

CADTH Reference List

HPV Self-Sampling for Primary Cervical Cancer Screening: A 2021 Update

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Key Message

Ten non-randomized studies were identified regarding diagnostic accuracy or agreement of self-sampled HPV tests and clinician-sampled HPV tests for asymptomatic cervical cancer screening.

Research Questions

1. What is the diagnostic test accuracy of self-sampled HPV tests compared with clinician-sampled HPV tests or cytology for asymptomatic cervical cancer screening?
2. What is the clinical evidence regarding the agreement or concordance of self-sampled HPV tests and clinician-sampled HPV tests or cytology for asymptomatic cervical cancer screening?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were self-sampling and HPV. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2018 and August 16, 2021. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

Results

Ten relevant references were identified for this report.¹⁻¹⁰ All relevant references were non-randomized studies examining diagnostic test accuracy of self-sampled HPV tests and clinician-sampled HPV tests for asymptomatic cervical cancer screening.¹⁻¹⁰ Three of the identified non-randomized studies also examined the agreement of self-sampled HPV tests and clinician-sampled HPV tests for cervical cancer screening.^{1,8,10} No relevant health technology assessments, systematic reviews, or randomized controlled trials were identified.

Table 1: Selection Criteria

Criteria	Description
Population	Asymptomatic adults eligible for cervical cancer screening (≥ 21 years of age, or age at which screening starts in the jurisdiction)
Intervention	Q1 and Q2: Self-sampled high-risk HPV tests for primary cervical cancer screening
Reference standard	Q1 only: Colposcopy with histologic examination of tissue specimens, when indicated
Comparator	Q1 and Q2: Clinician-sampled high-risk HPV tests for primary cervical cancer screening; cytology (conventional Pap smear or liquid based cytology)
Outcomes	Q1: Diagnostic test accuracy (e.g., sensitivity, specificity, positive predictive value, negative predictive value) Q2: Agreement between self-sampled HPV tests and clinician-sampled HPV tests or cytology (i.e., % agreement of positive test results, % agreement of negative test results)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Overall Summary of Findings

Ten non-randomized studies¹⁻¹⁰ were identified regarding diagnostic test accuracy of self-sampled HPV tests and clinician-sampled HPV testing for asymptomatic cervical cancer screening. Authors of 3 of the 10 identified non-randomized studies^{1,8,10} also examined the agreement of self-sampled HPV tests and clinician-sampled HPV tests for asymptomatic cervical cancer screening. Table 2 details the summary of findings from the relevant abstracts identified. Overall, self-collected samples (urine or vaginal swab) for HPV testing related to cervical cancer screening appears to be comparable to clinician collected swabs, depending on the test used.

Table 2: Overall Summary of Findings

Author, year	Population	Intervention(s)	Comparator(s)	Outcome(s)	Authors' conclusions
Bokan et al. (2021)¹	N = 209 women Colposcopy population from National Cervical Cancer Screening Programme ZORA	SC vaginal swab Qvintip (n = 111) HerSwab (n = 98)	CC cervical smears Conventional cytology HPV testing	Qvintip (SC) cytology vs. Qvintip (SC) HPV vs. CC HPV: Sensitivity: 71.8% vs. 83.1% vs. 94.4% Specificity: 75.0% vs. 51.3% vs. 57.5% PPV: 83.6% vs. 75.6% vs. 79.8% NPV: 60.0% vs. 62.5% vs. 85.2% HerSwab (SC) vs. HerSwab (SC) HPV vs. CC HPV: Sensitivity: 71.7% vs. 75.0% vs. 94.3% Specificity: 46.7% vs. 47.7% vs. 44.4% PPV: 61.3% vs. 62.9% vs. 66.7% NPV: 58.3% vs. 61.8% vs. 87.0% Percent agreement (SS [Qvintip] vs. CC): 81.8% (kappa = 0.534) Percent agreement (SS [HerSwab] vs. CC): 77.1% (kappa = 0.456)	"The results confirm that HPV self-sampling is not as accurate as clinician sampling when HC2 is used." ¹
Cho et al. (2021)²	N = 314 matched samples Referred for colposcopy following abnormal cytology	SC urine and vaginal samples	CC cervical samples	Sensitivity Vaginal vs. cervical: 0.91 (95% CI, 0.90 to 1.03) vs. 0.87 (95% CI, 0.75 to 1.02) Urine vs. cervical: 0.79 (95% CI, 0.70 to 0.92) vs. 0.74 (95% CI, 0.61 to 0.89)	"The detection performance for hrHPV and CIN2+ on self-collected vaginal samples was comparable to that of clinician-collected cervical samples. On the other hand, HPV tests using urine were inferior to those using clinician-collected cervical samples in terms of detecting hrHPV and CIN2+." ²
Klischke et al. (2021)³	N = 89 Colposcopy clinic	Dry SC cervico-vaginal samples	CC samples	SC vs. CC: Sensitivity (CIN2+): 26.1% (95% CI, 0.13 to 0.46) vs. 45.5% (95% CI, 0.27 to 0.65) Specificity (CIN2+): 95.6% (95% CI, 0.85 to 0.99) vs. 78.3% (95% CI, 0.64 to 0.88)	"...the results of the self-collected samples differed clearly in comparison to the reference samples." ³

