SYSTEMATIC REVIEW

Self-collected HPV Testing Improves Participation in Cervical Cancer Screening: A Systematic Review and Meta-analysis

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ABSTRACT

OBJECTIVE: HPV testing has emerged as an effective cervical cancer screening test. The use of HPV self-testing has the potential to address many barriers to screening and reach at-risk women through engagement in screening. However, there is a need to examine the evidence for whether offering self-collected HPV testing in practice increases screening compliance. The objective of this review is to determine to what extent providing self-collected HPV testing increases screening participation in women who are never or underscreened for cervical cancer.

METHODS: A systematic literature review conducted in the databases Medline and Embase identified articles examining the use of HPV self-testing on cervical cancer screening participation. A meta-analysis using a random-effects model was used to calculate the relative compliance, with an intent-to-treat analysis of HPV self-testing compared to Pap testing, with 95% confidence intervals (CI). All statistical tests were two-sided.

SYNTHESIS: Ten studies were reviewed, with 8 being European and 2 North American. Of the 10 studies, 9 employed a randomized design. In all studies, the relative compliance of HPV self-collected testing compared to Pap testing was significantly greater than 1.0 ($p<0.01$). The overall relative compliance was 2.14 (95% CI 1.30-3.52). There was large heterogeneity of screening compliance between studies for both HPV self-testing and Pap testing.

CONCLUSION: HPV self-collected testing significantly improved the participation of women who did not routinely attend cervical cancer screening programs. New approaches to HPV self-test delivery should be considered as HPV testing becomes more widely incorporated as a primary screening tool.

KEY WORDS: Human papillomavirus; cervical cancer screening; self collected specimens; under-screening; review

La traduction du résumé se trouve à la fin de l'article.

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Cervical cancer screening has dramatically reduced the incidence of cervical cancer in those countries that have implemented screening programs;[1] however, the majority of cervical cancers continue to occur in women who do not attend regular screening (underscreened) or who have never been screened.[2]

The Papanicolaou (Pap) test is one of the standard screening tests used for the detection of cervical cancer. The Pap test, which is administered during a pelvic examination, involves the examination of cervical cells for abnormal histological changes consistent with cervical cell dysplasia and cervical cancer. Barriers to Pap testing can be grouped into three broad categories: clinic-level, test-level, and personal-level barriers.[3-6] Clinic-level barriers include such factors as the lack of a family physician, inconvenient clinic hours and lack of available transportation to the clinic.[5,7] Barriers at the test level are reported as physical discomfort or anticipation of discomfort.[6] Personal-level barriers include those that pertain to religious and cultural beliefs, language barriers, and lack of knowledge around cervical cancer screening.[6,7]

The human papillomavirus (HPV) is a necessary cause, but not a sufficient cause, for cervical cancer.[8] More and more, HPV testing is being considered an important addition to cervical cancer screening programs, either by way of co-testing with the Pap test or as a primary screening test used to triage women for subsequent Pap testing.[9-14] HPV testing seeks to identify the presence of HPV in the vaginal canal. The presence of oncogenic HPV types confers an elevated risk for the future development of cervical cancer. In women over 30 years of age, HPV testing has been shown to be more sensitive than Pap testing for the detection of cervical interstitial neoplasia (CIN) grade 2/3+.[15-17] Due to the lower specificity of HPV testing compared to Pap screening, it has been recommended that HPV testing be used only as a screening modality in women older than 30, as a co-test or that those who test HPV-positive be triaged to undergo Pap testing.[9,16] In order for a two-phase double-screening regimen to take place, adequate follow-up procedures and infrastructure are required at the primary care and/or population level.

Trials comparing self-collected HPV test samples to physician-collected samples found that both methods provided equally viable samples for detecting HPV.[18-20] In addition, women who performed self-collection were found to have similar cancer-related outcomes to women who underwent HPV testing by a physician;[21] as such, self-collected HPV testing has been investigated as an alternative to physician-collected samples.

