confounding variables that reached p<0.2 in bivariable analysis. Level of significance was 0.05. All statistical analyses were performed in SAS 9.4 and R4.02.

Ethics Approval

Ethics approvals for survey was received by the University of British Columbia Research Ethics Board (H06-04032). In addition, a privacy review was undertaken to ensure the survey complied with provincial privacy legislation.

RESULTS

Survey invites were administered from August 2017 through to February 2018. A total of 14,535 participants from both the HPV and cytology arms in HPV FOCAL trial were identified as eligible to receive 48-months exit online survey, of which 13,176 were delivered to a valid email address FIGURE 1). There were 5,532 surveys completed, of which 4,938 were fully and 594 partially completed.

Characteristics of respondents

The median age of participants completing the survey was 54 years (IQR: 46,62) (Table 1). The median time of survey completion was 3 years after study exit. The majority of respondents (67%) had completed college or higher education and 77% reported living with a partner. Survey respondents were comparable to HPV FOCAL trial participants based on study arm, age at HPV FOCAL trial enrollment, and geographical location. Survey respondents and non-respondents were comparable by study arm and marital status, but those who responded to the survey were slightly older than non-responders, although this was not a meaningful difference.

Acceptability of HPV testing for Screening

Overall, 63% of survey respondents agreed or strongly agreed that HPV testing for cervical cancer screening was acceptable, with 37% not agreeing (11% disagree, 16% neutral, 10% don't know) (Table 1). There were no significant associations between acceptability of HPV testing and marital partnership status, time since study exit, education or income. Women who received an HPV positive result at any point during HPV FOCAL trial and who were older were more accepting of HPV testing compared to those who remained HPV negative during trial participation.

In multivariate analysis, women who reported HPV testing as acceptable were more likely to have received an HPV positive screen test result at some point during the trial (OR 1.41 95%CI 1.11,1.80, p=0.005), and were older (OR 1.01, 95%CI 1.00,1.02, p=0.01) (Table 2).

Over half of respondents (54%) agreed with the statement "I would be willing to have an HPV test every 4-5 years instead of a Pap every 3 years". There was a significant difference in acceptability of an extended screening interval between those who reported being accepting of HPV testing compared to those who were not accepting. Overall, 69% responded that HPV testing starting at age 30 was acceptable, with over 80% of those who were accepting of HPV testing reporting agreement with a higher screening age (30 years or over) compared to Pap testing (Table 1).

In addition, 66% of respondents reported that an extended screening would not result in less visits to their healthcare provider for other medical reasons, indicating that despite the extended interval recommended with HPV-based screening, women would continue to see their providers for medical reasons as needed.

Attitudes towards an HPV Positive Test Result:

Survey respondents were asked to rate their level of agreement with a variety of statements regarding attitudes surrounding receipt of HPV positive results (Table 3). Women were asked if they would be more concerned about receiving a positive HPV test or an abnormal Pap result, for which most respondents (73%) reported that both screening outcomes would concern them equally. However, those that reported HPV testing to be acceptable, reported that an HPV positive result would concern them more (14%) than an abnormal Pap. This was statistically different compared to those who were not accepting of HPV testing, who responded that abnormal Pap test results would concern them more. The difference in distribution between these responses was statistically significant.

Most respondents who were not accepting of HPV testing indicated that having a sexually acquired infection would concern them differently than having abnormal Pap results. The relationship between level of agreement with HPV testing acceptability and ones' level of concern about having a sexually acquired infection was significant. Regardless of a respondent's reported HPV testing acceptability, most respondents felt it important to them to know who gave them HPV and when they acquired HPV (72% and 78% respectively). Most respondents indicated they disagreed or were neutral regarding feeling judged for having HPV, and there was no significant relationship between feeling judged and level of agreement with HPV testing. More respondents who were accepting of HPV testing indicated they would feel comfortable telling their partner if they had HPV, which was in contrast to those who were not accepting of HPV testing; these differences indicated a significant relationship between HPV testing acceptance and comfort disclosing HPV status to a partner. Regardless of level of agreement with HPV testing, most respondents (79%) indicated they would feel concerned about transmitting HPV to their partner(s). More respondents who were accepting of HPV

testing would feel confident in the recommendations from their provider for the management of their HPV positive results. There was a significant association between level of agreement with HPV testing and degree of confidence with provider recommendations.

Sources of information for HPV testing and screening:

Overall, the most reported important sources of information were health care providers and BC Cancer, the agency that is responsible for the cervix screening program in British Columbia (Table 4). In addition, those that are accepting of HPV testing were more likely to look to their health care providers and BC Cancer as important sources of information. Regardless of one's level of agreement with HPV testing for screening, friends and family or social media were not as important as health care providers and BC Cancer for sources of information.

DISCUSSION

Acceptability of, and attitudes, towards primary HPV testing were analysed from 5,532 women who completed HPV testing as part of the HPV FOCAL trial, which was embedded within an organized population-based cervical cancer screening program. Most respondents (63%) were accepting of HPV testing for cervix screening and for screening with HPV testing to begin at age 30 (69%). Just over half were accepting of HPV testing with the extended screen interval of 4 to 5 years (54%). Although most women were accepting, the proportion of respondents indicating they disagreed with or were neutral in their acceptance of HPV testing and of extended intervals was higher than we expected considering this was a group of people who were provided with education and information about HPV, HPV testing, and cervical cancer. These findings are similar to other studies that indicate women have concerns about the extended interval recommended with HPV testing [10,17–19], stemming from a belief that a cancer diagnosis may be missed through extension of the interval. Considering study participants received information

regarding HPV, the natural history of HPV and cervical cancer, and the rationale for HPV testing compared to the Pap test, these findings indicate that additional research and patient engagement is needed to gain insights and identify and develop resources or procedures to address barriers to HPV testing and an extended screening interval.

This multivariate analysis found that those who received positive HPV test results at some point during the trial were more likely to be accepting of HPV testing for cervix screening than those who never received an HPV positive result. Those who tested HPV positive would have received additional information and counseling from their healthcare provider and or a Study nurse, which would have included information that would not necessarily have been provided to those who tested HPV negative. This additional reinforcement of education, and an opportunity for dialogue when receiving the positive result, may have facilitated improvement in knowledge and subsequently, enhanced acceptance of HPV testing. Other findings have indicated that increased HPV and HPV screening knowledge can be a facilitator of HPV screening acceptance[20].

One of the concerns with an extended screening interval is if women would be less likely to consult with the health care provider for other medical reasons. When we asked participants if they would be less willing to see a healthcare provider for other medical reasons if the interval for cervix screening were increased, most respondents said they would not be less willing, indicating that the extended interval for cervix screening would not prevent them from seeking care as needed. This finding can provide reassurance to healthcare professionals who have concerns that the extended screening interval recommended with HPV-based screening would lead to fewer visits to a clinician, given that the cervical screen visit is often an opportunity for the clinician to assess other preventive care or medical issues [21].

Respondents' concerns regarding receipt of HPV positive results were varied. Nearly 93% of the respondents never received an HPV positive result during the HPV FOCAL trial. As a result, the majority of responses evaluate attitudes and experiences for those who did not actually receive HPV positive results, and therefore, reflect how the respondents would hypothetically feel if they were to receive HPV positive results. Of the respondents, 7.5% had received an HPV positive result at some point during their trial participation.

Most participants indicated that having HPV would cause them concern about having cervical cancer. The majority of participants reported that having either an abnormal Pap or a positive HPV test would concern them; however, for those that had tested positive for HPV, they reported that an HPV test would concern them more compared to an abnormal Pap. Overall, participants' perceptions about HPV positive results and cervical cancer indicate that increased knowledge regarding the specificity of HPV testing for cervical cancer screening is needed.

Receipt of positive HPV results has been associated with higher anxiety and distress compared to receipt of abnormal Pap results[22–24], which may be due to the fact that HPV is a sexually transmitted infection and has been associated with levels of shame and stigma [25,26]. Most respondents in our survey indicated that receiving results for a sexually acquired HPV infection would concern them differently than having an abnormal Pap test result; however, this belief varied depending on a participant's acceptability of HPV testing. Women who were not accepting of HPV testing indicated that a HPV positive result would concern them differently than abnormal Pap results, compared to those who were accepting of HPV testing [22–24][25,26]. Most respondents, whether they accepted HPV testing or not, felt it important for them to know who gave them HPV and when they got it (71% and 78% respectively). These findings together are reflective of other research findings[9,27,28] and indicate that when developing education and communication strategies, emphasis should be placed on the high

prevalence of HPV in the population, the transient nature of most HPV infections, bringing awareness to the fact an infection may have been acquired several years prior to a positive test result. Differentiating HPV from other STIs may minimize anxiety and facilitate normalization and acceptance[25,29].

Almost 75% of the respondents indicated they felt an HPV positive result would affect their relationship with their partner, or they weren't sure, and almost 80% would be concerned about transmitting HPV to their partners, with many feeling they would be judged for being HPV positive. The stigma associated with HPV, concerns about infidelity and potential partner reactions to the HPV result may underlie these concerns. Previous research has indicated some women question whether partner notification with HPV is necessary [29,30]. Unlike other STIs such as chlamydia or gonorrhea where partner notification is recommended for testing and treatment purposes, there is usually no medical reason to notify the partner of a woman who tested positive for HPV.

Healthcare providers, as trusted and valued sources of information, can influence patients' decision-making patterns regarding health care decisions [17,31] Reflecting other findings, the respondents in this survey indicated that the most important sources of information for them were their healthcare providers and the provincial screening program [17,31]. As a result, program planning for HPV-based screening should ensure health care providers are provided with education and training surrounding HPV prior to program changes, to ensure they are prepared to address women's questions and concerns regarding the paradigm shift from cytology to HPV-based screening.

