

Title: HPV Self-Sampling for Cervical Cancer Screening: A Rapid Review

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Sources

This rapid review is being conducted by the Evidence Synthesis Group at the Complex Reviews Synthesis Unit (ESG @CRSU) to synthesise evidence relevant to the forthcoming publication of the YouScreen study, which estimated the impact of offering HPV self-sampling to non-attenders within the cervical screening programme in England.(1)

Sponsor

This study is funded by the NIHR Evidence Synthesis Programme.

Role of Sponsor or Funder

The protocol was developed independently of the funder of the study (NIHR). Feedback on a draft protocol, and approval of the final protocol, were sought from the UK National Screening Committee (NSC).

Conflict of interest

No authors have known conflicts of interest to declare.

Introduction

Rationale

Globally, cervical cancer is the fourth most frequent malignancy, and in the UK, has an approximate incidence of 3200 diagnoses annually.(2) Persistent genital infection with Human Papillomavirus (HPV), one of the most common sexually transmitted infections, is responsible for an estimated 99.7% cases of cervical cancer.(3) Indeed, the more than 200 HPV genotypes may be stratified into high-risk (hrHPV), and low-risk/non-oncogenic strains; the former includes types 16, 18, 31 and 33. Protracted HPV infection is associated with the development of cervical intraepithelial neoplasia (CIN), a precursor of cervical cancer which is classified according to the severity of dysplasia as CIN1 (low grade), CIN2 (moderate grade) and CIN3 (high grade).(4) The development of cervical cancer from CIN3 can take over a decade; owing to the considerable lag period between HPV infection and the development of cervical cancer, there is substantial opportunity for early detection of precancerous lesions via screening.(5)

The NHS cervical screening programme was introduced in 1988; currently, individuals with a cervix in England and Northern Ireland are invited for screening three-yearly between the ages of 25 and 49, and five-yearly between ages 50 and 64, whilst in Scotland and Wales, eligible individuals are screened at intervals of five years.(2) Owing to greater sensitivity in identifying CIN, hrHPV DNA detection has replaced cytological techniques as the preferred screening method. Those with a positive result are referred for cytology; individuals with abnormal cytology are invited for colposcopy. Clinical guidelines recommend monitoring CIN1 lesions for progression to more severe dysplasia, whilst CIN2+ lesions should be managed by removing the abnormal cells, most frequently by large loop excision of the cervical transformation zone (LLETZ).(4)

Whilst screening programmes have been demonstrated to mitigate the incidence of cervical cancer, coverage in many countries is suboptimal, and cervical cancer is most frequently diagnosed in those who are either underscreened or who have never participated in regular screening.(6, 7) Indeed, the reasons for non-participation are multifarious, but may include insufficient time to attend a clinic, lack of awareness, anxiety regarding a gynaecological examination, or physical discomfort during specimen collection. Participation is often reduced in some patient populations, including those in minority ethnic groups, those of low socio-economic status, and transgender and non-binary people with a cervix.(8, 9) A range of diagnostic HPV-DNA tests and sampling methods are available, and samples may be self-collected from the vagina, as an alternative to collection from the cervix by a healthcare professional.(10) Indeed, self-sampling has several advantages compared to clinician-based sampling, including reduced invasiveness, greater privacy, more convenient, and it has thus been proposed as a strategy to improve uptake of cervical screening. Furthermore, there is increasing evidence that self-sampling has good diagnostic accuracy is acceptable to screenees, and that it may improve cervical screening coverage.(11) Several countries, including France, Sweden and Australia, have incorporated self-sampling into their national screening programmes, either as a primary screening approach, or as a method targeted at underscreened individuals.

There is interest within the National Screening Committee to incorporate self-sampling into the cervical screening programme in the UK, specifically for non-attenders.(1) YouScreen was an

implementation feasibility study which evaluated the impact of opportunistically offering HPV self-sampling at primary care encounters to people that did not attend for cervical screening in England.

To contextualise, and better understand the potential policy implications of the findings of the YouScreen study, this rapid review is intended to address the following clinical questions:

- What is the accuracy of HPV testing in self-collected samples compared with health professional collected samples, and does this vary according to patient and test characteristics?
- In cervical screening non-attenders, what is the level of agreement between HPV-DNA testing in self-collected samples and clinician / health professional collected samples, and does this vary according to patient and test characteristics?
- What is the uptake of cervical screening in screening non-attenders offered HPV self-sampling compared with those offered health professional sampling, and does this vary according to patient and test characteristics?
- Are HPV self-sampling screening strategies acceptable to those that have not attended the regular cervical screening programme, and does this vary according to patient and test characteristics?

