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Implementation of HPV self-collection in cervical screening

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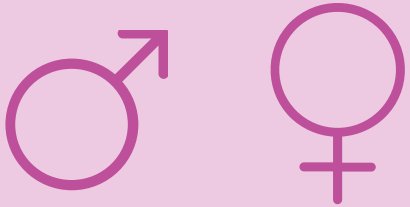
Happy
International Women's Day

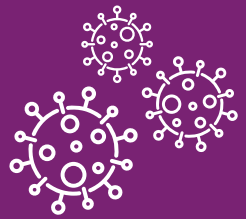
Cervical cancer is caused by human papillomavirus

1980s

Causative role of HPV established in the 1980s



Passed through any kind of sexual contact



Extremely common

13 of >100

known genotypes can cause cervical cancer

70%

HPV16/18 causes 70% of cervical cancers

Cervical cancer can be prevented

HPV vaccination:
prevention of persistent infections

Very effective when administered before the sexual debut

But only younger women are benefitting for now

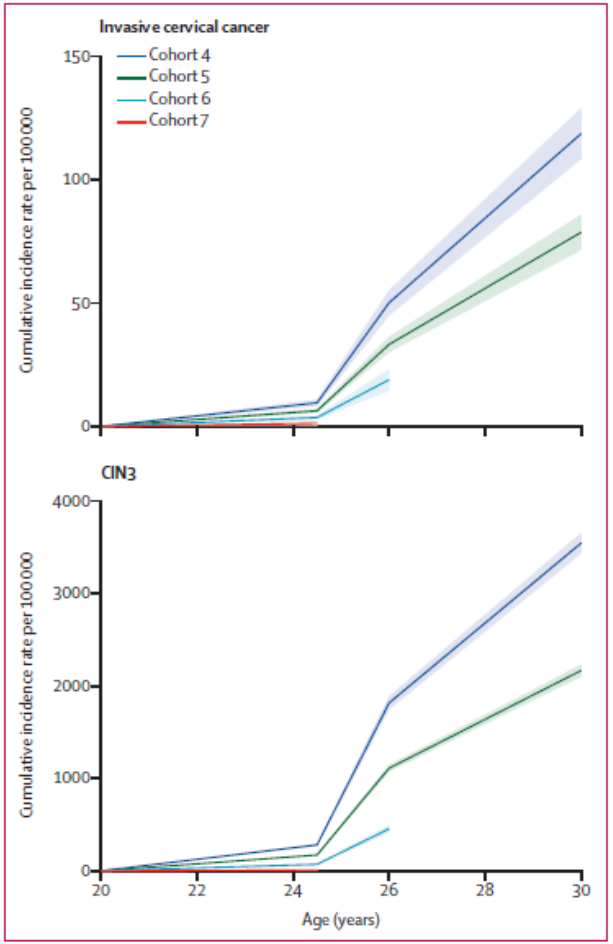


Figure 2: **Cumulative incidence rates of cervical cancer and CIN3 by birth cohort**
The shaded area indicates 95% CI. CIN=cervical intraepithelial neoplasia. Estimates from Model 3 with all other covariates fixed at their reference values.