This study is not without limitations. Survey participants were part of a large clinical trial and were given information about HPV, HPV testing and cervical cancer upon enrollment and,

therefore, may not be representative of the general screening population of British Columbia. The response rate may be considered low at 41%; however, those who have stronger opinions about their screening choices may have been more likely to respond to the survey than those who are more trusting of the health care system and accepting of any future policy changes. In addition, survey respondents were representative of overall participants in the HPV FOCAL trial. The majority of respondents completed the survey approximately 3 years after trial completion and it is possible there was loss of recall of HPV related information provided to them when they consented to participate in the trial, which for many was up to 7 years prior to survey completion. The potential lag time between trial entry and survey completion may impact women's attitudes and beliefs surrounding HPV testing. In addition, most of the participants in this trial were over the age of 50, highly educated and primarily from two urban geographic regions and may not be representative of all screen eligible people in various regions of British Columbia.

CONCLUSIONS

In this study, within an organized screening setting, evaluating acceptability and attitudes around HPV testing from women undergoing HPV-based screening, most are accepting of HPV testing for screening; however, further research is needed to understand factors that can increase acceptability. These findings contribute to the growing body of evidence demonstrating that concerns and experiences surrounding HPV testing and receipt of HPV positive results are complex and varied. As many cervix screening programs begin HPV-based screening and are planning implementation strategies, attention to patient engagement to address potential barriers will be important. As HPV-based screening becomes standard of care, it is plausible that concerns with this paradigm shift will eventually be alleviated with increasing knowledge

and familiarity. These findings provide insight into areas of importance that should be considered for development of education, information, and communication strategies.

Figure 1: Study flowchart and participant disposition

Table 1: Demographic characteristics of respondents and bivariable analysis of acceptability of HPV testing

			Having an HPV test instead of a Pap smear to screen for cervical cancer is acceptable to me		
		Total (N)	**Not acceptable (Disagree/Neutral/Don't know)**	**Acceptable (Agree)**	**p-value**
Total (N)		**5336**	1993 (37.4%)	3343 (62.6%)	
Age	median [IQR]	5336	53.35 [45.35, 61.19]	54.23 [45.64, 61.72]	0.051
Marital Status[a]					
	Living with a partner	3806	1438 (78.7)	2368 (76.6)	0.095
	Living without a partner	1115	390 (21.3)	725 (23.4)	
Education[a]					
	Complete College or higher	3317	1250 (68.5)	2067 (66.7)	0.221
	Incomplete post-secondary or less	1607	576 (31.5)	1031 (33.3)	
Income[a]					
	Less than $75000	1501	529 (32.0)	972 (34.0)	0.175
	$75,000 or more	3014	1126 (68.0)	1888 (66.0)	
HPV Testing Status during FOCAL trial					
	Never tested HPV positive	4937	1867 (93.7) 37.8%	3070 (91.8) 62.2%	0.015*
	At least one HPV positive result	399	126 (6.3) 31.6%	273 (8.2) 68.4%	
Time since exit from FOCAL trial, Years					
	median [IQR]	5336	3.09 [2.26, 3.91]	3.04 [2.23, 3.93]	0.616
I would be willing to have an HPV test every 4-5 years instead of a Pap every 3 years[a]					
	Agree	2858	386 (19.5)	2472 (74.2)	<0.001*
	Disagree	1096	744 (37.6)	352 (10.6)	
	Neutral	1353	847 (42.8)	506 (15.2)	
Receiving HPV testing starting at age 30 is acceptable to me[a]					
	Agree	3635	944 (47.8)	2691 (81.0)	<0.001*
	Disagree	682	423 (21.4)	259 (7.8)	
	Neutral	981	608 (30.8)	373 (11.2)	
If cervical cancer screening was to occur every 4 or 5 years, instead of every 3 years, I would be less likely to visit my health care provider for other health reasons. [a]					
	Agree	1062	405 (20.4)	657 (19.7)	0.814
	Disagree	3517	1303 (65.7)	2214 (66.4)	
	Neutral	735	274 (13.8)	461 (13.8)	

Table Notes: [a] Missing values up to 5,336 = not reported or prefer not to answer, * significant to p<0.05

Table 2: Multivariate analysis of predictors for participants who are accepting of HPV testing instead of Pap testing for cervical cancer screening.

Variable	OR (95% CI)	P-value
Age at survey completion (years)	1.01 (1.00,1.02)	0.01
Received HPV positive results during study (Yes vs No)	1.41 (1.11,1.80)	0.005
Education (Incomplete post-secondary or less vs Complete College or higher)	1.06 (0.93,1.21)	0.41
Marital status (Living without a partner vs Living with a partner)	1.04 (0.88,1.22)	0.67
Income ($75000 or more vs. less than $75000)	0.97 (0.84,1.12)	0.68

487 **Table 3:** Experiences receiving HPV positive results

		HPV testing instead of Pap testing for cervical cancer:		
	Total (N)	**Not acceptable**	**Acceptable**	p-value
	5336	1993 (36.0%)	3343 (60.4%)	
What would concern you most: Being told you had abnormal Pap results, or being told you had HPV?[a]				
Being told I have abnormal Pap test results	668	274 (14.0)	394 (11.9)	<0.001*
Being told I have HPV	683	197 (10.0)	486 (14.7)	
Both would concern me equally	3855	1464 (74.7)	2391 (72.2)	
Neither would concern me	67	26 (1.3)	41 (1.2)	
Having an infection that is sexually acquired (HPV) doesn't concern me any differently than abnormal Pap results would[a]				
Agree	1412	442 (24.8)	970 (31.5)	<0.001*
Disagree	2465	974 (54.6)	1491 (48.4)	
Neutral	987	369 (20.7)	618 (20.1)	
It would be important for me to know who gave me HPV[a]				
Agree	3468	1251 (70.3)	2217 (71.7)	0.094
Disagree	545	188 (10.6)	357 (11.5)	
Neutral	859	340 (19.1)	519 (16.8)	
It would be important for me to know when I got HPV[a]				
Agree	3795	1372 (76.9)	2423 (78.3)	0.131
Disagree	432	151 (8.5)	281 (9.1)	
Neutral	650	260 (14.6)	390 (12.6)	
I think people would judge me for having HPV[a]				
Agree	1775	663 (37.4)	1112 (36.0)	0.307
Disagree	1419	495 (27.9)	924 (30.0)	
Neutral	1666	617 (34.8)	1049 (34.0)	
I would feel comfortable telling my partner if I had HPV[a]				
Agree	3391	1198 (67.4)	2193 (71.3)	0.016*
Disagree	709	284 (16.0)	425 (13.8)	
Neutral	755	296 (16.6)	459 (14.9)	
I would not be concerned about transmitting HPV to my partner[a]				
Agree	515	174 (9.8)	341 (11.1)	0.095
Disagree	3825	1400 (78.7)	2425 (79.0)	
Neutral	509	205 (11.5)	304 (9.9)	
Being HPV positive would not affect my relationship with my partner[a]				
Agree	1249	445 (25.1)	804 (26.3)	0.035*
Disagree	2003	708 (39.9)	1295 (42.3)	
Neutral	1584	622 (35.0)	962 (31.4)	
Having HPV would not cause me any concern about cervical cancer[a]				
Agree	181	52 (2.9)	129 (4.2)	0.012*
Disagree	4112	1499 (84.1)	2613 (84.8)	
Neutral	569	231 (13.0)	338 (11.0)	
I would feel confident in the recommendations from my healthcare provider for follow-up of my HPV positive result[a]				
Agree	3876	1323 (74.0)	2553 (82.5)	<0.001*
Disagree	226	97 (5.4)	129 (4.2)	

	Neutral	780	369 (20.6)	411 (13.3)

Table Notes: : [a] Missing values up to 5,336 = not reported or prefer not to answer,, * significant to p<0.05

488
489

Table 4: Important sources of HPV information

			Having an HPV test instead of a Pap smear to screen for cervical cancer is acceptable to me		
		Total (N)	**Not acceptable**	**Acceptable**	p-value
		5336	1993 (36.0%)	3343 (60.4%)	
Health Care Provider[a]					
	Important	3405	1128 (59.3)	2277 (70.1)	<0.001*
	Neutral	1256	560 (29.5)	696 (21.4)	
	Not Important	487	213 (11.2)	274 (8.4)	
BC Cancer (organizes screening in BC)[a]					
	Important	2713	907 (48.7)	1806 (56.9)	<0.001*
	Neutral	1649	673 (36.1)	976 (30.8)	
	Not Important	673	283 (15.2)	390 (12.3)	
Govt Websites (ex: Canadian Cancer Society/Public Health Agency Canada)[a]					
	Important	2111	734 (39.9)	1377 (44.2)	0.011*
	Neutral	1914	748 (40.6)	1166 (37.5)	
	Not Important	928	359 (19.5)	569 (18.3)	
Other websites (WebMd, blogs)[a]					
	Important	1597	567 (31.3)	1030 (33.7)	0.112
	Neutral	1997	776 (42.8)	1221 (40.0)	
	Not Important	1273	469 (25.9)	804 (26.3)	
Friends/family[a]					
	Important	1336	453 (25.0)	883 (28.9)	0.012*
	Neutral	1865	725 (40.0)	1140 (37.3)	
	Not Important	1670	634 (35.0)	1036 (33.9)	
Social media[a]					
	Important	580	197 (10.9)	383 (12.6)	0.004*
	Neutral	1562	633 (35.1)	929 (30.7)	
	Not Important	2693	975 (54.0)	1718 (56.7)	

Table Notes: : [a] Missing values up to 5,336 = not reported or prefer not to answer,, * significant to p<0.05

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Contributors: LWS involved in conception, design and implementation of the research presented here, drafting and review of manuscript; CSR conducted statistical analysis and contributed to drafting and review of manuscript; LG conducted statistical analysis; MK, ML, REM, GS, SP ELF and DV are co-investigators on the HPV FOCAL Study and were involved in FOCAL trial design and trial management; AJC and GO are co-principal investigators of the FOCAL Study and oversaw conduct of the trial; all authors take responsibility for the credibility of the data and analysis and critically reviewed the paper and approved the final version.