Beyond the efficiency and effectiveness of HPV testing as a diagnostic test, studies have also considered women's attitudes toward self-collection and found that women have a high acceptance of and positive attitudes toward the use of self-collected HPV testing.[22-25]

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Table 1. The Key Words and Medical Subject Headings (MeSH) Used to Identify Peer-reviewed Articles in the Databases Medline and Embase From January 1, 1990-July 15, 2012

Medline	Embase
[Papillomavirus infections OR cervical intraepithelial neoplasia OR uterine cervical neoplasmas OR vaginal smears OR papillomaviridae]	[Vagina smear OR papilloma virus OR papillomavirus infection OR wart virus OR papilloma OR uterine cervix carcinoma OR uterine cervix carcinoma in situ]
AND	AND
[Self care OR patient acceptance of health care OR Self-sampl* or Self test*]	[Self evaluation OR patient participation OR patient compliance OR self care OR Self test* OR Self sampling OR Self sampl* OR Self sampling Human papillomavirus test]
AND	AND
[HPV test*]	[Cancer screening OR HPV test*]

Being able to collect one's own sample has the potential to address many of the current barriers around screening and improve the participation of women who are most at risk for cervical cancer, i.e., those who are underscreened and/or hard to reach.[26] Self-collected testing, especially when conducted at home, removes the dependence on clinic hours, transportation, discomfort with the physical exam, and language barriers with a care provider, and could provide a culturally or religiously safe procedure. In short, it appears that the use of self-collected testing could play a major role in the use of HPV testing for cervical cancer screening.[27,28]

While studies have examined and considered many aspects relating to HPV self-testing, there is a need to examine the evidence for whether self-collected HPV testing in practice increases participation and compliance in cervical cancer screening.

The objective of this review is to determine whether the option of self-collected HPV testing increases cervical cancer screening participation (through HPV testing) for women living in developed countries who are never or underscreened for cervical cancer.

METHODS

Selection of studies

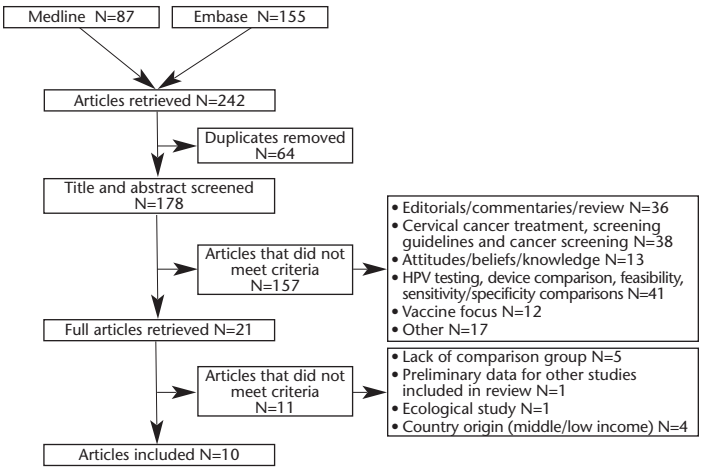
A systematic literature review was conducted to identify relevant articles that examined the use of HPV self-collected testing for cervical cancer screening in never- and underscreened women. The databases Medline and Embase were systematically searched for peer-reviewed articles published between January 1, 1990 and July 15, 2012, with 87 and 155 relevant citations identified within each respective database.

Keywords and Medical Subject Headings (MeSH) were chosen to capture the constructs of HPV infection, cervical cancer, self-sampling and HPV DNA testing (Table 1).

The literature search was restricted to peer-reviewed articles that clearly demonstrated the comparison of self-collected HPV testing as a primary screening test to standard Pap testing in women who did not routinely participate in cervical cancer screening programs. This review was restricted to developed countries where Pap testing is the standard for cervical cancer screening. One exception is Mexico. Mexican studies were also considered due to the importance of Mexico in the North American context both geopolitically and from an immigration perspective.

Studies were included if group allocation was clearly described and compliance was available for both the intervention group and the control group. Accepted control groups were those that offered a standard invitation to undergo Pap testing at a local Health Care Clinic or that offered Pap testing via the normal procedures of the jurisdiction within which the study was conducted.

Figure 1. Flow chart of the systematic search to retrieve studies on the compliance of self-collected HPV testing compared to Pap testing for cervical cancer screening from Medline and Embase (January 1, 1990-July 15, 2012).



The number of articles retrieved and removed based on the inclusion and exclusion criteria are provided. Ten articles met both the inclusion and exclusion criteria and were included in the review.