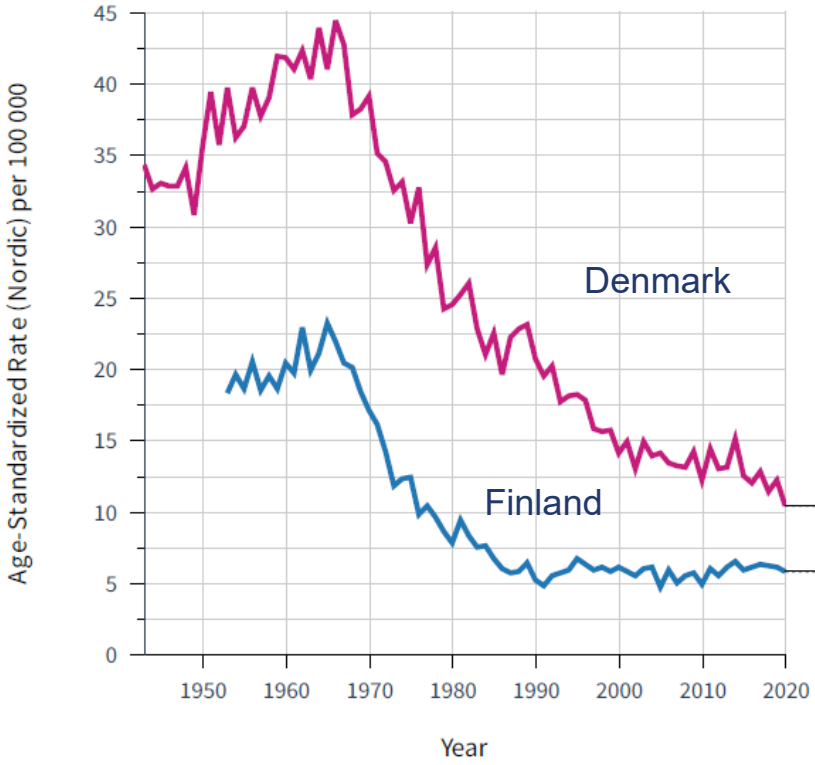
Falcaro et al. Lancet 2021

Cervical cancer can be prevented

Screening:
treatment of preinvasive lesions

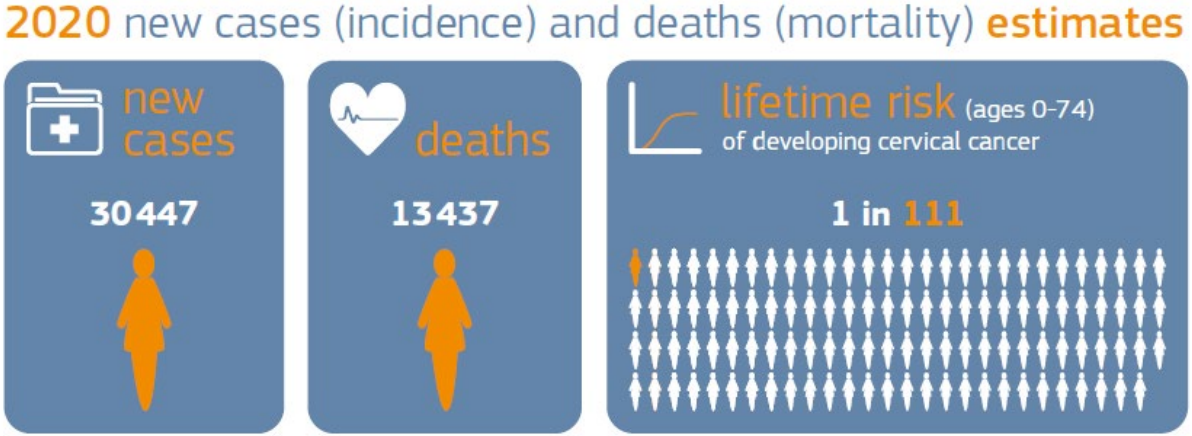
Very effective

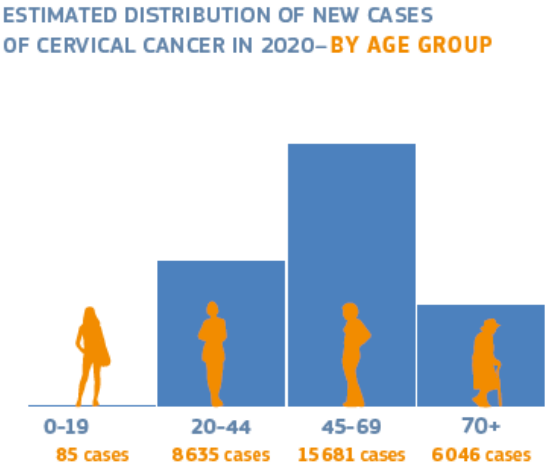
Available to all women
(usually 20's/30's to 60's)



NORDCAN (https://nordcan.iarc.fr/en)

Yearly burden of cervical cancer (EU-27)





European Cancer Information System, https://ecis.jrc.ec.europa.eu/pdf/factsheets/cervical_cancer_en-Nov_2021.pd

