Increasing cervical cancer screening response by home-based urine or vaginal self-sampling: first results from the Flemish randomized controlled trial ScreenUrSelf

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Rationale

- On January 1st, 2025, Belgium switched from cytology-based cervical cancer screening (25-64y, 3y interval) to primary hrHPV-based screening for the subgroup of women aged 30-64 (5y interval).
- Since June 1st, 2013, (recall) invitation letters are sent by CvKO (every 36-48 months) to women that are overdue for screening.
- Despite these efforts, 1 in 3 women are under-screened (34%), and 1 in 9 women are never screened (12%) *(2023 figures Flanders, CvKO)*.
- Self-sampling methods, including first-void urine, can increase screening accessibility.

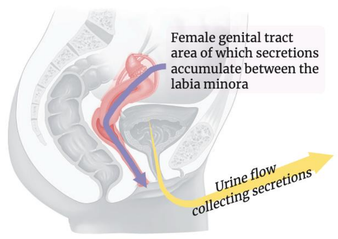
Research questions

Can we reach more un(der)-screened, Flemish women for cervical cancer screening by offering home-based self-sampling opportunities?

When screen-positive, what will the compliance to follow-up be?

Is first-void urine self-sampling more preferred compared to vaginal self-sampling?

Is first-void urine the solution?



- ✓ **Well-accepted method**[1-3]
- ✓ **Similar clinical accuracy** of hrHPV-DNA-based PCR testing in first-void urine[4] compared to clinician-taken cervical samples[5-14]

*Will first-void urine be received by (hard-to-reach) women as **easier to use?***

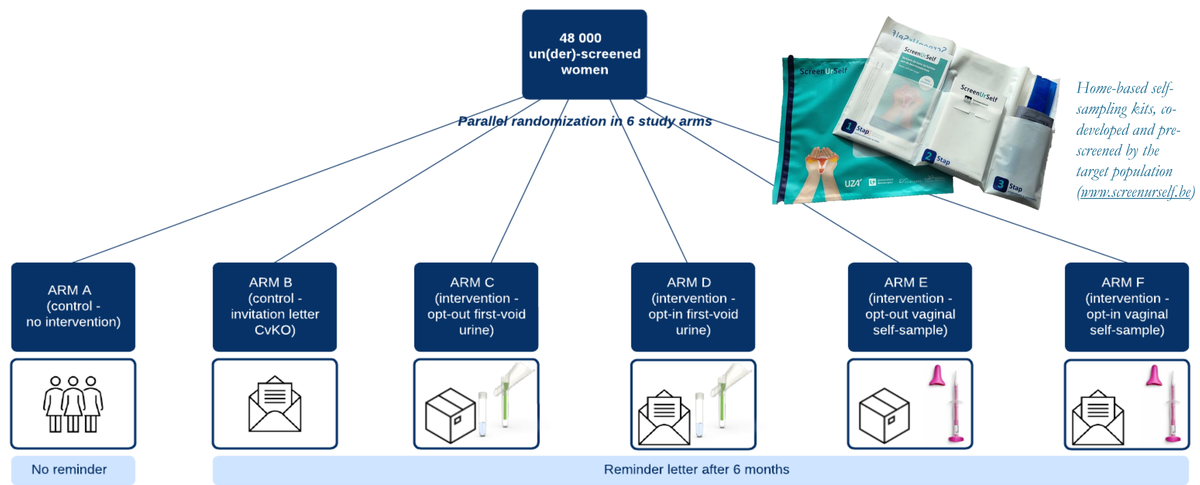
*Will women be **more confident** that they have collected the sample properly?*

*Will it be an alternative **when vaginal self-sampling is not possible** (e.g., cultural, religious beliefs, previous (sexual) trauma)?*

Will urine self-sampling be more (cost-)effective than vaginal self-sampling to reach un(der)-screened women?