Studies that employed an ecological design were excluded as individual-level crude rates of compliance in testing could not be determined. Conference abstracts, editorials, commentaries and other unpublished manuscripts were excluded, in addition to articles that included duplicate datasets or male participants. Studies involving male participants were excluded as the objective of this review was to examine compliance specifically in cervical cancer screening.

There were no language restrictions on publications included. Of all the publications, only one was published in a foreign language (French). For this paper, the data were extracted and confirmed by a second, independent reviewer comfortable in French.

Articles were reviewed in full if the study abstract met the inclusion criteria or if an article lacked sufficient information in the abstract to make an inclusion/exclusion judgement, so as to minimize errors of omission.

Data extraction and outcome measures

The following information was extracted for each study: first author, publication journal, date of publication, country and city of study, dates of study completion, HPV detection method, sample collection device, population description, age distribution of participants, definition of non-attending or underscreened, study design, total number of participants in each group, compliance in

Table 2. Summary Study Characteristics of Reviewed Studies Published Between January 1, 1990 and July 15, 2012 Examining HPV Self-collected Testing vs. Pap Testing Compliance for Women Who Do Not Normally Participate in Cervical Cancer Screening Programs

Study (reference), Year, Country	Number of Participants	Age Range (Yrs)	Estimated National Coverage of Cervical Cancer Screening	Study Characteristics (Randomization, HPV Detection Assay, Sampling Device and Setting)	Description of HPV Self-testing Arm and Control Arm Intervention	Definition of Underscreened Population
Gok et al.,[33] 2012, Netherlands	25,822	30-60	77%	Randomized. Hybrid-capture II assay with Cervovaginal brush sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who had not attended cervical cancer screening in the last year after a reminder invitation for screening.
Szarewski, et al.,[35] 2011, United Kingdom	3000	25-64	68%	Randomized. Hybrid-capture II assay with swab sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who did not respond to 2 invitations for screening.
Giorgi et al.,[34] 2011, Italy	1235	35-65	48-88%	Randomized. Hybrid-capture II assay with lavage sampling device. Urban and rural settings.	Mailed HPV self-test vs. Pap invitation letter.	Women who did not respond to 1 regular invitation for screening.
Wikstrom et al.,[36] 2011, Sweden	4060	39-60	NR*	Randomized. Hybrid-capture II assay with swab sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who had not participated in screening for >6 years.
Virtanen et al.,[37] 2011, Finland	8699	30-60	70%	Randomized. Hybrid-capture II assay with lavage sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who did not respond to 2 invitations for screening.
Castle et al.,[40] 2011, United States of America	119	26-65	NR	Not randomized. Hybrid-capture II assay with swab sampling device. Rural setting.	Direct door-to-door offering of HPV self-test vs. coupon for free Pap test at local clinic.	Women who had not had a Pap test in the last 3 years.
Lazcano-Ponce et al.,[39] 2011, Mexico	22,102	25-65	NR	Randomized. Hybrid-capture II assay with Cervovaginal brush sampling device. Rural setting.	Direct door-to-door offering of HPV self-test vs. door-to-door invitation to Pap testing at nearest clinic.	Women in a poverty-reduction program, with limited access to health services.
Piana et al.,[38] 2011, France	7854	35-69	60%	Randomized. PCR genotyping assay with swab sampling device. Urban setting.	Solicitation for HPV self-testing at home vs. Pap invitation letter.	Did not participate in cervical cancer screening after invitation.
Gok et al.,[32] 2010, Netherlands	27,163	30-60	77%	Randomized. Hybrid-capture II assay with lavage sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who had not had a Pap test in 5 years and did not respond to 1 invitation for screening.
Bias et al.,[31] 2007, Netherlands	2624	30-50	63%	Randomized. PCR genotyping with Cervovaginal brush sampling device. Urban setting.	Mailed HPV self-test vs. Pap invitation letter.	Women who did not respond to 2 invitations for screening.

* NR = Not reported.

each group by test (HPV and Pap), and percent positivity of high-risk HPV.

Two independent abstractors (SR and DW) extracted all data for quality control, and any discordance was resolved by consensus. The most recent article was included for articles that presented on the same dataset.