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Competing interests: MK and AC were principal investigators, and GO, DV and EF were co-investigators on industry funded (Hologic Inc, and Roche) investigator-led adjunct studies to the HPV FOCAL Trial, designed to compare the performance of different HPV testing assays. No investigators personally benefitted financially. Funding for these adjunct studies was not applied to the operation of the HPV FOCAL results presented in this paper. ELF served as an occasional advisor for companies involved with HPV vaccines (Merck, GSK) and HPV diagnostics (Roche). He also holds a patent "DNA methylation markers for early detection of cervical cancer," registered at the Office of Innovation and Partnerships, McGill University, Montreal, Quebec, Canada.

Patient consent for publication: Not required

Ethics approval: Ethics approvals for survey was received by the University of British Columbia Research Ethics Board (H06-04032).

Provenance and Peer review: Not commissioned; externally peer reviewed.

Data availability Statement: Deidentified participant data is available upon consideration and reasonable request.

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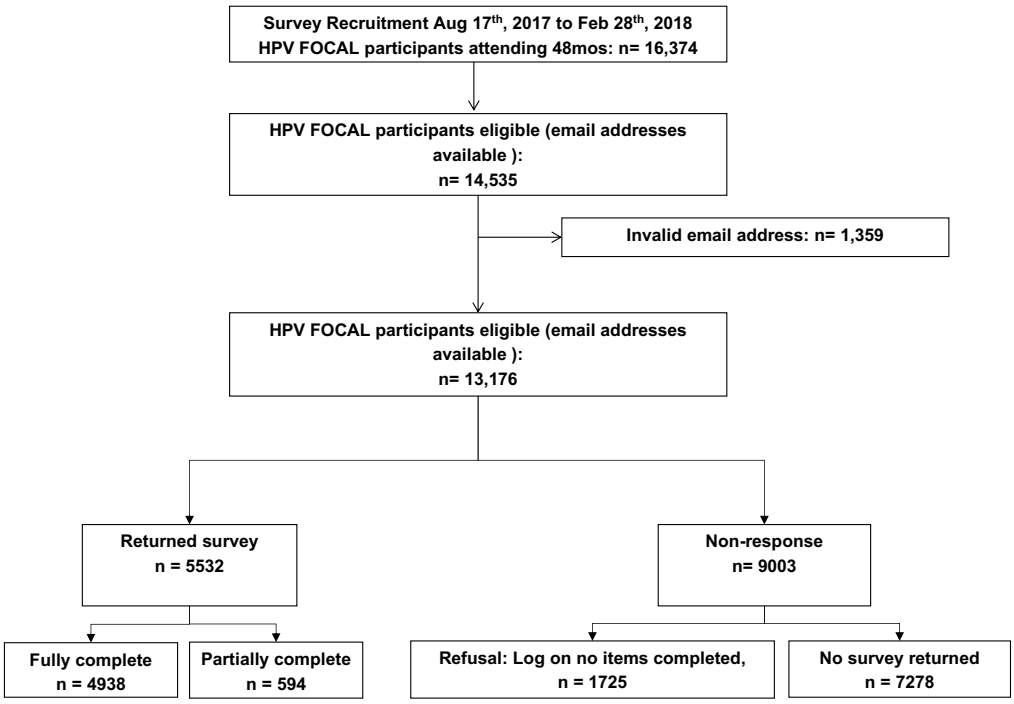
Figure 1: Study Flowchart and participant disposition



Thank you for contributing to the HPV FOCAL Study! As you know the purpose of the study was to evaluate HPV testing for cervical cancer screening in BC. The results of the FOCAL study will be very important as Canadian programs consider adopting HPV testing to screen for changes that may lead to cervical cancer. We are interested to learn about your experience and understanding of HPV testing for cervical cancer screening. ***As a reminder, ALL women who completed a 4 year exit screen received both a Pap smear and an HPV test***

Your input is important to us and can help plan for the future of cervical cancer screening in BC. Please take a few moments of your time to complete the attached survey. You do not have to answer any questions you do not feel comfortable answering.

First we would like to ask about your HPV knowledge before and during the study.

1) *Please rate the following question according to how much you agree or disagree with the statement:*
I know more about HPV and cervical cancer now than I did before I participated in the study:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Not Sure

2) I was aware of my cervical screen (Pap and HPV test) results at completion of the study:

- ☐ No
- ☐ Yes
- ☐ Not sure

3) *Please rate the following question according to how much you agree or disagree with the statement:*
I had enough time to ask my health care provider questions about HPV testing and/or my results.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know
- ☐ Not applicable

4) *Please rate the following question according to how much you agree or disagree with the statement:*
I feel my health care provider was able to answer my questions about HPV:

☐ Strongly Disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly agree
☐ Don't know
☐ Not applicable

5) *Please rate the following statements regarding HPV testing:*
Having my health care provider collect a sample for HPV testing for cervical cancer screening would be:

	<---	**<--**	**<-**	**Neutral**	**->**	**-->**	**--->**	
Accurate	☐	☐	☐	☐	☐	☐	☐	Inaccurate
Safe	☐	☐	☐	☐	☐	☐	☐	Unsafe
Protect my health	☐	☐	☐	☐	☐	☐	☐	Harm my health
Acceptable	☐	☐	☐	☐	☐	☐	☐	Unacceptable

6) Which of the following have been important sources of information for you about HPV/HPV testing?

	Not at all important	**Not that important**	**Neutral**	**Somewhat important**	**Very important**
My health care provider	☐	☐	☐	☐	☐
BC Cancer Agency (including the BC Cancer Agency website)	☐	☐	☐	☐	☐
Government websites (ie: Canadian Cancer Society, Health Canada, Public Health Agency of Canada, BC Ministry of Health)	☐	☐	☐	☐	☐
Other websites (ie: WebMD, blogs, etc)	☐	☐	☐	☐	☐
Friends/family	☐	☐	☐	☐	☐
Social Media (ie: facebook, twitter, etc)	☐	☐	☐	☐	☐

Other comments:……

……

Next we would like to ask how you feel about HPV testing to screen for cervical cancer.

As a reminder, there are over 100 types of the human papillomavirus (HPV), of which about 40 affect the genital region. HPV is very common and most sexually active people will have an infection at some point in their lives, however it usually disappears without a person experiencing any symptoms. Only in cases where a cancer causing HPV type persists for many years, is there a risk that it may lead to cervical cancer.

7) *Please rate the following question according to how much you agree or disagree with the statement:* **Having an HPV test to screen for cervical cancer instead of a Pap smear is acceptable to me:**

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments:……

8) I would be willing to have an HPV test <u>every 4 or 5 years</u> instead of a Pap test every 3 years:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments: ……

Evidence suggests that HPV testing is ideally started no earlier than 30 years of age. Should HPV testing be adopted in the province, it would be available for women starting at age 30 or 35. However, cervical cancer screening could still start at age 25 using the Pap smear as currently recommended in BC.

9) Receiving HPV testing for cervical cancer screening, starting at age 30 is acceptable to me.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

10) If cervical cancer screening was to occur every 4 or 5 years, instead of every 3 years, I would be less likely to visit my health care provider for other health reasons.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Next we would like to understand some of your thoughts about HPV testing compared to the Pap test.

11) What would concern you most: 1) being told you had "abnormal Pap test results" or 2) being told you were "positive for HPV"? (*Check ONE only*)

- ☐ Neither would concern me
- ☐ Being told I have abnormal Pap test results
- ☐ Being told I have HPV
- ☐ Both would concern me equally

Please explain: .....

.....

Next, we would like to learn about your experience of receiving HPV results.

12) If you tested HPV positive during the HPV FOCAL trial, or if you were to test positive for HPV, please rate your level of agreement with the following statements:

	Strongly disagree	**Disagree**	**Neutral/uncertain**	**Agree**	**Strongly Agree**
Although HPV is sexually acquired, having an infection that is sexually acquired does not concern me any differently than abnormal Pap results would.	☐	☐	☐	☐	☐
It would be important for me to know who gave me HPV.	☐	☐	☐	☐	☐
It would be important to me to determine when I got HPV.	☐	☐	☐	☐	☐
I think people might judge me for having HPV.	☐	☐	☐	☐	☐
I would feel comfortable telling my partner about my HPV positive result.	☐	☐	☐	☐	☐
I would not be concerned about transmitting HPV to a sexual partner.	☐	☐	☐	☐	☐
Receiving a positive HPV result would not affect my relationship with my sexual partner.	☐	☐	☐	☐	☐
Having HPV would not cause me any concern about developing cervical cancer.	☐	☐	☐	☐	☐
I would feel confident in the follow up and/or treatment my provider would recommend for my positive HPV result.	☐	☐	☐	☐	☐

Other comments:……
……

13) *Please rate the following statements according to how much you agree or disagree:*
If I tested positive for HPV I felt/would feel:

	Strongly disagree	**Disagree**	**Neutral/uncertain**	**Agree**	**Strongly agree**
Reassured	☐	☐	☐	☐	☐
Relieved	☐	☐	☐	☐	☐
Guilty	☐	☐	☐	☐	☐
Worried	☐	☐	☐	☐	☐
Upset	☐	☐	☐	☐	☐
Surprised	☐	☐	☐	☐	☐

Other comments: ……

14) If you were aware of your results at the end of the trial and they were negative/normal, how confident were you with the safety of these results?