Author, year	Population	Intervention(s)	Comparator(s)	Outcome(s)	Authors' conclusions
Lorenzi et al. (2021) ⁴	N = 232 Colposcopy clinic because of abnormal Pap smear	SC HRHPV samples	CC HRHPV samples	SC vs. CC: Accuracy (CIN2+): 78.1% vs. 75.2% PPV (CIN2+): 80.0% vs. 76.5% NPV (CIN2+): 64.3% vs. 66.7% PLV (CIN2+): 1.36 vs. 1.35 NLV (CIN2+): 0.19 vs. 0.21	"SC, when associated with testing with biomarkers, is as accurate as collection by HPs in the detection of women at risk for cervical cancer." ⁴
Van Keer et al. (2021) ⁵	N = NR VALHUDES study	SC HRHPV	CC HRHPV	Relative sensitivity (CIN2+): 0.95 (95% CI, 0.88 to 1.01) Relative specificity (CIN2+): 1.03 (95% CI, 0.95 to 1.13) Subgroup (women > 30 years) Relative sensitivity (CIN2+): 0.97 (95% CI, 0.89 to 1.05) Relative specificity (CIN2+): 1.02 (95% CI, 0.93-1.12)	"HrHPV-DNA based PCR testing on home-collected first-void urine has similar accuracy for detecting CIN2+ compared to cervical samples taken by a clinician." ⁵
Onuma et al. (2020) ⁶	N = NR Previous negative test for IEL or HPV positive and ASCUS+	SC with Evalyn brush	CC with endocervical brush	SC vs. CC Sensitivity (CIN2+): 100% vs 100% Specificity (CIN2+): 57.0% vs. 58.1%	"Self-sampling showed high sensitivity for CIN2+. Self-sampling using the Evalyn brush and Cobas 4800 may be feasible for screening Japanese individuals." ⁶
Rohner et al. (2020a) ⁷	N = 314 Women aged 25 to 65 at 2 colposcopy clinics	SC cervico-vaginal samples	CC cervical samples	Positive results (HRHPV): SC: 76% CC = 70% P = 0.009	"Overall sensitivity for CIN2+ detection was similar for both sample types, but the higher HPV-16 prevalence in self-collected samples could result in increased colposcopy referral rates." ⁷
Rohner et al. (2020b) ⁸	N = 307 Women aged 25 to 65 at 2 colposcopy clinics	SC urine and cervico-vaginal samples	CC cervical samples	Sensitivity (CIN2+): Urine SC: 80% (95% CI 71 to 88%) Cervico-vaginal SC: 94% (95% CI, 89 to 99%) Cervical CC: 94% (95% CI, 89 to 99%) Agreement, urine vs. CC sample: kappa = 0.54	"Urine-based hrHPV testing may be a promising approach to improve cervical cancer screening coverage, especially among women with limited access to health care." ⁸