Methodological quality of studies

Study quality was assessed by looking at factors of appropriate randomization, reporting of allocation and loss to follow-up or dropouts, and representativeness of the sample to the underlying target population. A modified Downs and Black Tool[29] was used to guide the quality assessment of the studies. This allowed for the assessment of both randomized and non-randomized health intervention studies, by examining both internal and external validity. The terms low, medium and high referred to a qualitative judgement of whether the studies met few (low), some (medium) or most (high) of the criteria around randomization, reporting of group allocation and loss to follow-up, and representativeness of sample to the underlying target population.

Statistical analysis

All studies included in this review were used in the analysis to produce a pooled estimate of the relative compliance of HPV self-collected testing compared to Pap testing. Additional sensitivity analyses were conducted based on different study designs to ensure that variations in study design did not meaningfully impact the overall pooled estimate. The study-specific relative compliances and the overall pooled relative compliance were calculated using an intention-to-treat analysis. Women randomized to the HPV arm who elected to undergo Pap testing were analyzed as belonging to the HPV arm. However, for each study the compliance was reported by testing modality for each study arm.

The overall pooled relative compliance, with 95% confidence intervals, between the HPV self-testing groups and the control groups was calculated using a random effects model. We had to decide between using a fixed or random effects model for our meta-analysis. A fixed effects model is commonly used when all studies are attempting to estimate one true (fixed) effect size with a narrow distribution. A study with low variance is given more weight in a fixed effect model because it is seen as a better estimation of the true effect. A random effects model is used when individual studies are estimating different true effects, with their own distributions. In our meta-analysis, each country has its own true and valid measure of the effect of HPV self-testing on cervical cancer screening participation, which is impacted by the social norms and values of that country's culture. To allow the true effect to vary

Table 3. Overall Results of Compliance and Relative Compliance for All Studies Reviewed, Including High-risk-HPV Percent Positivity

Study (reference), Year, Country	Number of Participants	HPV Self-test Arm				Pap Test Arm		Relative Compliance (95% CI)	p-value	% High-risk HPV
		HPV Self-test Arm (n)	HPV Self-Test Compliance n (%)	Pap Test Compliance	Total HPV Self-test Compliance n (%)	Pap Test Arm	Pap Test Compliance n (%)			
Gok et al.,[33] 2012, Netherlands	25,822	25,561	7870 (30.8%)	n/a	**7870** (30.8%)	261	**17** (6.5%)	**4.727** (2.98-7.49)*	<0.0001	8.31%
Szarewski,et al.,[35] 2011, United Kingdom	3000	1500	96 (6.4%)	57 (3.8%)	**153** (10.2%)	1500	**68** (4.5%)	**2.250** (1.70-2.97)*	<0.0001	8.42%
Giorgi et al.,[34] 2011, Italy	1235	616	103 (16.7%)	18 (2.9%)	**121** (19.6%)	619	**86** (13.9%)	**1.414** (1.10-1.82)*	0.0073	21.36%
Wikstrom et al.,[36] 2011, Sweden	4060	2000	679 (34.0%)	100 (5.0%)	**779** (39.0%)	2060	**188** (9.1%)	**4.268** (3.69-4.94)*	<0.0001	6.04%
Virtanen et al.,[37] 2011, Finland	8699	2397	663 (27.7%)	93 (3.9%)	**756** (31.5%)	6302	**1631** (25.9%)	**1.219** (1.13-1.31*)	<0.0001	12.22%
Castle et al.,[40] 2011, United States of America	119	77	62 (80.5%)	n/a	**62** (80.5%)	42	**17** (40.5%)	**1.989** (1.36-2.92)*	0.0004	14.52%
Lazcano-Ponce et al.,[39] 2011, Mexico	22,102	9371	9202 (98.2%)	n/a	**9202** (98.2%)	12,731	**11,054** (86.8%)	**1.131** (1.12-1.14)*	<0.0001	9.61%
Piana et al.,[38] 2011, France	7854	3552	939 (26.4%)	n/a	**939** (26.4%)	4305	**311** (7.2%)	**3.659** (3.25-4.13)*	<0.0001	6.18%
Gok et al.,[32] 2010, Netherlands	27,163	26,886	7404 (27.5%)	51 (0.19%)	**7455** (27.7%)	277	**46** (16.6%)	**1.670** (1.28-2.18)*	0.0001	10.25%
Bias et al.,[31] 2007, Netherlands	2624	2352	736 (31.3%)	70 (3.0%)	**806** (34.3%)	272	**48** (17.6%)	**1.942** (1.49-2.53)*	<0.0001	7.98%