[1]Leeman A (2017) BJOG; [2]Rohner E (2020) JWH; [3]De Pauw H (2021) APH; [4]Vorsters A(2012) EJCMID; [5]Ornskov D (2021) BMJ Open; [6]Van Keer S (2021) GO; [7]Van Keer S (2022) JCV; [8]Latsuzbaia A (2023) JMD; [9]Martinelli M (2023) Viruses; [10]Davies JC (2024) BJOG; [11]Van Keer S (2025) JMV; [12]Van Keer S (2025) JMD; [13]Tranberg M (2025) BMC Med; [14]van den Borst E (2025) GO

Study design

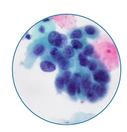


Home-based self-sampling kits, co-developed and pre-screened by the target population (www.screenurself.be)

Un(der)-screened women: no cytological, histological, pathological reports in Belgian Cancer Register for ≥2 screening rounds (31-64y), residing in Flanders, not included in other CvKO research projects, no history of total hysterectomy nor uterine/cervical cancer, not actively opted out of the organized screening program (ClinicalTrials.gov: NCT05996783).

(Riatol qPCR, AML, Belgium)

hrHPV-positive (HPV16/18/31/33/35/39/45/51/52/56/58/59/68)



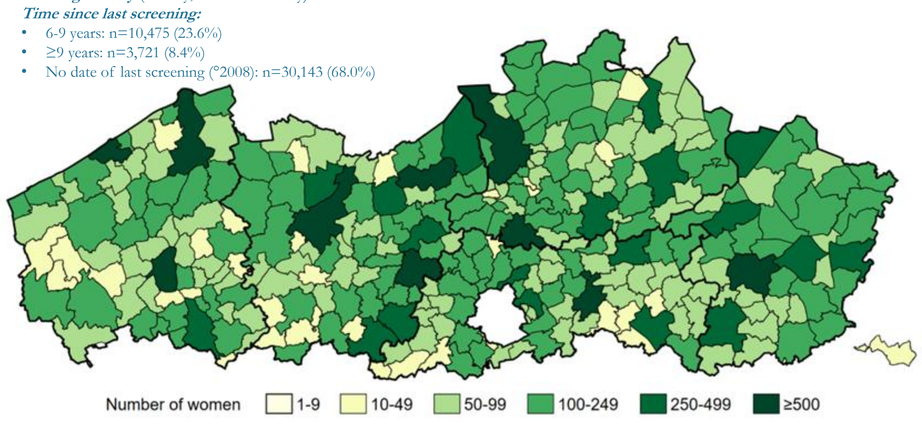
(PreCursor-M Gold, Self-Screen BV, The Netherlands)

Primary HPV test on self-sample → Cytology triage on cervical sample & Alternative triage test under study: DNA methylation triage (on self-sample)