☐ Very unconfident
☐ Somewhat unconfident
☐ Neutral
☐ Somewhat confident
☐ Very confident
☐ Didn't know my results
☐ Not applicable/results were positive

Next we would like to ask about your thoughts about the possibility of women collecting their own sample for HPV testing for cervical cancer screening by inserting a soft Q-tip or brush into the vagina that can then be returned to the laboratory and tested for the presence of HPV. With self-collection, a woman would not need to see a health care provider for pelvic exam for sample collection. Self-collected specimens tested for HPV have been shown to be equivalent to HPV samples taken by a health care provider for detecting abnormalities of the cervix.

15) *Please rate the following statements regarding self-collected samples:*

Collecting my own sample for cervical cancer screening would be:

	<---	**<--**	**<-**	**Neutral**	**->**	**-->**	**--->**	
Accurate	☐	☐	☐	☐	☐	☐	☐	Inaccurate
Safe	☐	☐	☐	☐	☐	☐	☐	Unsafe
Protect my health	☐	☐	☐	☐	☐	☐	☐	Harm my health
Acceptable	☐	☐	☐	☐	☐	☐	☐	Unacceptable

16) I would be willing to collect my own sample/specimen for cervical cancer screening:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments: ……..
……

Finally we'd like to ask some questions that may help us better understand associations between HPV and various other factors.

17) **What is the highest level of education you have achieved?**

- ☐ No formal education
- ☐ Some elementary school
- ☐ Completed elementary school
- ☐ Some high school
- ☐ Completed high school
- ☐ Some post-secondary training (Trades, college, university)
- ☐ Completed trade/vocational/apprenticeship program
- ☐ Completed college
- ☐ Completed university (bachelor degree)
- ☐ Completed university (master degree or higher)

18) Please indicate your current marital status:

- ☐ Single (living WITHOUT a partner)
- ☐ Single (living WITH a partner)
- ☐ Married or common law
- ☐ Divorced
- ☐ Separated (but still legally married)
- ☐ Widowed

19) Not including new partners you have had since you completed the HPV FOCAL study, please indicate to the best of your recollection, how many male partners you have had vaginal intercourse with:

- ☐ 0
- ☐ 1-10
- ☐ 11-49
- ☐ 50+

20) Please enter the total years you have used the following hormonal birth control methods. If never used, please enter "0". (survey build, enter in months)

Method	Total years used	Please place a checkmark in this column if you used this method while participating in the HPV FOCAL study
Oral contraceptive pill	_ _	☐
Contraceptive patch	_ _	☐
Contraceptive vaginal ring	_ _	☐
Hormonal IUD	_ _	☐
Injection (ie: Depo-provera)	_ _	☐
Morning after pill or emergency contraceptive pill	_ _	☐
Implant	_ _	☐

We are trying to better understand how use of specific substances (ie: alcohol, tobacco and marijuana) impacts a woman's potential to develop a long term HPV infection. These following questions help us determine if there is an association between HPV infection and different substances.

21) Have you ever smoked cigarettes?

☐ Yes (daily). For approximately how many years: _ _

☐ Yes (less than daily)

☐ Not at all

22) Were you a regular cigarette smoker during your participation in the HPV FOCAL Study?

☐ Every day…..Approximately how many cigarettes did you smoke per day? _ _

☐ Some days…Approximately how many days did you smoke each week? _ _

☐ Not at all

(Survey build). Only link to Q22 if answered "every day" or "some days" to Q21

23) During your participation in the HPV FOCAL Study, how often did you use marijuana:

- ☐ Never
- ☐ Less than once a month
- ☐ 1-3 times a month
- ☐ Once a week
- ☐ More than once a week
- ☐ Every day

Survey build: skip Q24 if answered "never" to Q23

24) Please indicate the ways you used marijuana during the HPV FOCAL study:

- ☐ Smoking
- ☐ Vaporizing
- ☐ Edible (ie: cakes, cookies, candy, drinks, etc)
- ☐ Pill/capsule
- ☐ Other

25) During your participation in the HPV FOCAL Study, how often did you drink alcoholic beverages?

- ☐ Never
- ☐ Once a month or less
- ☐ 2-3 times a month
- ☐ Once a week
- ☐ 2-3 times a week
- ☐ 4-6 times a week
- ☐ Every day

26) Please estimate your total household income (everyone in your household, excluding roommates):

☐ Less than $10,000

☐ $10,001-25,000

☐ $25,001-50,000

☐ $50,001-75,000

☐ $75,001-100,000

☐ More than $100,000

Thank you for completing this survey! Your responses are highly valued and impact guidelines and recommendations as the province of British Columbia considers changes to cervical cancer screening practices. If you have any questions or comments please feel free to contact the HPV FOCAL study at hpvfocal@bccancer.bc.ca

……

……

SURVEY BUILD: Link to a separate section where respondents can enter their name and contact info to be entered into a draw. We will offer an incentive for survey completion.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6,7*
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	17
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9, 18
Outcome data	15*	Report numbers of outcome events or summary measures	18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	18

		(*b*) Report category boundaries when continuous variables were categorized	n/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Women's acceptability of and experience with primary human papillomavirus testing for cervix screening: HPV FOCAL trial cross-sectional online survey results

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Women's acceptability of and experience with primary human papillomavirus testing for cervix screening: HPV FOCAL trial cross-sectional online survey results

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Objective: To study participant's acceptability of and attitudes towards human papillomavirus (HPV) testing compared to cytology for cervical cancer screening, and what impact having an HPV positive result may have in future acceptability of screening.

Design: Cross-sectional online survey of clinical trial participants.

Setting: Primary care, population-based Cervix Screening Program, British Columbia, Canada.

Participants: A total of 5,532 participants from the HPV FOCAL Trial, in which women received HPV and cytology testing at study exit were included in the analysis. Median age was 54 years. The median time of survey completion was 3 years after trial exit.

Outcome measures: Acceptability of HPV testing for primary cervical cancer screening (primary); attitudes and patient perceptions towards HPV testing and receipt of HPV positive screen results (secondary).

Results: Most respondents (63%) were accepting of HPV testing, with the majority (69%) accepting screening to begin at age 30 with HPV testing. Only half of participants (54%) were accepting of an extended screening interval of 4 to 5 years. In multivariable logistic regression, women who received an HPV positive screen test result during the trial (OR=1.41 95%CI: 1.11,1.80), or were older (OR= 1.01, 95%CI:1.00,1.02) were more likely to report HPV testing as acceptable.

Conclusions: In this evaluation of acceptability and attitudes regarding HPV testing for cervix screening, most are accepting of HPV testing for screening; however, findings indicate heterogeneity in concerns and experiences surrounding HPV testing and receipt of HPV positive results. These findings provide insights for the development of education, information, and communication strategies during implementation of HPV-based cervical cancer screening.

Trial Registration: ISRCTN79347302 and ClinicalTrials.gov Identifier: NCT00461760

ARTICLE SUMMARY

'Strengths and limitation of this Study'

- Measures of acceptability and patient perceptions of HPV testing within a primary cervix screening program.
- Reports on acceptability of increased screening interval and delayed onset of screening initiation, and impact of a positive HPV test result.
- Recommendations for key health promotion messaging to address potential barriers to HPV testing for primary cervical screening.
- Limitations include that participants were recruited from a large clinical trial on HPV testing for cervical cancer screening and may not be representative of the general screening population.

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INTRODUCTION

It is well established that persistent infection with an oncogenic strain of the human papillomavirus (HPV), the most common sexually transmitted infection around the world, is the causative agent for most cervical cancers [1,2]. There is a robust body of evidence regarding the superior performance of HPV vs. cytology screening in detection of cervical intraepithelial neoplasia (CIN) grade 2 or worse (CIN2+) and greater protection against cervical cancer [3–5]. As such, several countries around the world have implemented primary HPV testing for cervical cancer screening, including Australia, the Netherlands, and the UK, with many other jurisdictions in various planning stages for HPV-based screening implementation. A shift to an HPV-based screening approach results in different program guidelines and, thus, a different experience for the person undergoing screening. The very high negative predictive value of HPV testing permits the interval between screens to be extended to 5 or more years compared to cytology testing, recommended every 2 to 3 years in most jurisdictions [5–7]. Due to high prevalence and regression rates of HPV infection in younger women, HPV-based screening may not be recommended until 25 to 30 years of age [5,6]. In addition, being screened for cervical cancer with a test for a sexually transmitted infection can result in anxiety and concern for those undergoing screening [8,9].

With such a transformative change in what is arguably a well-established screening paradigm, it is crucial to examine women's readiness or acceptance of HPV testing compared to cytology testing for screening, to ensure engagement in screening is not hampered by a change in technology or guidelines. This unintended consequence was illustrated in Australia, prior to the change in the national program from cytology to HPV screening, when a 2017 petition opposing the changes garnered 70,000 signatures[10]. Respondents to the Australian survey indicated concerns about such things as the extended interval and missing cancer cases in younger

women as a result of the program change [10]. Despite enhancements to screening efficacy and safety, a successful change in technology requires acceptance by those who undergo screening. Anticipating women's questions and concerns prior to implementation of program changes can mitigate resistance to change and assist in the design of targeted education strategies.

This analysis is of the 48-month exit survey for the Human Papillomavirus For Cervical Cancer Screening Trial (HPV FOCAL). HPV FOCAL is currently the only North American trial comparing primary HPV testing to cytology (liquid-based) for screening within an organized program, which also provides us with the unique opportunity to assess women's experiences with HPV testing in a population-based program setting. The primary objective of this analysis was to explore participant's acceptability of and attitudes towards HPV testing compared to cytology for cervical cancer screening, and what impact having an HPV positive result may play in future acceptability of screening.