* Statistically significant p<0.01.

between studies, we used a random effects model so that each country could contribute equally (i.e., equal weights) to the overarching mean distribution of effect. The statistical heterogeneity was assessed using the I^2 statistic, which measures the variation across studies that is due to heterogeneity rather than chance.[30] All statistical tests were two-sided and analysis was performed using Stata 11.2 (Stata Corporation, College Station, TX, USA).

RESULTS

The systematic literature search identified a total of 242 articles, 87 from Medline and 155 from Embase (Figure 1). After removing duplicate articles, 178 article titles and abstracts were reviewed for inclusion. A total of 21 full-text articles were retrieved for full review, of which 10 met both the inclusion and exclusion criteria and were included in this review (Table 2).

Study characteristics

All studies were conducted between 2003 and 2010. The majority of the studies took place in Europe, specifically, the Netherlands,[31-33] Italy,[34] United Kingdom,[35] Sweden,[36] Finland,[37] and France.[38] All of the European studies used a randomized controlled trial design and took advantage of population registries to be able to identify non-attendees to cervical cancer screening programs. Non-attendees were subsequently randomized to either receive a HPV self-collection kit by mail or receive an invitation to undergo Pap testing.

Two studies were set in North America: one in Mexico[39] and one in the United States.[40] The North American studies differed from the European studies in their design and population definitions. In both North American settings, a door-to-door recruitment approach was used. The US study was non-randomized and was conducted in a neighbourhood that had a low rate of screening. Women who reported not receiving routine Pap testing were offered the option of performing a HPV self-test (delivered to the door) or of receiving a coupon to attend a free Pap-testing clinic. The Mexican study targeted underscreened women, i.e., those with "limited access to health services" and who would only be screened a few times over their lifetime.[39] Mexican participants were randomized from a database of women enrolled in a community-based program for women with limited access to health services. Randomized women received either an invitation to a free Pap-testing clinic, or a self-collected HPV testing kit delivered to her home by a study nurse. Despite the differences in study design, both of these studies employed similar methods for HPV self-testing and obtained similar HPV-positivity results comparable to those found in the European trials.