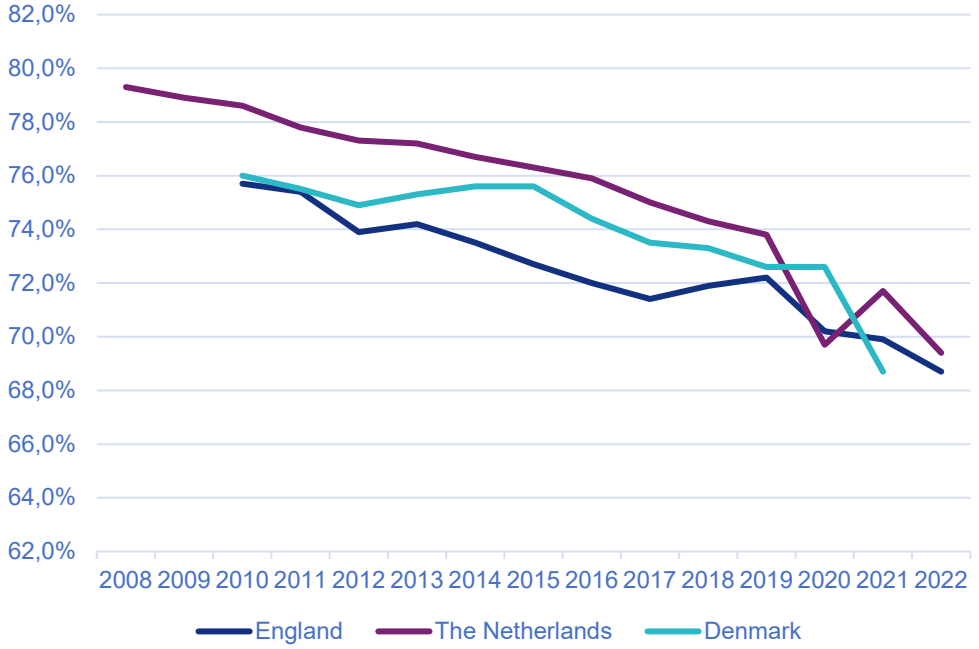
Why has cervical cancer not yet been eradicated?

Prevention is highly, but not 100% effective

Women (girls) are not vaccinated

Women are not screened →

- many reasons: sociodemographic factors, cultural factors, lack of knowledge, embarrassment, lack of access because of practical issues



https://www.rivm.nl/bevolkingsonderzoek-baarmoederhalskanker/professionals/monitoring-en-evaluatie, https://www.sundhed.dk/sundhedsfaglig/kvalitet/kliniske-kvalitetsdatabaser/screening/livmoderhalskraeftscreening/, and https://digital.nhs.uk/data-and-information/publications/statistical/cervical-screening-annual/england-2022-2023 (and similar for earlier years)