Objectives

The primary objectives of this rapid review are:

- To compare the diagnostic accuracy of HPV-DNA testing on self-collected samples with testing on samples collected by a healthcare professional, in individuals who do not participate in a regular cervical screening programme
- To compare the uptake of cervical screening and adherence to follow-up, for self-sampling compared to sample collection by a healthcare professional, in people who do not participate in a regular cervical screening programme
- To evaluate the acceptability of self-collection of samples for HPV-DNA testing in individuals who do not participate in a regular cervical screening programme, and the factors which influence acceptability.

The secondary objectives of this rapid review are:

- To determine if the diagnostic accuracy of HPV testing of self-collected samples varies according to patient characteristics, including socio-economic status, screening history, and clinical history, and test characteristics, including sampling device, storage medium, testing methodology, and setting.
- To assess the variation in uptake of cervical screening and adherence to follow-up for self-sampling in people who do not participate in a regular cervical screening programme, according to patient characteristics, including socio-economic status and clinical history, and test characteristics, including sampling device, storage medium, testing methodology, and setting.

Methods

The approach to this rapid review has primarily been developed based on recent recommendations and methodological guidance provided by the Cochrane Rapid Reviews Methods Group, and this protocol has been adapted from a template originally developed by Cochrane for rapid reviews on COVID-19.(12-17) However, it also accounts for the specific challenges of rapid reviews on diagnostic tests, namely the particular statistical methods for diagnostic accuracy and methodologies explicitly designed to evaluate the conduct of studies of diagnostic tests.(18)

To optimise the methodological rigour of this rapid review, preference is given to restriction, rather than omission, of systematic review components.(16) Indeed, given the required expediency of the evidence synthesis, this pragmatic approach leverages multiple existing well-conducted systematic reviews which are aligned with the respective objectives of this rapid review. Where applicable, these form the basis of our data extraction, with limited searches overlapping those utilised in the reviews, intended to identify new publications with which analyses can be updated. To meet stakeholder needs, evidence synthesis will be prioritised as a deliverable over the quality assessment of included studies. Furthermore, we will engage regularly with the NSC throughout the rapid review process to ensure that outputs are aligned with their requirements. Patient and public involvement activities were embedded within the YouScreen study, so are not included within this rapid review.

Criteria for Considering Studies for this Review and Search Methods for Identification of Relevant Studies

The eligibility criteria and search methods for each respective clinical question are outlined separately. The respective systematic reviews upon which each search strategy is based are reported, with the search strategies detailed in the Appendix. The start dates for the searches have been selected to allow for three months of overlap with the end date of the search in the prior review, to ensure that all relevant new publications are captured. The identification of ongoing studies is limited in this review to ClinicalTrials.gov, for instances in which a more comprehensive search of multiple trial registries has been conducted in the primary review(s).

What is the accuracy of HPV testing in self-collected samples compared with health professional collected samples, and does this vary according to patient and test characteristics?

A prior review by Arbyn et al. will be used as a basis in addressing this question.(19)

Population	Individuals eligible for cervical screening
Index Test	HPV testing on self-collected sample
Comparator Test	HPV testing on healthcare professional-collected sample
Reference Standard	Colposcopy +/- biopsy as indicated
Co-variates	<ul style="list-style-type: none"> • background risk of population • screening history of population (e.g under-screened, never screened) • clinical history of population (e.g HIV positive)