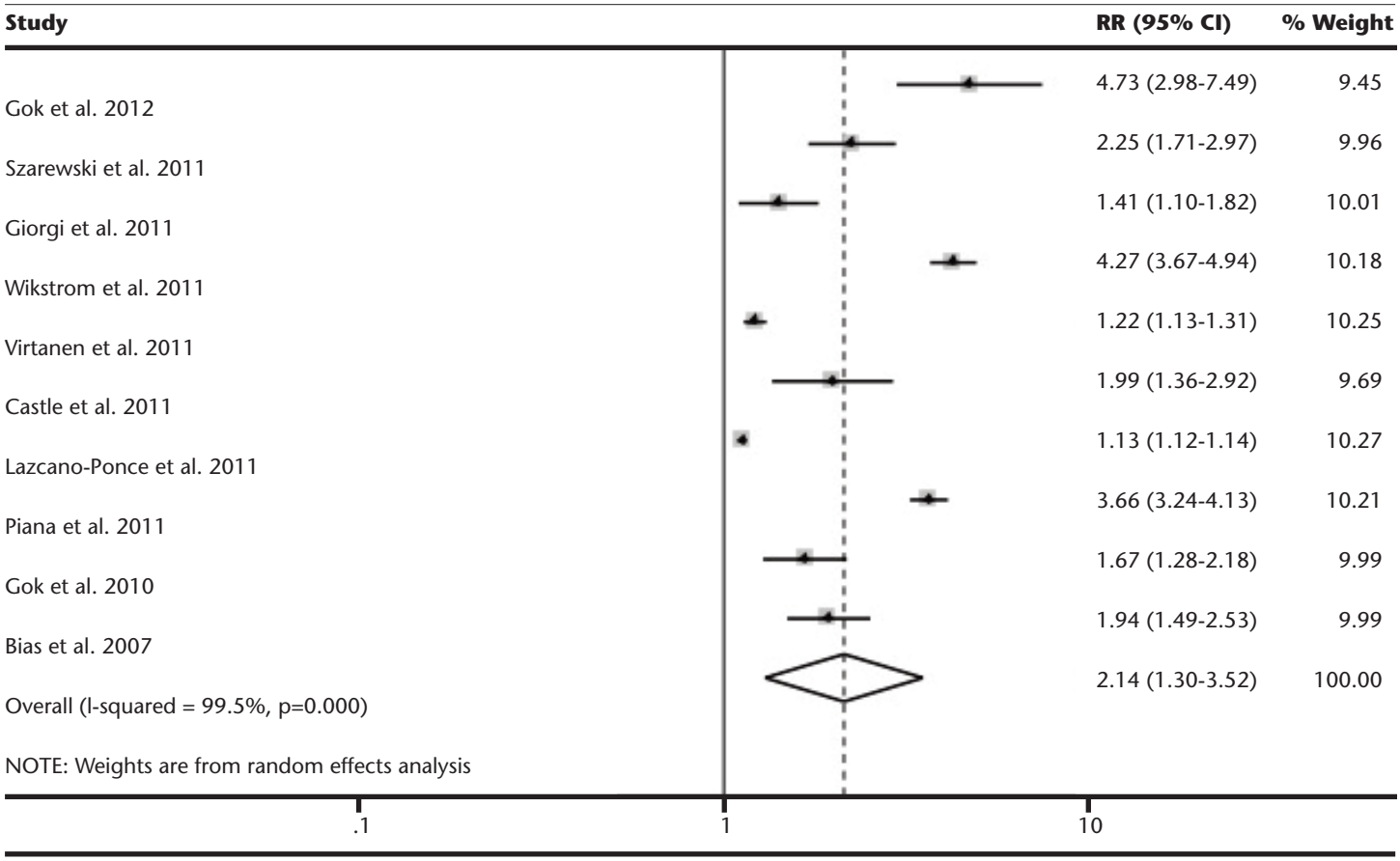
All of the studies included in the review were similar with regard to targeted age demographic, methods for HPV self-collection and Pap testing, and urban setting. In addition, all studies targeted women who were considered overdue for or who did not attend regular cervical cancer screening in their own jurisdictions.

The studies included did differ in the use of the self-collection device (Table 2). A wide variety of devices were employed across studies: cervovaginal brush,[31,33,39] vaginal swabs,[35,36,38,40] and lavage methods.[32,34,37]

Methodological quality of studies

Study quality was deemed to be high in all studies reviewed. All studies reported on allocation of participants and attrition, and

Figure 2. Forest plot for the pooled estimate of the relative screening compliance of women using HPV self-testing compared to invitation to Pap testing



9 out of 10 used a randomized allocation design. The level of compliance in testing varied between studies but was consistent within a given study, which provided confidence in the study recruitment and internal validity.

Compliance of HPV self-testing compared to Pap testing

The relative compliance of HPV self-collected testing compared to Pap testing was significantly greater than 1.0 in all reviewed studies; indicating that women were significantly more likely to participate in screening if they were offered HPV self-testing (Table 3). The pooled relative compliance was 2.14 (95% CI 1.30-3.52). These results indicate that women were twice as likely to participate in cervical screening if they were offered a HPV self-testing home kit compared to women who were invited to the clinic to undergo Pap testing. A Forest plot of the studies and the pooled effect estimate (Figure 2) indicated that statistical heterogeneity (I^2) was 99.5% ($p<0.0001$), representing significant heterogeneity between studies.