METHODS

Participants

Survey participants were recruited through the HPV FOCAL trial, a publicly funded randomized control trial comparing primary HPV testing every four years (HPV arm) to liquid-based cytology testing (cytology arm) every two years for cervical cancer screening (ISRCTN79347302). HPV FOCAL recruited women, 25-65 years of age, from two largely metro areas in British Columbia who were due for cervical cancer screening from 2008 through to 2012. Participants of the HPV FOCAL Trial were engaged in cervical cancer screening through a large population-based screening program, and representative of women at average risk of cervical cancer in North America [11] Trial design and primary outcome results have been previously described in detail [3,11–14]. Participants were provided with information on HPV, HPV testing (including differences between Pap and HPV testing, and the reasons behind an extended interval between negative HPV screens) and cervical cancer upon enrollment and throughout the trial follow-up period. A total of 9552 women were randomized to the HPV arm and 9457 women to the cytology arm. Women from both the HPV and cytology arms completed trial exit screening between 2012 and 2016, where they received HPV and cytology co-testing at the exit screen. Results were provided to their primary care provider, who then conveyed them to the participants. From August 2017-February 2018 women from both arms who had attended the 48-month exit screen were invited to complete the online exit survey (FIGURE 1).

HPV FOCAL exit survey

The survey included 26 items that asked participants about HPV knowledge and information seeking before and during the study, acceptability of HPV testing, willingness to increase the screening interval, commencement screening age for HPV testing, attitudes and concerns about test positive results and communication needs around screening results, in addition to demographic details (SUPPLEMENTARY FILE). Reponses included 7- and 5-point Likert

scales, and survey responses were linked to HPV FOCAL trial screen test results. Survey items were based upon previous HPV FOCAL surveys assessing HPV testing acceptance [15] The survey was distributed and managed using the web-based platform of Fluidsurveys (www.fluidsurveys.com). The survey was pilot tested and revised for face and content validity with approximately 20 women, aged 30 and above prior to distribution to FOCAL participants.

Patient and public involvement

Patient concerns and questions raised during the trial period identified the need for the study, but patients were not involved in the construction of the survey[16]. However, a sample of women who undergo cervical cancer screening in BC were involved in pilot testing of the survey for the purposes of face validity and survey flow and logistics. Based on this feedback, revisions were made to the survey to clarify wording of questions and format of layout.

Response rate and inclusion criteria

Participants from the HPV FOCAL trial from both the HPV and cytology arms who had completed their study 48 month exit screen, had indicated consent to be contacted for future research, and for whom email addresses were available were eligible for survey invitation. The invite to complete the survey was sent via email, with one reminder sent a month later for those who had not initiated or completed the survey. Participants were provided with a unique study identifier to access the survey and no personal identifiers were captured during survey completion. Participants were informed they had the option to complete none, some, or all of the survey with completion of survey questions as indication of consent.

Survey completeness was reviewed, and duplicate surveys, where the same woman completed all or some of the survey more than once, were identified. For those with a duplicate entry, the

first complete survey was used in the analysis with all other survey attempts discarded. Response rate (%) was the sum of completed surveys plus partial surveys, divided by the number of invitations sent to eligible valid email addresses, as per the American Association for Public Opinion Research guidelines[17]. Non-response included: refusals (clicked the survey link, but did not complete consent or any items), and those assumed eligible with no response received. Email addresses that were undeliverable were considered invalid and not included in the analysis.

Statistical analysis

Survey respondents were compared to HPV FOCAL trial participants on age, study arm, and location of trial recruitment to explore if survey sample was representative of FOCAL trial population.

Our main outcome of HPV testing acceptability was assessed by response to the question "having an HPV test instead of a Pap to screen for cervical cancer is acceptable to me", which was dichotomized from a 5-point Likert scale, with those reporting strongly agree or agree, categorized as 'accepting', and those reporting neutral, don't know, disagree and strongly disagree as 'not accepting' of HPV testing. This categorization was chosen to capture those who were truly accepting and biased towards the null. Only complete surveys were included, with those who were missing or preferred not to answer excluded. Participants were classified as being HPV positive, if they received an HPV positive screening result at any point during their participation in the HPV FOCAL trial, otherwise a participant was classified as HPV negative.

Bivariable analysis explored differences in acceptability of HPV testing based on demographic factors such as age, income, and education, in addition to HPV screening test result, and length of time since study exit. Factors shown to be potentially associated with acceptability,

such as HPV screening starting at 30 years of age and increased screening interval, were also examined[16,18,19].

Socio-demographics and attitudes towards HPV testing were explored descriptively with Chi-square for categorical variables and median score test for continuous variables.

Multivariate logistic regression was used to explore the association of the acceptability of HPV testing with *a priori* identified confounding variables that reached $p \leq 0.2$ in bivariable analysis. Level of significance was 0.05. All statistical analyses were performed in SAS 9.4 and R4.02.

Ethics Approval

Ethics approvals for survey was received by the University of British Columbia Research Ethics Board (H06-04032). In addition, a privacy review was undertaken to ensure the survey complied with provincial privacy legislation.

RESULTS

Survey invites were administered from August 2017 through to February 2018. A total of 14,535 participants from both the HPV and cytology arms in HPV FOCAL trial were identified as eligible to receive 48-months exit online survey, of which 13,176 were delivered to a valid email address FIGURE 1). There were 5,532 surveys completed, of which 4,938 were fully and 594 partially completed.

Characteristics of respondents

The median age of participants completing the survey was 54 years (IQR: 46,62) (Table 1). The median time of survey completion was 3 years after study exit. The majority of respondents (67%) had completed college or higher education and 77% reported living with a partner. Survey respondents were comparable to HPV FOCAL trial participants based on study arm, age at HPV FOCAL trial enrollment, and geographical location. Survey respondents and non-respondents were comparable by study arm and marital status, but those who responded to the survey were slightly older than non-responders (median of 51 years vs. 49 years), although the difference was not clinically significant.

Acceptability of HPV testing for Screening

Overall, 63% of survey respondents agreed or strongly agreed that HPV testing for cervical cancer screening was acceptable, with 37% not agreeing (11% disagree, 16% neutral, 10% don't know) (Table 1). There were no significant associations between acceptability of HPV testing and marital partnership status, time since study exit, education or income. Women who received an HPV positive result at any point during HPV FOCAL trial and who were older were more accepting of HPV testing compared to those who remained HPV negative during trial participation.

In multivariate analysis, women who reported HPV testing as acceptable were more likely to have received an HPV positive screen test result at some point during the trial (OR 1.41 95%CI 1.11,1.80, p=0.005), and were older (OR 1.01, 95%CI 1.00,1.02, p=0.01) (Table 2).

Over half of respondents (54%) agreed with the statement “I would be willing to have an HPV test every 4-5 years instead of a Pap every 3 years”. There was a significant difference in acceptability of an extended screening interval between those who reported being accepting of HPV testing compared to those who were not accepting. Overall, 69% responded that HPV testing starting at age 30 was acceptable, with over 80% of those who were accepting of HPV testing reporting agreement with a higher screening age (30 years or over) compared to Pap testing (Table 1).

In addition, 66% of respondents reported that an extended screening would not result in less visits to their healthcare provider for other medical reasons, indicating that despite the extended interval recommended with HPV-based screening, women would continue to see their providers for medical reasons as needed.

Attitudes towards an HPV Positive Test Result:

Survey respondents were asked to rate their level of agreement with a variety of statements regarding attitudes surrounding receipt of HPV positive results (Table 3). Women were asked if they would be more concerned about receiving a positive HPV test or an abnormal Pap result, for which most respondents (73%) reported that both screening outcomes would concern them equally. However, those that reported HPV testing to be acceptable, reported that an HPV positive result would concern them more (14%) than an abnormal Pap. This was statistically different compared to those who were not accepting of HPV testing, who responded that abnormal Pap test results would concern them more. The difference in distribution between these responses was statistically significant.

Most respondents who were not accepting of HPV testing indicated that having a sexually acquired infection would concern them differently than having abnormal Pap results. The relationship between level of agreement with HPV testing acceptability and ones' level of concern about having a sexually acquired infection was significant. Regardless of a respondent's reported HPV testing acceptability, most respondents felt it important to them to know who gave them HPV and when they acquired HPV (72% and 78% respectively). Most respondents indicated they disagreed or were neutral regarding feeling judged for having HPV, and there was no significant relationship between feeling judged and level of agreement with HPV testing. More respondents who were accepting of HPV testing indicated they would feel comfortable telling their partner if they had HPV, which was in contrast to those who were not accepting of HPV testing; these differences indicated a significant relationship between HPV testing acceptance and comfort disclosing HPV status to a partner. Regardless of level of agreement with HPV testing, most respondents (79%) indicated they would feel concerned about transmitting HPV to their partner(s). More respondents who were accepting of HPV testing would feel confident in the recommendations from their provider for the management of their HPV positive results. There was a significant association between level of agreement with HPV testing and degree of confidence with provider recommendations.

Sources of information for HPV testing and screening:

Overall, the most reported important sources of information were health care providers and BC Cancer, the agency that is responsible for the cervix screening program in British Columbia (Table 4). In addition, those that are accepting of HPV testing were more likely to look to their health care providers and BC Cancer as important sources of information. Regardless of one's level of agreement with HPV testing for screening, friends and family or social media were not as important as health care providers and BC Cancer for sources of information.

DISCUSSION

Acceptability of, and attitudes, towards primary HPV testing were analysed from 5,532 women who completed HPV testing as part of the HPV FOCAL trial, which was embedded within an organized population-based cervical cancer screening program. Most respondents (63%) were accepting of HPV testing for cervix screening and for screening with HPV testing to begin at age 30 (69%). Just over half were accepting of HPV testing with the extended screen interval of 4 to 5 years (54%). Although most women were accepting, the proportion of respondents indicating they disagreed with or were neutral in their acceptance of HPV testing and of extended intervals was higher than we expected considering this was a group of people who were provided with education and information about HPV, HPV testing, and cervical cancer. These findings are similar to other studies that indicate women have concerns about the extended interval recommended with HPV testing [10,20–22], stemming from a belief that a cancer diagnosis may be missed through extension of the interval. Considering study participants received information regarding HPV, the natural history of HPV and cervical cancer, and the rationale for HPV testing compared to the Pap test, these findings indicate that additional research and patient engagement is needed to gain insights and identify and develop resources or procedures to address barriers to HPV testing and an extended screening interval.