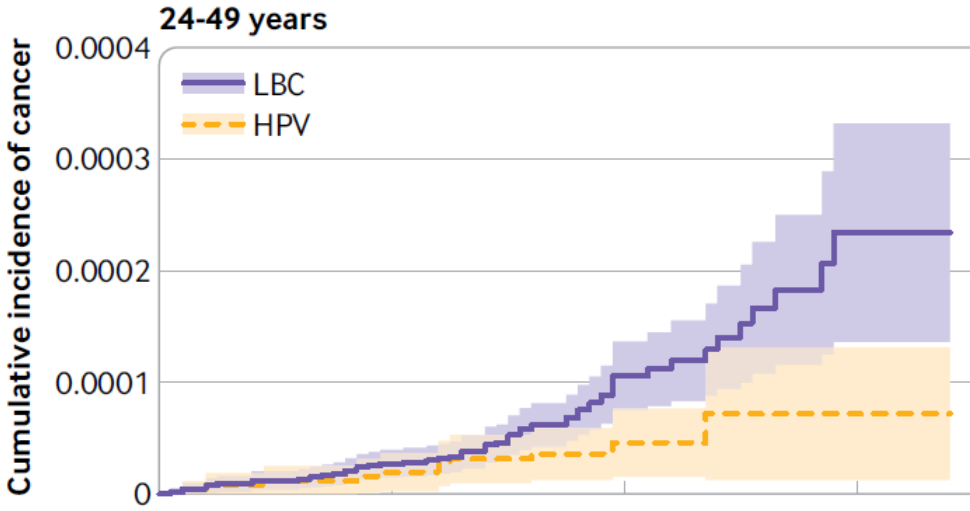
New, better tools for screening

HPV test is a better screening test

Instead of cytology
as the first (“primary”) test

Positive: additional investigations

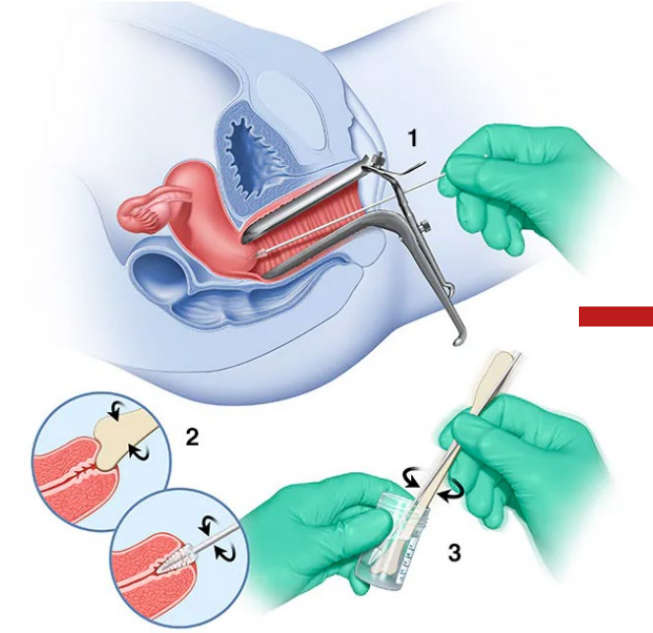
Negative: back to a routine recall



Rebolj et al, BMJ 2022

New, better tools for screening

Clinician collection: sample from the cervix



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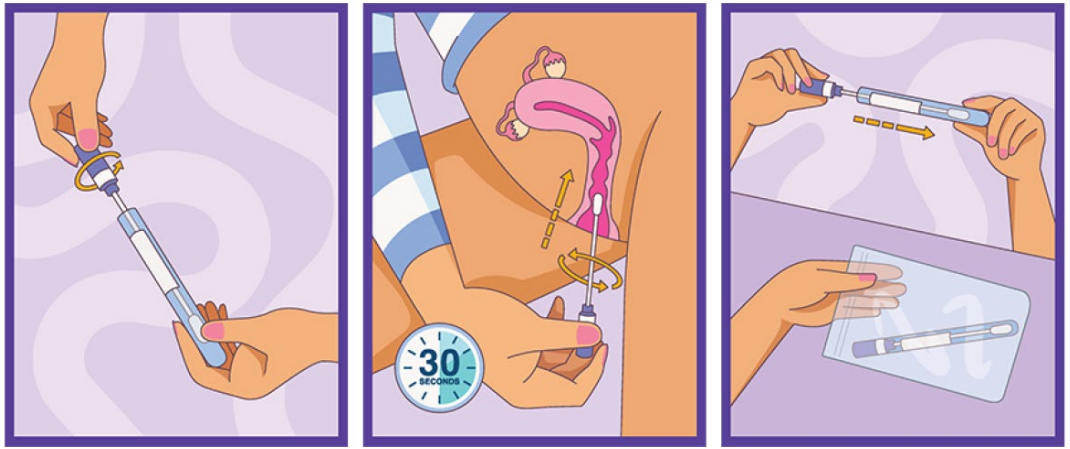
HPV self-collection



“As good as clinician collection”

https://www.mayoclinic.org/tests-procedures/pelvic-exam/about/pac-20385135, https://www.health.gov.au/self-collection-for-the-cervical-screening-test

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Main advantages: convenience, privacy

What research studies have shown

10-30%

Of **under-screened** women take up the self-sampling offer **when invited by mail ("opt-in", "opt-out" offers)**

60%

Of **under-screened** women take up the self-sampling offer **when invited by their GP ("opportunistic offer")**

40%

Of **well-screened** women might consider switching from clinician sampling to self-sampling

Proceed to implementation

Drysdale et al. J Med Screen 2021, Lim et al. preprint 2023, Rebolj et al. Int J Cancer 2023

Early adopter countries

Two approaches:

Only to under-screened women

- multiple research studies
- might lead to switching

As a choice to all women

- not studied in research studies
- a likely model for several countries
(overburdened primary care, women's preferences, ?same accuracy)


Denmark since 2017


Netherlands since 2017


Australia since 2018


Italy since 2020 (regional and pilots)


Sweden since 2021


New Zealand since 2023



Elsewhere: Research and pilots

How does HPV self-sampling work in routine health care?