Overall, the compliance in screening varied widely between studies, with compliance reported in the HPV arms of between 10.2% and 98.2% and in the Pap test arms of between 4.5% and 86.8%. The highest study-specific compliances for both HPV testing and Pap testing were reported in the US and Mexican studies. All compliance and relative compliance estimates were unadjusted for any additional covariates, such as age, educational and marital status. Only the non-randomized study (US) examined age and education level, and found that younger age and higher education were associated with HPV self-testing compliance.[40]

HPV prevalence

All of the studies reported high specimen quality from self-collected samples for HPV testing. The percent positivity of high-risk HPV among those who administered the self-collected test ranged from 6.04% to 21.34%. Of the 10 studies, 8 used the hybrid-two capture assay for HPV detection,[32-37,39,40] and 2 used PCR genotype specific assays.[31,38]

DISCUSSION

To our knowledge, this is the first systematic literature review and meta-analysis that addresses the specific question of whether offering HPV self-testing, compared to Pap testing, improves participation in cervical cancer screening among women who are never or underscreened for cervical cancer. We found that never/underscreened women offered HPV self-testing were twice as likely to comply with/participate in cervical cancer screening. A large variety of self-collection devices were used so it is still unclear what the best HPV self-collection devices are for collecting reliable samples and maximizing comfort for women.

Many studies have examined the acceptance, reliability, and accuracy of self-collected HPV testing.[22-25] Overwhelmingly, HPV self-testing has been shown to have high acceptance among women, and women are able to collect good samples for testing using this method.[18-20] These factors support the notion that HPV self-collected testing has the potential to significantly improve cervical cancer screening compliance in women. Given that the studies reviewed in this analysis provided significant evidence that offering HPV self-testing did improve participation, HPV self-testing should be pur-

sued as a complement or alternative to Pap testing in women older than 30 who do not attend regular screening programs.

It is worth noting that HPV testing can potentially produce a relatively larger number of false positives (compared to Pap testing), due to transient infections. Infrastructure to provide timely and effective follow-up is an important component of any health care system that provides wide-scale HPV testing to ensure that women who are at an increased risk of cervical cancer are provided with appropriate follow-up care.[10]

Limitation of the studies reviewed

Large heterogeneity in compliance was observed between studies with reported compliance of HPV self-testing as high as 80.5% and others as low as 10.2%. The magnitude of the compliance was study-specific, however the relative compliance between studies was largely similar. This wide difference in observed compliance between studies was the main rationale for selecting a random-effects model. It was theorized that these studies and their populations were measuring different true effects and reflected the possible distribution of participation.

The studies included were predominately conducted in urban settings, with the exception of those in the US, Mexico, and one substudy site in rural Italy. The Italian study did find a significantly different relative compliance overall, favouring the use of HPV self-testing; however, within the rural substudy site, the compliance was not significantly different between the HPV self-test and the Pap test. The authors did note that the recruitment time period for this rural site was not optimal and so it is inconclusive whether there are true urban–rural differences. The US and Mexico studies both used door-to-door recruitment methods and had much higher response rates to both HPV self-testing and Pap testing; however, the door-to-door recruitment may have artificially increased their overall participation rates, plus – unfortunately – screening programs using door-to-door delivery are not sustainable in many areas.

The US and Mexico studies were included in the pooled estimate, despite obvious differences from the European trials. The four main differences were: rural locale, high overall response rate, lack of randomization in the US study, and lack of definitive Pap testing history in the Mexican study. A sensitivity analysis was conducted to estimate the pooled relative compliance without the inclusion of those two studies. The sensitivity analysis yielded an estimated pooled relative compliance of 2.34 (95% CI 1.47-3.70), which indicated that the addition of these two community trials did not alter the overall results, and if anything their inclusion provides a more conservative estimate of effect. However, potential differences in compliance between rural and urban women may still exist due to the observed lower relative compliance when both rural studies are taken into account, coupled with the non-significant finding in the rural Italian substudy site. Differences between rural and urban settings should continue to be elucidated, especially given that rural areas have been shown to have lower screening participation and increased burden of cervical cancer.[41-43]

Limitations of the review

One of the limitations of this review is the scope of articles included. The exclusion of middle-/low-income study sites led to the omission of four studies – three from India and one from China – that explored HPV self-testing in a developing country context.[44-46] The authors of the three Indian studies concluded that self-collected testing improved screening participation in women. Despite not including the data in the review, the overarching message of increased participation with the provision of HPV self-testing was echoed throughout these studies. Four additional studies, which examined uptake of HPV self-testing, were omitted due to a lack of comparison group.[24,47-49] Within this group of studies, the uptake of HPV self-test was reported as between 32.0% and 58.0%, a comparable estimation to the HPV self-testing uptake reported by the studies included in this review.