This multivariate analysis found that those who received positive HPV test results at some point during the trial were more likely to be accepting of HPV testing for cervix screening than those who never received an HPV positive result. Those who tested HPV positive would have received additional information and counseling from their healthcare provider and or a Study nurse, which would not necessarily have been provided to those who tested HPV negative. This additional information would have reinforced the education participants were provided at trial baseline, including the prevalence of HPV in the population, the transient nature of HPV and the

long natural history between HPV infection and cervical dysplasia development. In addition, those with HPV positive results would have received additional follow-up and management by the time the survey was administered. The reinforcement of education, an opportunity for dialogue when receiving the positive result, and the fact that those with a positive HPV result would have received treatment for detected dysplasia, may have facilitated improvement in knowledge and subsequently, enhanced acceptance of HPV testing. Other findings have indicated that increased HPV and HPV screening knowledge can be a facilitator of HPV screening acceptance[18].

One of the concerns with an extended screening interval is if women would be less likely to consult with the health care provider for other medical reasons[16]. When we asked participants if they would be less willing to see a healthcare provider for other medical reasons if the interval for cervix screening were increased, most respondents said they would not be less willing, indicating that the extended interval for cervix screening would not prevent them from seeking care as needed. This finding can provide reassurance to healthcare professionals who have concerns that the extended screening interval recommended with HPV-based screening would lead to fewer visits to a clinician, given that the cervical screen visit is often an opportunity for the clinician to assess other preventive care or medical issues [23].

Respondents' concerns regarding receipt of HPV positive results were varied. Nearly 93% of the respondents never received an HPV positive result during the HPV FOCAL trial. As a result, the majority of responses evaluate attitudes and experiences for those who did not actually receive HPV positive results, and therefore, reflect how the respondents would hypothetically feel if they were to receive HPV positive results. Of the respondents, 7.5% had received an HPV positive result at some point during their trial participation.

Most participants indicated that having HPV would cause them concern about having cervical cancer. The majority of participants reported that having either an abnormal Pap or a positive HPV test would concern them; however, for those that had tested positive for HPV, they reported that an HPV test would concern them more compared to an abnormal Pap. Overall, participants' perceptions about HPV positive results and cervical cancer indicate that increased knowledge regarding the specificity of HPV testing for cervical cancer screening is needed.

Receipt of positive HPV results has been associated with higher anxiety and distress compared to receipt of abnormal Pap results[24–26], which may be due to the fact that HPV is a sexually transmitted infection and has been associated with levels of shame and stigma[27,28]. Most respondents in our survey indicated that receiving results for a sexually acquired HPV infection would concern them differently than having an abnormal Pap test result; however, this belief varied depending on a participant's acceptability of HPV testing. Women who were not accepting of HPV testing indicated that a HPV positive result would concern them differently than abnormal Pap results, compared to those who were accepting of HPV testing. Most respondents, whether they accepted HPV testing or not, felt it important for them to know who gave them HPV and when they got it (71% and 78% respectively). These findings together are reflective of other research findings[9,29,30] and indicate that when developing education and communication strategies, emphasis should be placed on the high prevalence of HPV in the population, the transient nature of most HPV infections, bringing awareness to the fact an infection may have been acquired several years prior to a positive test result. Differentiating HPV from other STIs may minimize anxiety and facilitate normalization and acceptance[16,27].

Almost 75% of the respondents indicated they felt an HPV positive result would affect their relationship with their partner, or they weren't sure, and almost 80% would be concerned about transmitting HPV to their partners, with many feeling they would be judged for being HPV

positive. The stigma associated with HPV, concerns about infidelity and potential partner reactions to the HPV result may underlie these concerns. Previous research has indicated some women question whether partner notification with HPV is necessary[16,31]. Unlike other STIs such as chlamydia or gonorrhea where partner notification is recommended for testing and treatment purposes, there is usually no medical reason to notify the partner of a woman who tested positive for HPV.

Healthcare providers, as trusted and valued sources of information, can influence patients' decision-making patterns regarding health care decisions[20,32] Reflecting other findings, the respondents in this survey indicated that the most important sources of information for them, were their healthcare providers and the provincial screening program [[20,32]]. In this cohort, the least important sources of information were social media and friends and family, providing reassurance that women in this cohort seek information from reputable sources such as health care providers and the screening program compared to the internet, or friends and family. These findings demonstrate that program planning for HPV-based screening should prepare health care providers with adequate education and training surrounding HPV prior to program changes, to ensure they are equipped to address women's questions and concerns regarding the paradigm shift from cytology to HPV-based screening.

This study is not without limitations. Survey participants were part of a large clinical trial and were given information about HPV, HPV testing and cervical cancer upon enrollment and, therefore, may not be representative of all people eligible for cervix screening in British Columbia. However, participants of this study are reflective of the current population engaged in the screening program, who receive cytology testing with the Pap smear, and not HPV testing as standard of care. As a result, their concerns and feedback are informative for programs planning for a shift from cytology to HPV-based screening. The response rate may be

considered low at 41%; however, those who have stronger opinions about their screening choices may have been more likely to respond to the survey than those who are more trusting of the health care system and accepting of any future policy changes. In addition, survey respondents were representative of overall participants in the HPV FOCAL trial. The majority of respondents completed the survey approximately 3 years after trial completion and it is possible there was loss of recall of HPV related information provided to them when they consented to participate in the trial, which for many was up to 7 years prior to survey completion. The potential lag time between trial entry and survey completion may have introduced recall bias and impacted women's attitudes and beliefs surrounding HPV testing; however, the impact of this potential bias would be small as we found no significant difference between acceptability and time between trial entry and survey completion. In addition, most of the participants in this trial were over the age of 50, highly educated and primarily from two urban geographic regions and may not be representative of all screen eligible people in various regions of British Columbia.

CONCLUSIONS

In this study, within an organized screening setting, evaluating acceptability and attitudes around HPV testing from women undergoing HPV-based screening, most are accepting of HPV testing for screening; however, further research is needed to understand factors that can increase acceptability. These findings contribute to the growing body of evidence demonstrating that concerns and experiences surrounding HPV testing and receipt of HPV positive results are complex and varied. As many cervix screening programs begin HPV-based screening and are planning implementation strategies, attention to patient engagement to address potential barriers will be important. As HPV-based screening becomes standard of care, it is plausible that concerns with this paradigm shift will eventually be alleviated with increasing knowledge

and familiarity. These findings provide insight into areas of importance that should be considered for development of education, information, and communication strategies.

Figure 1: Study flowchart and participant disposition

Table 1: Demographic characteristics of respondents and bivariable analysis of acceptability of HPV testing

			Having an HPV test instead of a Pap smear to screen for cervical cancer is acceptable to me		
		Total (N)	**Not acceptable (Disagree/Neutral/Don't know)**	**Acceptable (Agree)**	**p-value**
Total (N)		**5336**	1993 (37.4%)	3343 (62.6%)	
Age	median [IQR]	5336	53.35 [45.35, 61.19]	54.23 [45.64, 61.72]	0.051
Marital Status[a]					
	Living with a partner	3806	1438 (78.7)	2368 (76.6)	0.095
	Living without a partner	1115	390 (21.3)	725 (23.4)	
Education[a]					
	Complete College or higher	3317	1250 (68.5)	2067 (66.7)	0.221
	Incomplete post-secondary or less	1607	576 (31.5)	1031 (33.3)	
Income[a]					
	Less than $75000	1501	529 (32.0)	972 (34.0)	0.175
	$75,000 or more	3014	1126 (68.0)	1888 (66.0)	
HPV Testing Status during FOCAL trial					
	Never tested HPV positive	4937	1867 (93.7)	3070 (91.8)	0.015*
	At least one HPV positive result	399	126 (6.3)	273 (8.2)	
Time since exit from FOCAL trial, Years					
	median [IQR]	5336	3.09 [2.26, 3.91]	3.04 [2.23, 3.93]	0.616
I would be willing to have an HPV test every 4-5 years instead of a Pap every 3 years[a]					
	Agree	2858	386 (19.5)	2472 (74.2)	<0.001*
	Disagree	1096	744 (37.6)	352 (10.6)	
	Neutral	1353	847 (42.8)	506 (15.2)	
Receiving HPV testing starting at age 30 is acceptable to me[a]					
	Agree	3635	944 (47.8)	2691 (81.0)	<0.001*
	Disagree	682	423 (21.4)	259 (7.8)	
	Neutral	981	608 (30.8)	373 (11.2)	
If cervical cancer screening was to occur every 4 or 5 years, instead of every 3 years, I would be less likely to visit my health care provider for other health reasons. [a]					
	Agree	1062	405 (20.4)	657 (19.7)	0.814
	Disagree	3517	1303 (65.7)	2214 (66.4)	
	Neutral	735	274 (13.8)	461 (13.8)	

Table Notes: [a] Missing values up to 5,336 = not reported or prefer not to answer, * significant to p<0.05

Table 2: Multivariate analysis of predictors for participants who are accepting of HPV testing instead of Pap testing for cervical cancer screening.