Return to routine recall

Screening service

HPV-negative

Clinician-collected sample

Invitations

HPV-positive: triage on the same sample

3

3

Clinical follow-up

Switching from clinician to self-collection

2

HPV-positive

Triage sample (clinician collected)

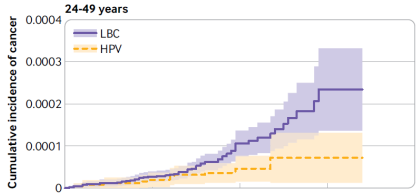
(early recall
+/- colposcopy
+/- treatment

No sample

Self-collected sample

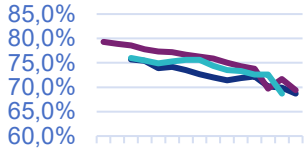
HPV-negative

2



Fewer women without a sample

1



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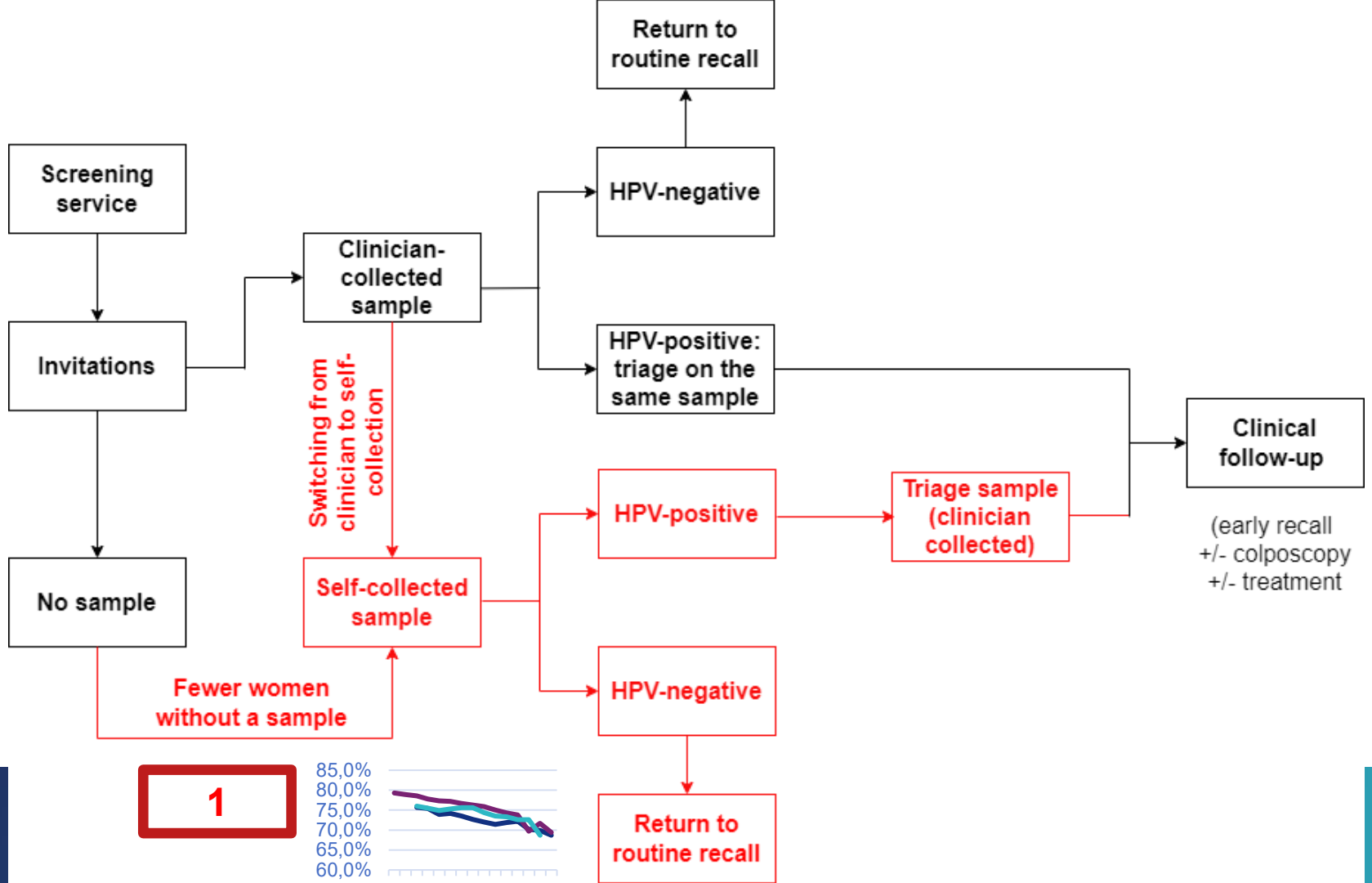
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+/- treatment
No sample
Self-collected sample
HPV-negative
Fewer women without a sample
1
85,0%
80,0%
75,0%
70,0%
65,0%
60,0%
Return to routine recall

What have we learnt from early adopter countries?