Another limitation of this review is that studies employing multiple intervention arms were only analyzed based on the comparison between the Pap testing control group and the intervention arm that employed the use of mailed HPV self-collection test kits. The other intervention arms that were included in some trials consisted of providing HPV testing in a clinic setting or having participants request a self-collection kit by phone. The restriction to only analyze participants who were provided with HPV self-collected testing by mail was to improve comparability across studies. Additionally, if a study employed a multi-phase or crossover design, only the initial phase of the study was included in the analysis, again to ensure that the comparison groups across the trials were as similar as possible, as participation response in subsequent phases may have been impacted due to increased study exposure from a prior invitation or study information relating to cervical cancer screening. This review attempted to simplify the complexity in many of these trials so that they could be reasonably compared, which allowed the authors to identify the overarching trend in women's participation in cervical cancer screening programs when provided with an offer of HPV self-collected testing.

Potential publication bias (for null results) was addressed by searching conference proceedings. All conference abstracts were accounted for by identified publications. Despite the potential for outstanding null effect studies, a null effect would not change the pooled effect from these 10 positive studies. A broad search criterion was used to reduce the potential for missing relevant articles. It is unlikely that the literature is missing a large negative study, and though one negative study might pull the pooled effect towards the null, it would not negate the significantly positive effect.

CONCLUSION

HPV self-testing could significantly improve cervical cancer screening participation, especially in those who are never or under-screened for cervical cancer. As HPV testing becomes more widely accepted as a primary screening tool or co-testing approach with Pap testing, new approaches to cervical cancer screening delivery should be considered. However, appropriate follow-up and treatment for women who do test high-risk HPV-positive need to develop concurrently with HPV self-testing delivery. Future research efforts in HPV self-testing should focus on exploring effective HPV self-test delivery methods and infrastructure, and examining the uptake in rural areas, where the use of HPV self-testing has the potential to make dramatic improvements in those communities.

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RÉSUMÉ

OBJECTIF : Le test du VPH se montre efficace pour dépister le cancer du col utérin. Le recours à l'autotest du VPH pourrait potentiellement surmonter un bon nombre des obstacles au dépistage et joindre les

femmes à risque en les faisant participer au dépistage. Il faut cependant examiner les preuves pour voir si le fait d'offrir l'autotest du VPH augmente en pratique le recours au dépistage. Nous avons cherché à déterminer dans quelle mesure le fait d'offrir l'autotest du VPH augmente le recours au dépistage chez les femmes qui ne sont jamais ou qui sont insuffisamment examinées pour le cancer du col utérin.

MÉTHODE : Une revue systématique de la littérature spécialisée dans les bases de données Medline et Embase a permis de recenser les articles traitant de l'utilisation de l'autotest du VPH pour dépister le cancer du col utérin. Nous avons effectué une méta-analyse à l'aide d'un modèle à effets aléatoires pour calculer la conformité relative, avec une analyse en intention de traiter de l'autotest du VPH comparativement au dépistage par frottis de Papanicolaou, avec des intervalles de confiance (IC) de 95 %. Tous les tests statistiques étaient bilatéraux.

SYNTHÈSE : Dix études ont été examinées dont huit européennes et deux nord-américaines. Sur les 10 études, neuf employaient un plan d'étude aléatoire. Dans toutes les études, la conformité relative de l'autotest du VPH par rapport au frottis était significativement plus élevée que 1,0 ($p<0,01$). La conformité relative globale était de 2,14 (IC de 95 % : 1,30-3,52). La conformité au dépistage était très hétérogène d'une étude à l'autre, tant pour l'autotest du VPH que pour le dépistage par frottis.

CONCLUSION : L'autotest du VPH améliorait significativement la participation des femmes qui n'avaient pas systématiquement recours aux programmes de dépistage du cancer du col utérin. De nouvelles approches de prestation de l'autotest du VPH devraient être envisagées à mesure que l'intégration du test du VPH en tant qu'outil de dépistage primaire se généralise.

MOTS CLÉS : papillomavirus humain; dépistage du cancer du col utérin; échantillons auto-prélevés; sous-dépistage; examen