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	<ul style="list-style-type: none"> • testing methodology • sampling method/kit • storage medium • home-based vs in clinic self-sampling • age • Socioeconomic background • Ethnicity 		
Outcomes (where available)	<ul style="list-style-type: none"> • Absolute sensitivity and specificity of HPV self-sampling for the detection of CIN2+ and CIN3+ of index and comparator tests. • Relative sensitivity and specificity of HPV self-sampling for CIN2+ and CIN3+ of HPV self-sampling versus clinician-based sampling • False-positive and false-negative rates of HPV self-sampling versus clinician-based sampling • PPV and NPV of HPV self-sampling • Proportion of self selected samples in which HPV status cannot be determined (e.g. insufficient sample, failed lab tests). • Proportion of women with a 'failed' test/sample who are asked to provide a second sample. • Proportion of women with a positive test result who attend clinic for diagnostic investigations and treatment (including cytology follow-up) 		
Study designs	Cross-sectional studies, cohort studies, RCTs, systematic reviews.		
Electronic databases	Database <input checked="" type="checkbox"/> MEDLINE <input checked="" type="checkbox"/> CENTRAL <input checked="" type="checkbox"/> EMBASE <input type="checkbox"/> Other (please specify, e.g. PsycINFO) <input checked="" type="checkbox"/> Clinical Trial Registry (ClinicalTrials.gov)	From: <i>1st January 2018</i> <i>(overlap with Arbyn et al. 2018)</i>	To: March 2024

Methods for screening search results

Expertise	Screening will be performed by RM and NT
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Screening methods	Dual; second reviewer checks all excluded records	<input checked="" type="checkbox"/>	<input type="checkbox"/>
	Dual; second reviewer checks 20% of excluded records	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Dual; independent screen and cross check	<input type="checkbox"/>	<input type="checkbox"/>
Discrepancy resolution	<input checked="" type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)		
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies		
Inclusion of abstracts and conference proceedings	<input checked="" type="checkbox"/> Exclude all <input type="checkbox"/> Include if clearly eligible and have usable data <input type="checkbox"/> Include if clearly eligible regardless of usable data <input type="checkbox"/> Include if eligibility is unclear and add to section in report		
Inclusion of non-English language studies	<input type="checkbox"/> Include abstracts and full texts <input type="checkbox"/> Include full texts only <input checked="" type="checkbox"/> Exclude		
	<input type="checkbox"/> All potentially relevant abstracts will progress to full text screen <input type="checkbox"/> [Single/dual] title/abstract screen by foreign-language speaker(s) <input type="checkbox"/> [Abstract/ <u>methods</u> /full text] will be translated for abstract/ <u>full text</u> screen <input checked="" type="checkbox"/> Listed as non-English language and not assessed further		

In cervical screening non-attenders, what is the level of agreement between HPV-DNA testing in self-collected samples and health professional collected samples, and does this vary according to relevant patient and test characteristics?

A prior review by Arbyn et al. will be used as a basis in addressing this question, with specific additional consideration of an updated review and meta-analysis on concordance between self-collected and clinician-collected samples for HPV testing.(19, 20)

Population	Individuals eligible for cervical screening
Index test	HPV testing on self-collected specimens
Comparator/reference standard	HPV testing on healthcare professional-collected specimens in index test subject
Co-variates	<ul style="list-style-type: none"> • background risk of population • clinical history of population • testing methodology • sampling method / kit • storage medium • home-based vs in clinic self-sampling • age?

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	<ul style="list-style-type: none"> • Socioeconomic background? • Ethnicity? • Comorbidities are those captured by clinical history? 		
Outcomes (where available)	<ul style="list-style-type: none"> • HPV status • Test positivity ratio • Percent positive agreement • Percent negative agreement • Cohen’s Kappa statistic • Positive concordance • Negative concordance 		
Study designs	RCTs, cohort studies, systematic reviews.		
Electronic databases	Database <input checked="" type="checkbox"/> MEDLINE <input checked="" type="checkbox"/> CENTRAL <input checked="" type="checkbox"/> EMBASE <input type="checkbox"/> Other (please specify, e.g. PsycINFO) <input checked="" type="checkbox"/> Clinical Trial Registry (ClinicalTrials.gov)	From: <i>1st January 2018</i> <i>(overlap with Arbyn et al. 2018)</i>	To: March 2024

Methods for screening search results			
Expertise	Screening will be performed by RM and NT		
Screening methods	Dual; second reviewer checks all excluded records Dual; second reviewer checks 20% of excluded records Dual; independent screen and cross check	<i>Abstract</i> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<i>Full text</i> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/>
Discrepancy resolution	<input checked="" type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)		
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies		
Inclusion of abstracts and conference proceedings	<input checked="" type="checkbox"/> Exclude all <input type="checkbox"/> Include if clearly eligible and have usable data <input type="checkbox"/> Include if clearly eligible regardless of usable data <input type="checkbox"/> Include if eligibility is unclear and add to section in report		
Inclusion of non-English language	<input type="checkbox"/> Include abstracts and full texts <input type="checkbox"/> Include full texts only		