Denmark (initially only the Capital region): under-screened women

An increase in the coverage by 3% (17% of under-screened women self-collected a sample)

Australia: initially only under-screened women

- Initially disappointing results
- Lack of clarity on regulatory approval, unclear messaging, strict requirement for collection at a health care facility
- ? Unified messaging and system support is required

Italy: under-screened ± well-screened women

- Hard to increase coverage
- ? Some regions implemented as response to the COVID-19 pandemic

Netherlands: all women (initially as opt-in)

- No increase in overall coverage, relatively little self-collection
- ? Uniform invitation letter: both well-screened and under-screened women

What can we do?

? Effective communication

- Invitation letters
- Other venues (community-based etc.)

? Practical obstacles

- Help with planning

? Why not screened

- Improve the understanding of who are non-responders and the reasons behind it

? Multi-pronged offer

- Basic offer (opt-in, opt-out) + opportunistic + additional outreach

? Any other

- To be made part of the policy

Return to routine recall

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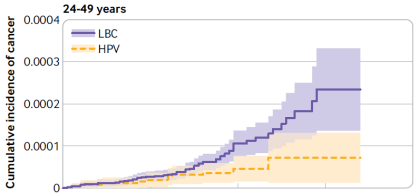


Assumptions on HPV self-sampling test sensitivity

Context:

- Very few manufacturer claims
- Repurposing for self-sampling purposes
- Some proposed, but no internationally agreed validation frameworks
- A large number of research and local “validation” studies, mostly from women with abnormal cytology

Agreement:

Self-sampling is ~equally good as clinician sampling

(Meta-analysis of the available studies)

What have we learnt from early adopter countries?

Estimates: test sensitivity reduction of 10-25%

(for the detection of high-grade preinvasive lesions or worse)

(But: suboptimal study designs)

Why this difference?

1. Previous studies: women with abnormal cytology, hardly any lesions with HPV+/neg-cytology
2. HPV+/neg-cytology likely to emit a weaker signal to detect the infection → more difficult to detect
3. Early adopters: data correctly include women with HPV+/neg-cytology lesions
4. (Would self-sampling prevent fewer cervical cancers?)

https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcSHLllwS2k9XmKKallmCzOf1GujJNkzM7sq1A&usqp=CAU

How should we interpret these findings?

Self-collection is still a useful screening test, likely better than cytology

Accept: uncertainty about the reduction in the sensitivity

- A potential for more cancers than with clinician sampling (in the worst-case scenario)
- Especially an issue when women are given a choice

https://btshealth.com/light-at-he-end-of-the-tunnel/

What can we do?