Author, year	Population	Intervention(s)	Comparator(s)	Outcome(s)	Authors' conclusions
El-Zein et al. (2019) ⁹	N = 700 (subset of CASSIS study)	HerSwab	CC samples	SC vs. CC PPV (CIN2+) : 28% (95% CI, 23.2 to 33.1) vs. 29.7% (95% CI, 24.8 to 34.9) NPV (CIN2+) : 96.4% (95% CI, 93.9 to 98.1) vs. 97.8% (95% CI, 95.6 to 99)	"Our results confirm that HPV self-sampling has comparable performance with a physician-collected sample in detecting cervical lesions." ⁹
Nutthachote et al. (2019) ¹⁰	N = 400	SC	CC	Detection rate: SC vs. CC (HPV DNA) 10.0% vs. 7.5% kappa = 0.73	"HPV DNA test positive for detection CIN+ was not significantly different between self-collected and clinician-collected testing." ¹⁰

ASCUS+ = atypical squamous cells of undetermined significance or worse; CASSIS = Cervical And Self-Sample In Screening; CC = clinician collected; CI = confidence interval; CIN2+ = cervical intraepithelial neoplasia grade 2 or higher; HC2 = Hybrid Capture 2; HRHPV = high risk HPV; IEL = intraepithelial lesions; NR = not reported; NLV = negative likelihood value; NPV = negative predictive value; PLV = positive likelihood value; PPV = positive predictive value; SC = self-collected.

References

Health Technology Assessments

No literature identified

Systematic Reviews and Meta-analyses

No literature identified

Randomized Controlled Trials

No literature identified

Non-Randomized Studies

1. Bokan T, Ivanus U, Jerman T, et al. Long term results of follow-up after HPV self-sampling with devices Qvintip and HerSwab in women non-attending cervical screening programme. *Radiol Oncol.* 2021 01;55(2):187-195. doi: [10.2478/raon-2021-000110.2478/raon-2021-0001](https://doi.org/10.2478/raon-2021-000110.2478/raon-2021-0001)
2. Cho HW, Hong JH, Min KJ, et al. Performance and Diagnostic Accuracy of Human Papillomavirus Testing on Self-Collected Urine and Vaginal Samples in a Referral Population. *Cancer Res Treat.* 2021 07;53(3):829-836. doi: [10.4143/crt.2020.116510.4143/crt.2020.1165](https://doi.org/10.4143/crt.2020.116510.4143/crt.2020.1165)
3. Klischke L, von Ehr J, Kohls F, et al. Performance of a six-methylation-marker assay on self-collected cervical samples - A feasibility study. *J Virol Methods.* 2021 09;295:114219. doi: [10.1016/j.jviromet.2021.11421910.1016/j.jviromet.2021.114219](https://doi.org/10.1016/j.jviromet.2021.11421910.1016/j.jviromet.2021.114219)
4. Lorenzi NPC, Termini L, Ferreira-Filho ES, et al. A positive HPV test with positive p16/Ki-67 double staining in self-sampled vaginal material is an accurate tool to detect women at risk for cervical cancer. *Cancer Cytopathol.* 2021 08;10:10. doi: [10.1002/cncy.2249810.1002/cncy.22498](https://doi.org/10.1002/cncy.2249810.1002/cncy.22498)
5. Van Keer S, Peeters E, Vanden Broeck D, et al. Clinical and analytical evaluation of the RealTime High Risk HPV assay in Colli-Pee collected first-void urine using the VALHUDES protocol. *Gynecol Oncol.* 2021 06;162(3):P575-583. doi: [10.1016/j.ygyno.2021.06.01010.1016/j.ygyno.2021.06.010](https://doi.org/10.1016/j.ygyno.2021.06.01010.1016/j.ygyno.2021.06.010)
6. Onuma T, Kurokawa T, Shinagawa A, et al. Evaluation of the concordance in HPV type between self- and physician-collected samples using a brush-based device and a PCR-based HPV DNA test in Japanese referred patients with abnormal cytology or HPV infection. *Int J Clin Oncol.* 2020 09;25(10):1854-1860. doi: [10.1007/s10147-020-01727-510.1007/s10147-020-01727-5](https://doi.org/10.1007/s10147-020-01727-510.1007/s10147-020-01727-5)
7. Rohner E, Edelman C, Sanusi B, et al. Extended HPV Genotyping to Compare HPV Type Distribution in Self- and Provider-Collected Samples for Cervical Cancer Screening. *Cancer Epidemiol Biomarkers Prev.* 202012;29(12):2651-2661. doi: [10.1158/1055-9965.EPI-20-067410.1158/1055-9965.EPI-20-0674](https://doi.org/10.1158/1055-9965.EPI-20-067410.1158/1055-9965.EPI-20-0674)
8. Rohner E, Rahangdale L, Sanusi B, et al. Test Accuracy of Human Papillomavirus in Urine for Detection of Cervical Intraepithelial Neoplasia. *J Clin Microbiol.* 2020 02;58(3). doi: [10.1128/JCM.01443-1910.1128/JCM.01443-19](https://doi.org/10.1128/JCM.01443-1910.1128/JCM.01443-19)
9. El-Zein M, Bouten S, Louvanto K, et al. Predictive Value of HPV Testing in Self-collected and Clinician-Collected Samples Compared with Cytology in Detecting High-grade Cervical Lesions. *Cancer Epidemiol Biomarkers Prev.* 2019 07;28(7):1134-1140. doi: [10.1158/1055-9965.EPI-18-133810.1158/1055-9965.EPI-18-1338](https://doi.org/10.1158/1055-9965.EPI-18-133810.1158/1055-9965.EPI-18-1338)
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Appendix 1: References of Potential Interest