HPV Self-sampling for Cervical Screening: Rapid Review Protocol

studies	<input checked="" type="checkbox"/> Exclude
	<input type="checkbox"/> All potentially relevant abstracts will progress to full text screen
	<input type="checkbox"/> [Single/dual] title/abstract screen by foreign-language speaker(s)
	<input type="checkbox"/> [Abstract/ <u>methods</u> /full text] will be translated for abstract/ <u>full text</u> screen
	<input checked="" type="checkbox"/> Listed as non-English language and not assessed further

What is the uptake of cervical screening in screening non-attenders offered HPV self-sampling compared with those offered health professional sampling, and does this vary according to relevant patient and test characteristics?

A prior review by Arbyn et al. will be used as a basis in addressing this question.(19)

Population	Individuals eligible for cervical screening who did not participate in the standard cervical screening programme, did not respond to invitations to attend for clinician-based cervical screening, are under-screened
Intervention	Invitation to HPV based cervical screening - self sampling: opt-in, mailed, door-to-door, opportunistic
Comparator	Invitation to HPV based cervical screening - clinician / health professional sampling
Co-variates	<ul style="list-style-type: none"> • invitation strategy (including opt-in; opt-out; opportunistic) • screening history • time from invitation for clinician / health professional sampling • clinical history of population • sampling method (brush, swab, lavage) • location of test (home vs. clinic/primary care) • use of reminders (e.g. SMS) • age? • Socioeconomic background? • Ethnicity? • Comorbidities?
Outcomes	<ul style="list-style-type: none"> • Uptake of HPV based cervical screening (absolute response rate) • Relative response rate • Response difference • Adherence to follow-up in individuals that receive a positive screening test result

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	<ul style="list-style-type: none"> • PPV for CIN2+ in individuals with a positive screening test that attended for follow-up • Proportion of self-sampling individuals with unsatisfactory test results i.e in which HPV status cannot be determined (e.g. insufficient sample, failed lab tests). • Proportion of women with a ‘failed’ test/sample who are asked to provide a second sample • CIN2+ detection rate • Frequency of screening across rounds 		
Study designs	RCTs, cohort studies, systematic reviews.		
Electronic databases	Database <input checked="" type="checkbox"/> MEDLINE <input checked="" type="checkbox"/> CENTRAL <input checked="" type="checkbox"/> EMBASE <input type="checkbox"/> Other (please specify, e.g. PsycINFO) <input checked="" type="checkbox"/> Clinical Trial Registry (ClinicalTrials.gov)	From: <i>1st January 2018</i> <i>(overlap with Arbyn et al. 2018)</i>	To: March 2024

Methods for screening search results			
Expertise	Screening will be performed by RM and NT		
Screening methods	Dual; second reviewer checks all excluded records Dual; second reviewer checks 20% of excluded records Dual; independent screen and cross check	<i>Abstract</i> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<i>Full text</i> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/>
Discrepancy resolution	<input checked="" type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)		
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies		
Inclusion of abstracts and conference proceedings	<input checked="" type="checkbox"/> Exclude all <input type="checkbox"/> Include if clearly eligible and have usable data <input type="checkbox"/> Include if clearly eligible regardless of usable data <input type="checkbox"/> Include if eligibility is unclear and add to section in report		
Inclusion of non-English language studies	<input type="checkbox"/> Include abstracts and full texts <input type="checkbox"/> Include full texts only <input checked="" type="checkbox"/> Exclude		
	<input type="checkbox"/> All potentially relevant abstracts will progress to full text screen		

	<input type="checkbox"/> [Single/dual] title/abstract screen by foreign-language speaker(s) <input type="checkbox"/> [Abstract/ <u>methods</u> /full text] will be translated for abstract/ <u>full text</u> screen <input checked="" type="checkbox"/> Listed as non-English language and not assessed further
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Are HPV self-sampling screening strategies acceptable to those that have not attended the regular cervical screening programme, and does this vary according to relevant patient and test characteristics?