Research

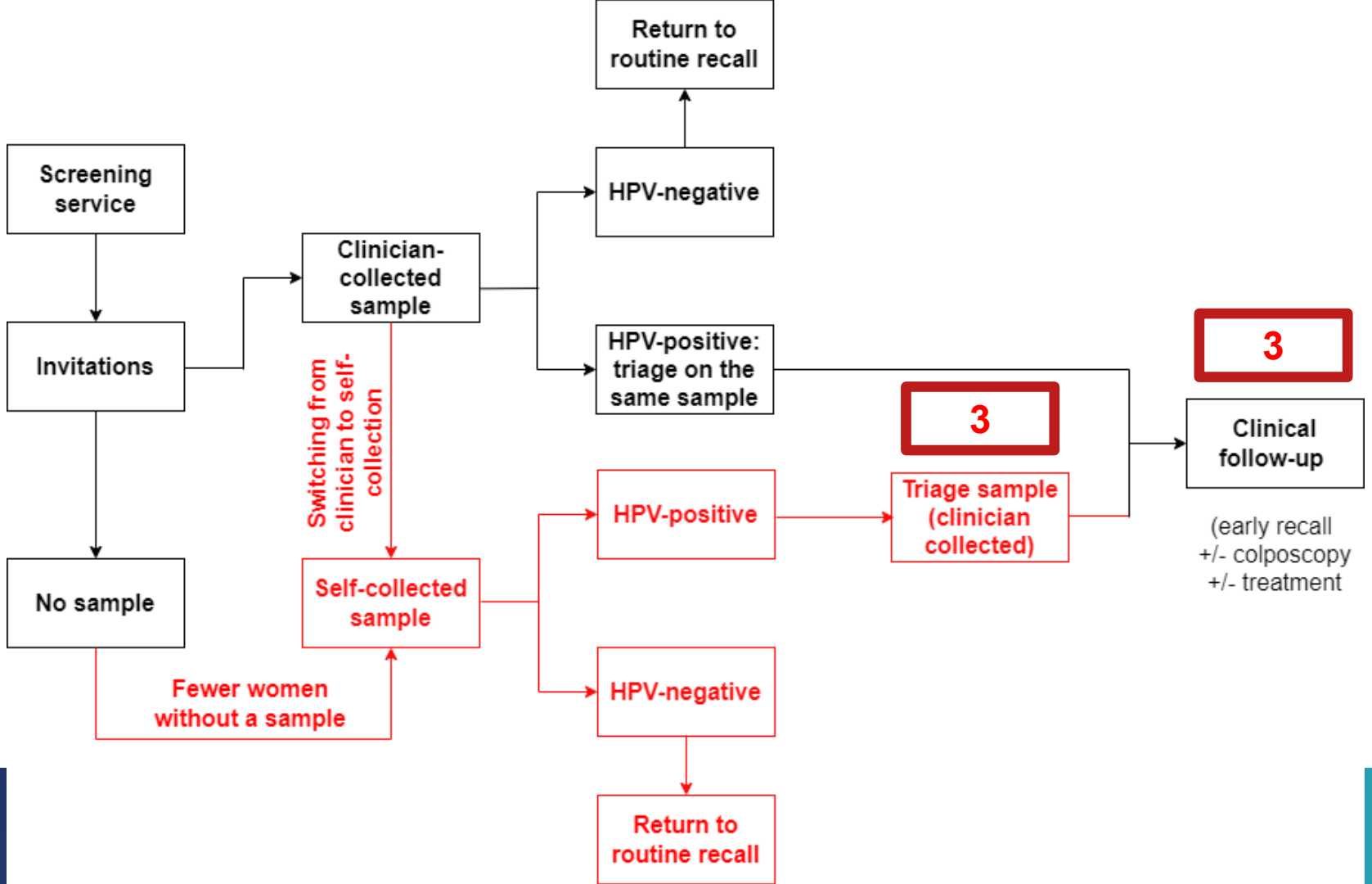
- Stronger evidence
- Improvement of the technology

Communication

- Communicate the uncertainty
- Balanced, understandable
- Without scaring women away (It is not a bad test! It is not a cost-cutting exercise!)

Mitigation

- Manage expectations
- Consider adjusting screening intervals
- Consider a different approach for under-screened vs. well-screened women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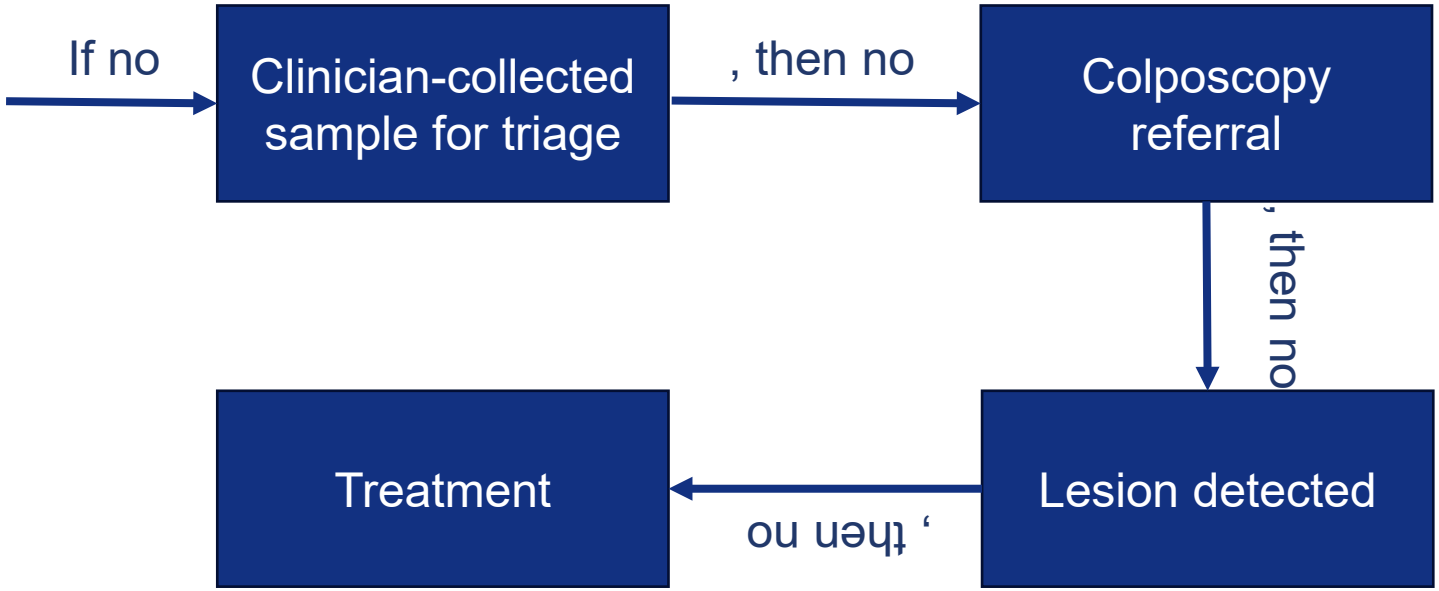
Screening only works if all the steps are completed:



What have we learnt from early adopter countries?

Adherence: 80-90%	Even in previously well-screened women	Defeats the purpose of increasing the screening uptake
Mitigation:	Development and validation of biomarkers on self-collected samples	Support HPV-positive women in completing the follow-up

Summary

- Exciting new option for cervical screening
- Potential to reduce the burden of cancer among under-screened women

- Effective routine implementation is not straightforward
  - It is a complex intervention

- How to design the service so that:
  - The uptake will be significantly increased
  - Women will be comfortable with making the choice
  - Women will be satisfied with the choice they will make
  - Women will complete the clinical follow-up

Thank you

Questions?

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How does HPV self-sampling work outside of research studies?

1. Does it increase the number of women who undergo screening?

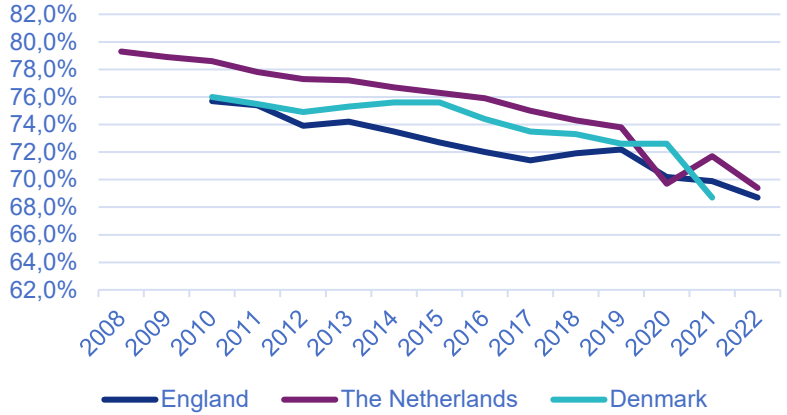
(screening uptake)

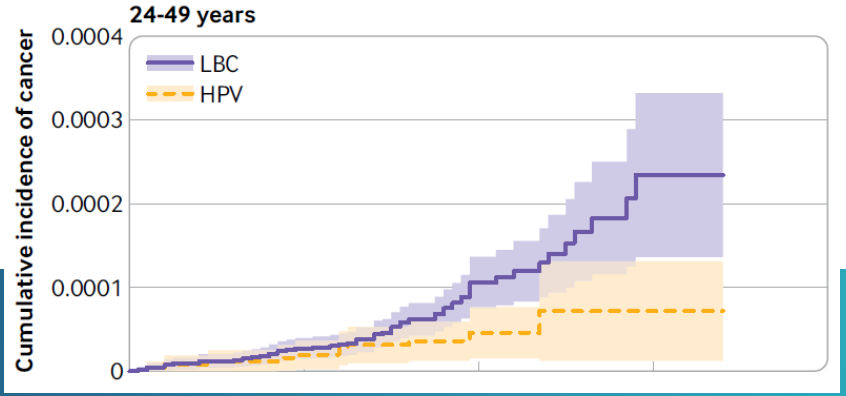
2. Does a negative self-sampling test identify women at low risk of a serious lesion?

(test sensitivity)

3. Do women with positive self-sampling tests proceed to treatment, if necessary?

(adherence to follow-up)





(Usual) differences between the two approaches of offering HPV self-sampling

<u>When offered only to under-screened women:</u>

- An invitation addresses these women's specific situations
- Explains the risks of remaining unscreened (and those of undergoing screening)
- The self-sampling kit offered as:
  - Opt-in, opt-out, opportunistic

<u>When offered as a choice to all women:</u>

- A standardised invitation
- (In some countries) explains the risks of remaining unscreened and those of undergoing screening
- The self-sampling kit offered as:
  - Opt-in, opt-out