Variable	OR (95% CI)	P-value
Age at survey completion (years)	1.01 (1.00,1.02)	0.01
Received HPV positive results during study (Yes vs No)	1.41 (1.11,1.80)	0.005
Education (Incomplete post-secondary or less vs Complete College or higher)	1.06 (0.93,1.21)	0.41
Marital status (Living without a partner vs Living with a partner)	1.04 (0.88,1.22)	0.67
Income ($75000 or more vs. less than $75000)	0.97 (0.84,1.12)	0.68

512 **Table 3:** Experiences receiving HPV positive results

		HPV testing instead of Pap testing for cervical cancer:		
	Total (N)	**Not acceptable**	**Acceptable**	p-value
	5336	1993 (36.0%)	3343 (60.4%)	
What would concern you most: Being told you had abnormal Pap results, or being told you had HPV?[a]				
Being told I have abnormal Pap test results	668	274 (14.0)	394 (11.9)	<0.001*
Being told I have HPV	683	197 (10.0)	486 (14.7)	
Both would concern me equally	3855	1464 (74.7)	2391 (72.2)	
Neither would concern me	67	26 (1.3)	41 (1.2)	
Having an infection that is sexually acquired (HPV) doesn't concern me any differently than abnormal Pap results would[a]				
Agree	1412	442 (24.8)	970 (31.5)	<0.001*
Disagree	2465	974 (54.6)	1491 (48.4)	
Neutral	987	369 (20.7)	618 (20.1)	
It would be important for me to know who gave me HPV[a]				
Agree	3468	1251 (70.3)	2217 (71.7)	0.094
Disagree	545	188 (10.6)	357 (11.5)	
Neutral	859	340 (19.1)	519 (16.8)	
It would be important for me to know when I got HPV[a]				
Agree	3795	1372 (76.9)	2423 (78.3)	0.131
Disagree	432	151 (8.5)	281 (9.1)	
Neutral	650	260 (14.6)	390 (12.6)	
I think people would judge me for having HPV[a]				
Agree	1775	663 (37.4)	1112 (36.0)	0.307
Disagree	1419	495 (27.9)	924 (30.0)	
Neutral	1666	617 (34.8)	1049 (34.0)	
I would feel comfortable telling my partner if I had HPV[a]				
Agree	3391	1198 (67.4)	2193 (71.3)	0.016*
Disagree	709	284 (16.0)	425 (13.8)	
Neutral	755	296 (16.6)	459 (14.9)	
I would not be concerned about transmitting HPV to my partner[a]				
Agree	515	174 (9.8)	341 (11.1)	0.095
Disagree	3825	1400 (78.7)	2425 (79.0)	
Neutral	509	205 (11.5)	304 (9.9)	
Being HPV positive would not affect my relationship with my partner[a]				
Agree	1249	445 (25.1)	804 (26.3)	0.035*
Disagree	2003	708 (39.9)	1295 (42.3)	
Neutral	1584	622 (35.0)	962 (31.4)	
Having HPV would not cause me any concern about cervical cancer[a]				
Agree	181	52 (2.9)	129 (4.2)	0.012*
Disagree	4112	1499 (84.1)	2613 (84.8)	
Neutral	569	231 (13.0)	338 (11.0)	
I would feel confident in the recommendations from my healthcare provider for follow-up of my HPV positive result[a]				
Agree	3876	1323 (74.0)	2553 (82.5)	<0.001*
Disagree	226	97 (5.4)	129 (4.2)	

	Neutral	780	369 (20.6)	411 (13.3)

Table Notes: : [a] Missing values up to 5,336 = not reported or prefer not to answer,, * significant to p<0.05

513
514

Table 4: Important sources of HPV information

			Having an HPV test instead of a Pap smear to screen for cervical cancer is acceptable to me		
		Total (N)	**Not acceptable**	**Acceptable**	p-value
		5336	1993 (36.0%)	3343 (60.4%)	
Health Care Provider[a]					
	Important	3405	1128 (59.3)	2277 (70.1)	<0.001*
	Neutral	1256	560 (29.5)	696 (21.4)	
	Not Important	487	213 (11.2)	274 (8.4)	
BC Cancer (organizes screening in BC)[a]					
	Important	2713	907 (48.7)	1806 (56.9)	<0.001*
	Neutral	1649	673 (36.1)	976 (30.8)	
	Not Important	673	283 (15.2)	390 (12.3)	
Govt Websites (ex: Canadian Cancer Society/Public Health Agency Canada)[a]					
	Important	2111	734 (39.9)	1377 (44.2)	0.011*
	Neutral	1914	748 (40.6)	1166 (37.5)	
	Not Important	928	359 (19.5)	569 (18.3)	
Other websites (WebMd, blogs)[a]					
	Important	1597	567 (31.3)	1030 (33.7)	0.112
	Neutral	1997	776 (42.8)	1221 (40.0)	
	Not Important	1273	469 (25.9)	804 (26.3)	
Friends/family[a]					
	Important	1336	453 (25.0)	883 (28.9)	0.012*
	Neutral	1865	725 (40.0)	1140 (37.3)	
	Not Important	1670	634 (35.0)	1036 (33.9)	
Social media[a]					
	Important	580	197 (10.9)	383 (12.6)	0.004*
	Neutral	1562	633 (35.1)	929 (30.7)	
	Not Important	2693	975 (54.0)	1718 (56.7)	

Table Notes: : [a] Missing values up to 5,336 = not reported or prefer not to answer,, * significant to p<0.05

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Contributors: LWS involved in conception, design and implementation of the research presented here, drafting and review of manuscript; CSR conducted statistical analysis and contributed to drafting and review of manuscript; LG conducted statistical analysis; MK, ML, REM, GS, SP ELF and DV are co-investigators on the HPV FOCAL Study and were involved in FOCAL trial design and trial management; AJC and GO are co-principal investigators of the FOCAL Study and oversaw conduct of the trial; all authors take responsibility for the credibility of the data and analysis and critically reviewed the paper and approved the final version.

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Competing interests: MK and AC were principal investigators, and GO, DV and EF were co-investigators on industry funded (Hologic Inc, and Roche) investigator-led adjunct studies to the HPV FOCAL Trial, designed to compare the performance of different HPV testing assays. No investigators personally benefitted financially. Funding for these adjunct studies was not applied to the operation of the HPV FOCAL results presented in this paper. ELF served as an occasional advisor for companies involved with HPV vaccines (Merck, GSK) and HPV diagnostics (Roche). He also holds a patent "DNA methylation markers for early detection of cervical cancer," registered at the Office of Innovation and Partnerships, McGill University, Montreal, Quebec, Canada.

Patient consent for publication: Not required

Ethics approval: Ethics approvals for survey was received by the University of British Columbia Research Ethics Board (H06-04032).

Provenance and Peer review: Not commissioned; externally peer reviewed.

Data availability Statement: Deidentified participant data is available upon consideration and reasonable request.

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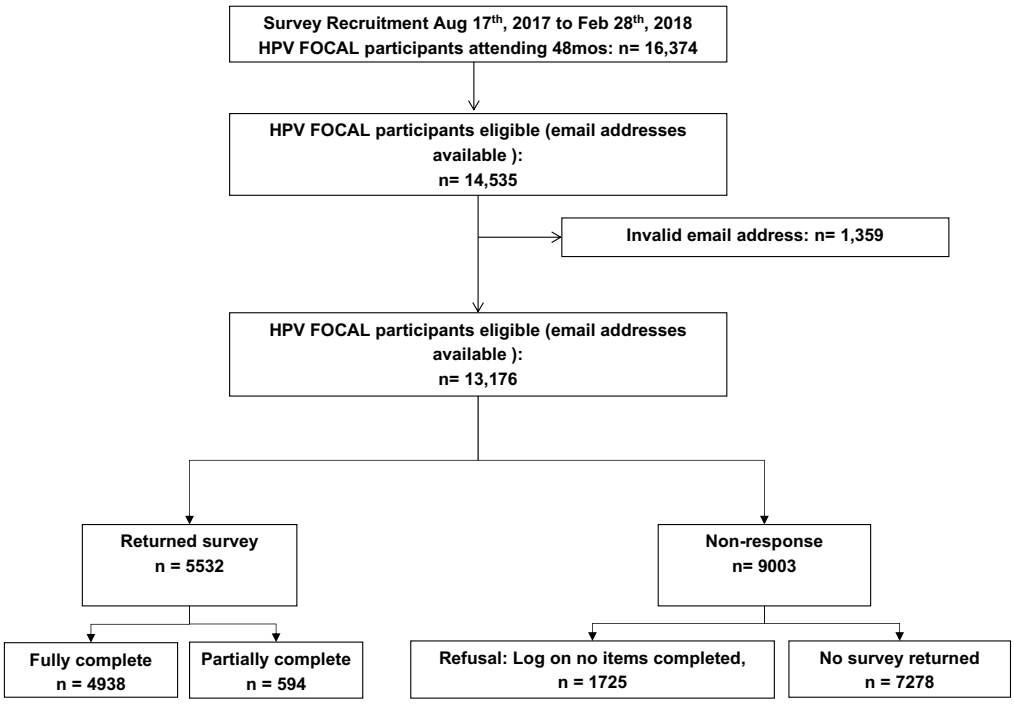
Figure 1: Study Flowchart and participant disposition



Thank you for contributing to the HPV FOCAL Study! As you know the purpose of the study was to evaluate HPV testing for cervical cancer screening in BC. The results of the FOCAL study will be very important as Canadian programs consider adopting HPV testing to screen for changes that may lead to cervical cancer. We are interested to learn about your experience and understanding of HPV testing for cervical cancer screening. ***As a reminder, ALL women who completed a 4 year exit screen received both a Pap smear and an HPV test***

Your input is important to us and can help plan for the future of cervical cancer screening in BC. Please take a few moments of your time to complete the attached survey. You do not have to answer any questions you do not feel comfortable answering.

First we would like to ask about your HPV knowledge before and during the study.