A prior review by Nelson et al. will be utilised as the basis for addressing this question, with particular consideration of additional reviews by Yeh et al. and Nishimura et al.(21-23)

Population	Individuals eligible for cervical screening who do not attend for health professional testing		
Intervention	Invitation to HPV based cervical screening - self sampling		
Comparator	Invitation to HPV based cervical screening - health professional sampling		
Co-variates	<ul style="list-style-type: none"> • invitation strategy • sampling method (brush, swab, lavage) • screening history • clinical history of population • population subgroup (eg SES, ethnicity, LGBT+) 		
Outcomes	<p>Overall:</p> <ul style="list-style-type: none"> • stated overall acceptability • stated preference in compared with clinician-based screening • stated preference for setting of self-collection of sample • stated willingness to repeat screening <p>Individual characteristics of acceptability / experience including:</p> <ul style="list-style-type: none"> • Logistic measures of acceptability (eg convenience, accessibility) • Procedure related measures of acceptability (eg pain/physical discomfort, ease of use, confidence in result, self-efficacy to do the test) • Psychosocial measures of acceptability (eg stigma, embarrassment, anxiety, fit with values) 		
Study designs	RCTs, cohort studies, feasibility studies, mixed methods studies, surveys and / or focus groups, qualitative interview studies, systematic reviews.		
Electronic databases	Database <input checked="" type="checkbox"/> MEDLINE	From: <i>1st December 2014</i> <i>(overlap with Nelson et</i>	To: March 2024

HPV Self-sampling for Cervical Screening: Rapid Review Protocol

	<input type="checkbox"/> CENTRAL <input checked="" type="checkbox"/> EMBASE <input checked="" type="checkbox"/> Other (CINAHL, LILACS, SCOPUS, OpenGrey, ProQuest, Cochrane Library) <input checked="" type="checkbox"/> Clinical Trial Registry (ClinicalTrials.gov)	<i>al. 2015)</i>	
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Methods for screening search results			
Expertise	Screening will be performed by RM and NT		
Screening methods		<i>Abstract</i>	<i>Full text</i>
	Dual; second reviewer checks all excluded records	<input checked="" type="checkbox"/>	<input type="checkbox"/>
	Dual; second reviewer checks 20% of excluded records	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Dual; independent screen and cross check	<input type="checkbox"/>	<input type="checkbox"/>
Discrepancy resolution	<input checked="" type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)		
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies		
Inclusion of abstracts and conference proceedings	<input checked="" type="checkbox"/> Exclude all <input type="checkbox"/> Include if clearly eligible and have usable data <input type="checkbox"/> Include if clearly eligible regardless of usable data <input type="checkbox"/> Include if eligibility is unclear and add to section in report		
Inclusion of non-English language studies	<input type="checkbox"/> Include abstracts and full texts <input type="checkbox"/> Include full texts only <input checked="" type="checkbox"/> Exclude		
	<input type="checkbox"/> All potentially relevant abstracts will progress to full text screen <input type="checkbox"/> [Single/dual] title/abstract screen by foreign-language speaker(s) <input type="checkbox"/> [Abstract/ <u>methods</u> /full text] will be translated for abstract/ <u>full text</u> screen <input checked="" type="checkbox"/> Listed as non-English language and not assessed further		

Data Extraction

Where feasible, data will be extracted from existing systematic reviews, using published data or by obtaining data extraction files from authors. Co-variate data may be extracted from the original studies in instances where this has not been recorded in a prior review. Data extraction will then be completed for additional studies identified in the searches which have not been captured in prior reviews.

Data extraction	
Expertise	Data extraction will be performed by MT and NT.
Software	Data will be extracted using pilot-tested data extraction forms in Excel