Previous CADTH Reports

11. HPV Self-Sampling for Primary Cervical Cancer Screening: A Review of Diagnostic Test Accuracy and Clinical Evidence – An Update. Ottawa (ON): CADTH; 2019 05. <https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1124%20HPV%20Self-Sampling%20Update%20Final.pdf>
12. HPV Testing for Primary Cervical Cancer Screening: A Health Technology Assessment. Ottawa (ON): CADTH; 2019 03. <https://www.cadth.ca/sites/default/files/ou-tr/op0530-hpv-testing-for-pcc-report.pdf>

Systematic Reviews

Alternative Outcome – Clinical Utility

13. Tesfahunei HA, Ghebreyesus MS, Assefa DG, et al. Human papillomavirus self-sampling versus standard clinician-sampling for cervical cancer screening in sub-Saharan Africa: a systematic review and meta-analysis of randomized controlled trials. *Infect Agent Cancer*. 2021 06;16(1). doi: [10.1186/s13027-021-00380-5](https://doi.org/10.1186/s13027-021-00380-5)

Unclear Methodology

14. Chaichan S, Sawanyawisuth K, Limpawattana P, et al. Roles of self-sampling for human papillomavirus in developing countries. *J Med Assoc Thai*. 2020;103(1):68-72. <http://www.jmatonline.com/index.php/jmat/article/view/10753>

Randomized Controlled Trials

Unclear Outcome

15. Aarnio R, Isacson I, Sanner K, et al. Comparison of vaginal self-sampling and cervical sampling by medical professionals for the detection of HPV and CIN2+: A randomized study. *Int J Cancer*. 2021 06;148(12):3051-3059. doi: [10.1002/ijc.33482](https://doi.org/10.1002/ijc.33482)

Non-Randomized Studies

Alternative Population – Non-Asymptomatic Patients

16. Ornskov D, Jochumsen K, Steiner PH, et al. Clinical performance and acceptability of self-collected vaginal and urine samples compared with clinician-taken cervical samples for HPV testing among women referred for colposcopy. A cross-sectional study. *BMJ Open*. 2021 05;11(3):e041512. doi: [10.1136/bmjopen-2020-041512](https://doi.org/10.1136/bmjopen-2020-041512)
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