Outcomes

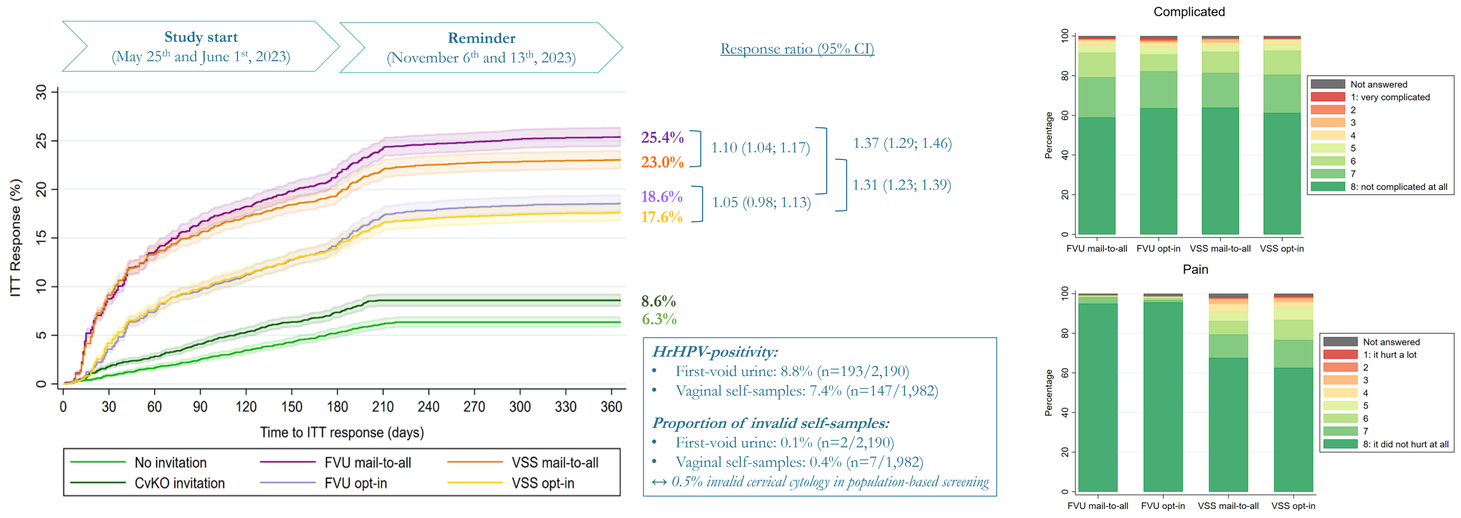
Study population

N=44,339 women across all Flemish municipalities
Mean age of 50y (SD:10y; min-max: 31-64y)
Time since last screening:
- 6-9 years: n=10,475 (23.6%)
- ≥9 years: n=3,721 (8.4%)
- No date of last screening (°2008): n=30,143 (68.0%)



Upcoming analyses will examine the percentage of screened women with a follow-up exam (compliance to follow-up), detection rate of cervical neoplasia, differences in response by age- and socio-economic status, women's attitudes, and evaluation of the clinical performance of an objective, non-morphological triage test on self-samples. This ASCL1/LHX8 methylation test, feasibly in combination with HPV16/18 genotyping, could offer an alternative for cytology triage when self-sampling, bypassing the need for a clinician-collected cervical sample.

Preference – response & questionnaire outcomes

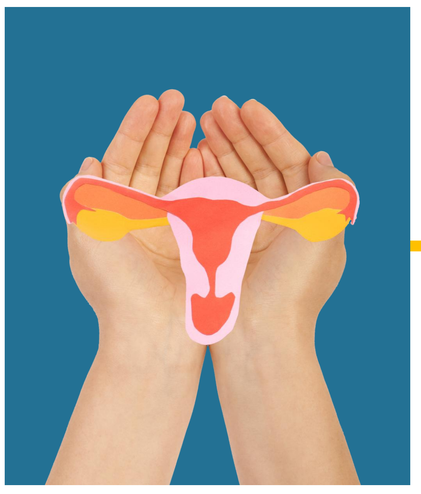


HrHPV-positivity:
- First-void urine: 8.8% (n=193/2,190)
- Vaginal self-samples: 7.4% (n=147/1,982)

Proportion of invalid self-samples:
- First-void urine: 0.1% (n=2/2,190)
- Vaginal self-samples: 0.4% (n=7/1,982)

↔ *0.5% invalid cervical cytology in population-based screening*

A significantly higher intention to treat (ITT; response in the intervention arms measured by self-samples and clinician-collected cervical samples) and per protocol (PP; response in the intervention arms measured by self-samples only) response (PP response ratio: 1.14; 95% CI: 1.06–1.23) was measured when women directly received a urine kit (FVU mail-to-all [opt-out]) compared to a vaginal kit (VSS mail-to-all [opt-out]). In both scenario's, the benefit of urine over vaginal self-sampling was not significant when people needed to order the kit first (opt-in) (PP response ratio: 1.05; 95% CI: 0.96-1.15). In the PP analysis, women in the mail-to-all (opt-out) arms were 65% (urine response ratio: 1.65; 95% CI: 1.53–1.79) and 52% (vaginal response ratio: 1.52; 95% CI: 1.40–1.66) more likely to respond compared to those in the opt-in arms.



- **ScreenUrSelf data confirm a response benefit of mail-to-all outreach over opt-in strategies, and a response benefit of first-void urine over vaginal self-sampling.**
- This was measured in women who have not attended cervical cancer screening for at least six years.
- Data will be used to estimate the cost-effectiveness of these interventions.

Utilization trajectory
- Generating data to formulate an evidence-based conclusion on the most (cost-)effective self-sampling strategy for reaching un(der)-screened Flemish women.

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