Data to be extracted	Author Year Study design Setting Participant characteristics (age, socioeconomic status, co-morbidities, clinical history, screening history, other [HIV status, ethnicity, LGBTQ+]) Intervention characteristics and comparator characteristics [sampling device, setting, invitation strategy] Outcomes assessed (outcomes of interest as previously specified) Numerical data for outcomes of interest	
Data extraction methods	<input type="checkbox"/> Single, no second reviewer <input type="checkbox"/> Dual; second reviewer checks all data <input checked="" type="checkbox"/> Dual; second reviewer checks 20% <input type="checkbox"/> Dual; independent screen and cross check	
Risk of bias tool*	<input type="checkbox"/> No risk of bias assessment <input checked="" type="checkbox"/> Cochrane RCT risk of bias tool (ROB-1) <input checked="" type="checkbox"/> Newcastle-Ottawa Scale for non-randomised studies <input checked="" type="checkbox"/> QUADAS-2 for systematic reviews of diagnostic test accuracy; otherwise AMSTAR-2 <input checked="" type="checkbox"/> CASP for qualitative studies <input type="checkbox"/> ROBINS-I	
Method of risk of bias assessment*	<input type="checkbox"/> Single, no second reviewer <input checked="" type="checkbox"/> Dual; second reviewer checks all judgements <input type="checkbox"/> Dual; second reviewer checks [add proportion] <input type="checkbox"/> Dual; independent screen and cross check	<input type="checkbox"/> All outcomes <input checked="" type="checkbox"/> Primary only
Discrepancy resolution	<input checked="" type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)	
Contacting study authors	<input type="checkbox"/> Authors will be contacted for missing information and data <input type="checkbox"/> Authors will be contacted for missing outcome data only <input checked="" type="checkbox"/> Authors will not be contacted	

* To meet stakeholder needs, evidence synthesis will be prioritised as a deliverable over the risk of bias assessment of included studies. Risk of bias assessment will be undertaken after the delivery of the rapid review and will be included in the final manuscript.

Data Synthesis

Narrative data synthesis will be conducted to address the respective clinical questions. For new diagnostic accuracy publications, contingency tables will be constructed and values for relevant outcome parameters described will be computed if not reported. Both intention-to-treat and per protocol analyses will be completed. Analyses will be conducted according to the methods recommended in the Cochrane Handbook for Systematic Review of Diagnostic Test Accuracy.(24) Meta-analyses will completed using CRSU apps MetaDTA/MetaBayesDTA where feasible.(25, 26)

Data synthesis	
Assessment of heterogeneity	<input checked="" type="checkbox"/> Inspecting forest plots <input type="checkbox"/> Statistical test (chi-squared) for heterogeneity <i>[specify p-value]</i> <input type="checkbox"/> I ² statistic <input type="checkbox"/> Explore potential sources of the heterogeneity among study results <i>[state which characteristics will be used]</i> <input type="checkbox"/> Sensitivity analysis by excluding outlying studies
Assessment of reporting biases	<input type="checkbox"/> Funnel plots <input type="checkbox"/> Test for funnel plot asymmetry (e.g. Begg, Egger test) <input type="checkbox"/> Trim and fill technique
Data synthesis	<input checked="" type="checkbox"/> Forest plots <input type="checkbox"/> Qualitative synthesis <input type="checkbox"/> Synthesis without meta-analysis
Model	<input type="checkbox"/> Fixed-effect meta-analyses <input checked="" type="checkbox"/> Random-effects meta-analyses (DerSimonian and Laird method) <input type="checkbox"/> Other <i>[please specify]</i>
Subgroup analyses	The following subgroups will be explored: as per co-variates for respective research questions
Sensitivity analysis	<input type="checkbox"/> Excluding studies at high risk of bias <i>[specify domains]</i> <input type="checkbox"/> Excluding studies with dubious eligibility <input type="checkbox"/> Alternative analysis methods <i>[specify]</i> <input checked="" type="checkbox"/> Other <i>[excluding non-randomised studies]</i> Any <i>post hoc</i> sensitivity analyses that arise during the review process will be justified in the final report.
GRADE approach	<input checked="" type="checkbox"/> GRADE will be used for the primary outcomes and results presented in a summary of findings table. Existing certainty of evidence grades will be derived from prior well-conducted systematic reviews where available. For new publications, one reviewer will determine a certainty of evidence rating to be verified by a second reviewer.