1) *Please rate the following question according to how much you agree or disagree with the statement:*
I know more about HPV and cervical cancer now than I did before I participated in the study:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Not Sure

2) I was aware of my cervical screen (Pap and HPV test) results at completion of the study:

- ☐ No
- ☐ Yes
- ☐ Not sure

3) *Please rate the following question according to how much you agree or disagree with the statement:*
I had enough time to ask my health care provider questions about HPV testing and/or my results.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know
- ☐ Not applicable

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4) *Please rate the following question according to how much you agree or disagree with the statement:*
I feel my health care provider was able to answer my questions about HPV:

☐ Strongly Disagree
☐ Disagree
☐ Neutral
☐ Agree
☐ Strongly agree
☐ Don't know
☐ Not applicable

5) *Please rate the following statements regarding HPV testing:*
Having my health care provider collect a sample for HPV testing for cervical cancer screening would be:

	<---	**<--**	**<-**	**Neutral**	**->**	**-->**	**--->**	
Accurate	☐	☐	☐	☐	☐	☐	☐	Inaccurate
Safe	☐	☐	☐	☐	☐	☐	☐	Unsafe
Protect my health	☐	☐	☐	☐	☐	☐	☐	Harm my health
Acceptable	☐	☐	☐	☐	☐	☐	☐	Unacceptable

6) Which of the following have been important sources of information for you about HPV/HPV testing?

	Not at all important	Not that important	Neutral	Somewhat important	Very important
My health care provider	☐	☐	☐	☐	☐
BC Cancer Agency (including the BC Cancer Agency website)	☐	☐	☐	☐	☐
Government websites (ie: Canadian Cancer Society, Health Canada, Public Health Agency of Canada, BC Ministry of Health)	☐	☐	☐	☐	☐
Other websites (ie: WebMD, blogs, etc)	☐	☐	☐	☐	☐
Friends/family	☐	☐	☐	☐	☐
Social Media (ie: facebook, twitter, etc)	☐	☐	☐	☐	☐

Other comments:……

……

Next we would like to ask how you feel about HPV testing to screen for cervical cancer.

As a reminder, there are over 100 types of the human papillomavirus (HPV), of which about 40 affect the genital region. HPV is very common and most sexually active people will have an infection at some point in their lives, however it usually disappears without a person experiencing any symptoms. Only in cases where a cancer causing HPV type persists for many years, is there a risk that it may lead to cervical cancer.

7) *Please rate the following question according to how much you agree or disagree with the statement:* **Having an HPV test to screen for cervical cancer instead of a Pap smear is acceptable to me:**

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments:……

8) I would be willing to have an HPV test <u>every 4 or 5 years</u> instead of a Pap test every 3 years:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments: ……

Evidence suggests that HPV testing is ideally started no earlier than 30 years of age. Should HPV testing be adopted in the province, it would be available for women starting at age 30 or 35. However, cervical cancer screening could still start at age 25 using the Pap smear as currently recommended in BC.

9) Receiving HPV testing for cervical cancer screening, starting at age 30 is acceptable to me.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

10) If cervical cancer screening was to occur every 4 or 5 years, instead of every 3 years, I would be less likely to visit my health care provider for other health reasons.

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Next we would like to understand some of your thoughts about HPV testing compared to the Pap test.

11) What would concern you most: 1) being told you had "abnormal Pap test results" or 2) being told you were "positive for HPV"? (*Check ONE only*)

- ☐ Neither would concern me
- ☐ Being told I have abnormal Pap test results
- ☐ Being told I have HPV
- ☐ Both would concern me equally

Please explain: .....

.....

Next, we would like to learn about your experience of receiving HPV results.

12) If you tested HPV positive during the HPV FOCAL trial, or if you were to test positive for HPV, please rate your level of agreement with the following statements:

	Strongly disagree	**Disagree**	**Neutral/uncertain**	**Agree**	**Strongly Agree**
Although HPV is sexually acquired, having an infection that is sexually acquired does not concern me any differently than abnormal Pap results would.	☐	☐	☐	☐	☐
It would be important for me to know who gave me HPV.	☐	☐	☐	☐	☐
It would be important to me to determine when I got HPV.	☐	☐	☐	☐	☐
I think people might judge me for having HPV.	☐	☐	☐	☐	☐
I would feel comfortable telling my partner about my HPV positive result.	☐	☐	☐	☐	☐
I would not be concerned about transmitting HPV to a sexual partner.	☐	☐	☐	☐	☐
Receiving a positive HPV result would not affect my relationship with my sexual partner.	☐	☐	☐	☐	☐
Having HPV would not cause me any concern about developing cervical cancer.	☐	☐	☐	☐	☐
I would feel confident in the follow up and/or treatment my provider would recommend for my positive HPV result.	☐	☐	☐	☐	☐

Other comments:……
……

13) *Please rate the following statements according to how much you agree or disagree:*
If I tested positive for HPV I felt/would feel:

	Strongly disagree	**Disagree**	**Neutral/uncertain**	**Agree**	**Strongly agree**
Reassured	☐	☐	☐	☐	☐
Relieved	☐	☐	☐	☐	☐
Guilty	☐	☐	☐	☐	☐
Worried	☐	☐	☐	☐	☐
Upset	☐	☐	☐	☐	☐
Surprised	☐	☐	☐	☐	☐

Other comments: ……

14) If you were aware of your results at the end of the trial and they were negative/normal, how confident were you with the safety of these results?

☐ Very unconfident
☐ Somewhat unconfident
☐ Neutral
☐ Somewhat confident
☐ Very confident
☐ Didn't know my results
☐ Not applicable/results were positive

Next we would like to ask about your thoughts about the possibility of women collecting their own sample for HPV testing for cervical cancer screening by inserting a soft Q-tip or brush into the vagina that can then be returned to the laboratory and tested for the presence of HPV. With self-collection, a woman would not need to see a health care provider for pelvic exam for sample collection. Self-collected specimens tested for HPV have been shown to be equivalent to HPV samples taken by a health care provider for detecting abnormalities of the cervix.

15) *Please rate the following statements regarding self-collected samples:*

Collecting my own sample for cervical cancer screening would be:

	<---	**<--**	**<-**	**Neutral**	**->**	**-->**	**--->**	
Accurate	☐	☐	☐	☐	☐	☐	☐	Inaccurate
Safe	☐	☐	☐	☐	☐	☐	☐	Unsafe
Protect my health	☐	☐	☐	☐	☐	☐	☐	Harm my health
Acceptable	☐	☐	☐	☐	☐	☐	☐	Unacceptable

16) I would be willing to collect my own sample/specimen for cervical cancer screening:

- ☐ Strongly Disagree
- ☐ Disagree
- ☐ Neutral
- ☐ Agree
- ☐ Strongly agree
- ☐ Don't know

Comments: ……..
…….

Finally we'd like to ask some questions that may help us better understand associations between HPV and various other factors.

17) **What is the highest level of education you have achieved?**

- ☐ No formal education
- ☐ Some elementary school
- ☐ Completed elementary school
- ☐ Some high school
- ☐ Completed high school
- ☐ Some post-secondary training (Trades, college, university)
- ☐ Completed trade/vocational/apprenticeship program
- ☐ Completed college
- ☐ Completed university (bachelor degree)
- ☐ Completed university (master degree or higher)

18) Please indicate your current marital status:

- ☐ Single (living WITHOUT a partner)
- ☐ Single (living WITH a partner)
- ☐ Married or common law
- ☐ Divorced
- ☐ Separated (but still legally married)
- ☐ Widowed

19) Not including new partners you have had since you completed the HPV FOCAL study, please indicate to the best of your recollection, how many male partners you have had vaginal intercourse with:

- ☐ 0
- ☐ 1-10
- ☐ 11-49
- ☐ 50+

20) Please enter the total years you have used the following hormonal birth control methods. If never used, please enter "0".

Method	Total years used	Please place a checkmark in this column if you used this method while participating in the HPV FOCAL study
Oral contraceptive pill	_ _	☐
Contraceptive patch	_ _	☐
Contraceptive vaginal ring	_ _	☐
Hormonal IUD	_ _	☐
Injection (ie: Depo-provera)	_ _	☐
Morning after pill or emergency contraceptive pill	_ _	☐
Implant	_ _	☐

We are trying to better understand how use of specific substances (ie: alcohol, tobacco and marijuana) impacts a woman's potential to develop a long term HPV infection. These following questions help us determine if there is an association between HPV infection and different substances.

21) Have you ever smoked cigarettes?

☐ Yes (daily). For approximately how many years: _ _

☐ Yes (less than daily)

☐ Not at all

22) Were you a regular cigarette smoker during your participation in the HPV FOCAL Study?

☐ Every day…..Approximately how many cigarettes did you smoke per day? _ _

☐ Some days…Approximately how many days did you smoke each week? _ _

☐ Not at all

23) During your participation in the HPV FOCAL Study, how often did you use marijuana:

- ☐ Never
- ☐ Less than once a month
- ☐ 1-3 times a month
- ☐ Once a week
- ☐ More than once a week
- ☐ Every day

24) Please indicate the ways you used marijuana during the HPV FOCAL study:

- ☐ Smoking
- ☐ Vaporizing
- ☐ Edible (ie: cakes, cookies, candy, drinks, etc)
- ☐ Pill/capsule
- ☐ Other

25) During your participation in the HPV FOCAL Study, how often did you drink alcoholic beverages?

- ☐ Never
- ☐ Once a month or less
- ☐ 2-3 times a month
- ☐ Once a week
- ☐ 2-3 times a week
- ☐ 4-6 times a week
- ☐ Every day

26) Please estimate your total household income (everyone in your household, excluding roommates):

- ☐ Less than $10,000
- ☐ $10,001-25,000
- ☐ $25,001-50,000
- ☐ $50,001-75,000
- ☐ $75,001-100,000
- ☐ More than $100,000

Thank you for completing this survey! Your responses are highly valued and impact guidelines and recommendations as the province of British Columbia considers changes to cervical cancer screening practices.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6,7*
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	17
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9, 18
Outcome data	15*	Report numbers of outcome events or summary measures	18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	18

		(*b*) Report category boundaries when continuous variables were categorized	n/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.