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Appendix

Search Strategies

Clinical Accuracy (per Arbyn et al.)(19)

Database	Search
PubMed	<p>#1: Cervix OR cervico* OR cervica*</p> <p>#2: Cancer OR carcinoma OR neoplas* OR dysplas* OR CIN[tw] OR CINII*[tw] OR CIN2*[tw] OR CINIII*[tw] OR CIN3[tw] OR SIL[tw] OR SIL OR HSIL[tw] OR H-SIL OR LSIL[tw] OR L-SIL OR OR "low grade" OR low-grade OR mild OR equivocal OR borderline.</p> <p>#3: #1 AND #2.</p> <p>#4: HPV OR "Human Papillomavirus DNA Tests"[Mesh] OR "human papillomavirus" OR papillomavir* OR viral OR virus</p> <p>#5: self-collection OR "self collection" OR self-sampling OR self-collect* OR self-sampl* OR self OR "Self- Examination"[Mesh]</p> <p>#6: #4 AND #5</p> <p>#7: #3 AND #6</p> <p>#8: Publication Date from January 2018 to March 2024.</p> <p>#9: #7 AND #8</p>
Embase	<p>#1: 'cervix'/exp OR cervix OR cervico* OR cervica*</p> <p>#2: 'cancer'/exp OR cancer OR 'carcinoma'/exp OR carcinoma OR neoplas* OR dysplas* OR cin OR 'cin2' OR 'cin3' OR sil OR hsil OR h+sil OR lsil OR l+sil OR 'low grade' OR low+grade OR mild OR equivocal OR 'borderline'/exp OR borderline</p> <p>#3: 'hpv'/exp OR hpv OR 'human papillomavirus'/exp OR 'human papillomavirus' OR papillomavir* OR viral OR 'virus'/exp OR virus</p> <p>#4: self+collection OR 'self collection' OR self+sampling OR 'self-sampling' OR self+collect* OR self+sampl* OR 'self'/exp OR self</p> <p>#5: #1 AND #2 AND #3 AND #4</p> <p>With the following limits:</p> <ul style="list-style-type: none"> • - Map to preferred terminology (with

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	<p>spell check)</p> <ul style="list-style-type: none"> - Also search as free text - Include sub-terms/derivatives (explosion search)
Cochrane Library	<p>#1: Cervix or cervico* or cervica*</p> <p>#2: Cancer or carcinoma or neoplas* or dysplas* or CIN or CIN2 or CIN3 or SIL or SIL or HSIL or H-SIL or LSIL or L-SIL or "low grade" or low-grade or mild or equivocal or borderline.</p> <p>#3: HPV or "human papillomavirus" or papillomavir* or viral or virus</p> <p>#4: self-collection or "self collection" or self-sampling or "self-sampling" or self-collect* or self-sampl* or self</p> <p>With the following limits:</p> <ul style="list-style-type: none"> Cochrane reviews (reviews + protocols) Other reviews Search for word variations

Strategies to increase population coverage of cervical screening (Albyn et al.)(19)

Database	Search
PubMed	(Cervix OR cervical) AND (HPV OR papillomavirus) AND (self-sampling OR self sampling OR self-collection OR self collection) AND (screening OR coverage OR participation OR knowledge OR acceptance)

Acceptability

(per Nelson et al)(21)

Database	Search
ProQuest Dissertations and Theses	(Prefer* OR feasib* OR accept* OR barrier OR cost OR attitude) AND (HPV OR "Human papillomavirus") AND (self-collect* OR self-sampl* OR self-screen*)

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PubMed	((("human papillomavirus"[All Fields] OR HPV[All Fields]) AND (accept[All Fields] OR prefer[All Fields] OR ("attitude"[MeSH Terms] OR "attitude"[All Fields]) OR barrier[All Fields] OR fesi[All Fields] OR ("economics"[Subheading] OR "economics"[All Fields] OR "cost"[All Fields] OR "costs and cost analysis"[MeSH Terms] OR ("costs"[All Fields] AND "cost"[All Fields] AND "analysis"[All Fields]) OR "costs and cost analysis"[All Fields]))) AND (self-collection[All Fields] OR self-collect[All Fields] OR self-sampling[All Fields] OR self-sample[All Fields] OR self-screen[All Fields]))
SCOPUS	(TITLE-ABS-KEY ("human papillomavirus" OR hpv) AND TITLE-ABS-KEY (accept OR prefer OR attitude OR barrier OR feasib OR cost) AND TITLE- ABS-KEY (self-collection OR self-collect OR self-sampling OR self-sample OR self-screen))
Web of Science	TOPIC: ("human papillomavirus" OR HPV) AND TOPIC: (accept OR prefer OR attitude OR barrier OR cost OR feasib) AND TOPIC: (self-collection OR self-collect OR self- sampling OR self-sample OR self-screen) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI.
OpenGrey	(HPV OR "Human papillomavirus") AND (collect* OR Sampl* OR screen*) HPV OR "Human papillomavirus"
Cochrane Database of Systematic Reviews	HPV OR "Human papillomavirus"

(per Yeh et al. and Nishimura et al)(22, 23)

Database	Search
PubMed	("human papillomavirus"[tiab] OR HPV[tiab] OR "cervical"[tiab] OR "cervix"[tiab]) AND ("self-test" [tiab] OR "self-testing" [tiab] OR

	<p>"home-based test"[tiab] OR "home-based testing"[tiab] OR "home test"[tiab] OR "home testing"[tiab] OR "clinic-based test"[tiab] OR "clinic-based testing"[tiab] OR "community-based test"[tiab] OR "pharmacy-based test"[tiab] OR "self-administer"[tiab] OR "self-sampling"[tiab] OR "self-collecting"[tiab] OR "self-collected"[tiab] OR "self-collection"[tiab] OR "self- versus provider-collected"[tiab] OR "self- and provider-collected"[tiab] OR "self-versus physician- collected"[tiab] OR "self- and physician-collected"[tiab] OR "self care"[Mesh] OR self- administration[Mesh] OR "self assessment"[Mesh])</p>
<p>CINAHL</p>	<p>(TI "human papillomavirus" OR TI HPV OR TI cervical OR TI cervix OR AB "human papillomavirus" OR AB HPV OR AB cervical OR AB cervix) AND (TI "self-test" OR AB "self-test" OR TI "self-testing" OR AB "self-testing" OR TI "home-based test" OR AB "home-based test" OR TI "home-based testing" OR AB "home-based testing" OR TI "home test" OR AB "home test" OR TI "home testing" OR AB "home testing" OR TI "clinic-based test" OR AB "clinic-based test" OR TI "clinic-based testing" OR AB "clinic-based testing" OR TI "community-based test" OR AB "community-based test" OR TI "pharmacy-based test" OR AB "pharmacy-based test" OR TI "self-administer" OR AB "self-administer" OR TI "self-sampled" OR AB "self-sampled" OR TI "self-sample" OR AB "self-sample" OR TI "self-sampling" OR AB "self-sampling" OR TI "self-collecting" OR AB "self-collecting" OR TI "self-collected" OR AB "self-collected" OR TI "self-collection" OR AB "self-collection" OR TI "self-versus provider-collected" OR AB "self-versus provider-collected" OR TI "self- and provider-collected" OR AB "self- and provider-collected" OR TI "self-versus physician-collected" OR AB "self-versus physician-collected" OR TI "self-and physician-collected" OR AB "self-and physician-collected")</p>

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<p>Embase</p>	<p>('human papillomavirus':ab,ti OR HPV:ab,ti OR cervical:ab,ti OR cervix:ab,ti) AND ('self-test':ab,ti OR 'self-testing':ab,ti OR 'home-based test':ab,ti OR 'home-based testing':ab,ti OR 'home test':ab,ti OR 'home testing':ab,ti OR 'clinic-based test':ab,ti OR 'clinic-based testing':ab,ti OR 'community-based test':ab,ti OR 'pharmacy-based test':ab,ti OR 'self-administer':ab,ti OR 'self-sampled':ab,ti OR 'self-sample':ab,ti OR 'self-sampling':ab,ti OR 'self-collecting':ab,ti OR 'self-collected':ab,ti OR 'self-collection':ab,ti OR 'self-versus provider-collected':ab,ti OR 'self-and provider-collected':ab,ti OR 'self-versus physician-collected':ab,ti OR 'self-and physician-collected':ab,ti)</p>
<p>LILACS</p>	<p>("human papillomavirus" OR HPV OR cervical OR cervix) [words] AND ("self-test" OR "self-testing" OR "home-based test" OR "home-based testing" OR "home test" OR "home testing" OR "clinic-based test" OR "clinic-based testing" OR "community-based test" OR "pharmacy-based test" OR "self-administer" OR "self-sampling" OR "self-collecting" OR "self-collected" OR "self-collection" OR "self-versus provider-collected" OR "self-and provider-collected" OR "self-versus physician-collected" OR "self-and physician-collected") [words]</p>