

Cost-effectiveness analysis of the YouScreen Trial: a modelling study

An Executive Summary

August 2024

Executive Summary

Self-sampling is cost effective

Offering self-sampling to never screened and under-screened women in England across a range of ages as part of the national cervical screening programme, particularly when offered in a GP setting, is both effective and cost-effective and is likely to reduce health inequalities.

An approach which relies entirely on direct mail-out is predicted to be both more costly and less effective than offering self-sampling in a GP setting. However, direct mail-out could supplement a GP-based approach to self-sampling and potentially be cost-effective provided HPV test costs are low enough.

Background to YouScreen Cost-Effectiveness Analysis

This Cost-Effectiveness Analysis (CEA) was commissioned by YouScreen on the advice of the UKNSC to support a policy discussion and enable future recommendations. The Daffodil Centre (a joint venture between Cancer Council NSW and the University of Sydney) carried out the primary economic analysis and the Health Economics team at Kings College London provided a partial Probabilistic Sensitivity Analysis (PSA) to assess the impact of uncertainty in input parameters on the results of the model. Both health economics teams worked closely with the YouScreen researchers in sourcing costs and other trial data.

Policy1-Cervix is a modelling platform developed by the Daffodil Centre. It is an extensively validated dynamic model of HPV transmission, HPV vaccination, type-specific natural history, cervical precancer, cancer survival, screening, diagnosis and treatment to simulate the lifetime costs and health outcomes following each of the screening strategies. This platform has been used to evaluate cervical screening programmes in many countries (Brisson, Kim, Canfell et al 2020; *Lancet* 2020; 395: 575-90) including England (Kitchener, Canfell, Gilham et al 2014; *Health Technol Assess* 2014;18(23)).

Methodology

Using the modelling platform *Policy1-Cervix*, several scenarios for economic modelling were developed and the model was calibrated to HPV prevalence, cervical cancer incidence, treatment and death in England based on the previously developed comprehensive model of natural history and cervical screening. The first stage used simulated cohorts of various ages, vaccination status and screening history included in the YouScreen Trial to model estimated short-term outcomes over five years of an intervention first offered in 2021 and continuing for one screening round over five years. The second stage created scenarios based on five assumptions (about screening behaviour over multiple rounds) with a range of inputs for a single birth cohort to model cost-effectiveness by estimating the impact of these inputs on lifetime screening participation and outcomes.

Short-term outcomes:

The assumptions and scenarios created for short term outcomes are as follows:

1. **Cervical Screening Programme Status Quo** – Assumes no self-sampling is offered to never and late screeners; uses the screening coverage aggregated for the five London boroughs in the YouScreen trial (approximately 60% in 2018).
2. **YouScreen Mail-out only** – assumes that self-sampling kits are only offered to non-attenders under the YouScreen trial protocol via the direct mail-out pathway.
3. **YouScreen Opportunistic only** – assumes that self-sampling kits are only offered to non-attenders under the YouScreen trial protocol via the GP opportunistic pathway.

4. **YouScreen as it occurred (combined GP opportunistic and direct mail-out)** – assumes that self-sampling kits are offered to non-attenders under the YouScreen trial protocol via both the GP opportunistic and direct mail-out pathways.

See **Table 1** and **Figure 1** in the report for the modelling description and data used. The model uses the total female population from the five boroughs in YouScreen, deduced from published data. The model assumes a proportion of under-screened women every year will receive and return a self-sample and women who are newly 12 months overdue cervical screening will receive a mail out offer and a proportion will return it. (In YouScreen this offer was made at 15 months overdue, however, the *Policy1-Cervix model* could only apply 12 months due to its annualised modelling programme).

The primary outcomes for the trial-based analysis over 2021-2025 at the multi-cohort/population level are:

- Additional women screened due to the YouScreen trial.
- Percentage increase in screening participation (in 2021 only) due to the YouScreen trial.
- Additional CIN2+ detected due to the YouScreen trial.
- Additional CIN3+ detected due to the YouScreen trial.
- Additional costs due to the YouScreen trial.
- Incremental cost per extra woman screened, per CIN2+ detected and per CIN3+ detected.

Lifetime cost-effectiveness:

The following scenarios were created for a hypothetical cohort of 10 million unvaccinated women in England who turned 26 in 2021 and thus be eligible for YouScreen offers. Results are presented per 100,000 women. The model assumes women who return a self-sample will continue to receive and return a self-sample to age 64. The assumptions and scenarios were created for lifetime outcomes as follows:

- 1) A counterfactual “**no screening**” scenario in which there is no cervical screening at all;
- 2) **Routine Cervical Screening Programme “No YouScreen”** i.e., self-sampling is not offered to never- and late-screeners; uses the screening coverage for England;
- 3) **YouScreen “Direct mail-out only”** i.e., never- and late-screeners are offered self-sampling under the YouScreen trial protocol via the mail-out pathway;
- 4) **YouScreen “GP opportunistic only”** i.e., never- and late-screeners are offered self-sampling under the YouScreen trial protocol via the opportunistic pathway; and
- 5) **“YouScreen as it occurred”** where both GP opportunistic and direct mail-out are offered to never- and late-screeners.

The primary outcomes for the cost-effectiveness analysis (CEA), over the lifetime of a single cohort of 100,000 women aged 25, up to when they are aged 84 years, are:

- Incremental cost-effectiveness ratio (ICER) (i.e. incremental cost per quality-adjusted life-year [QALY] gained relative to the next most effective intervention; discounted at 3.5% per annum).
- Screening programme costs (from the perspective of the NHS and personal social services) per woman screened and per CIN2/3 detected.
- Additional women screened due to ongoing self-sampling.
- Additional CIN2+ detected due to ongoing self-sampling.
- Additional CIN3+ detected due to ongoing self-sampling.
- Number of cervical cancer cases and deaths, by age.
- Resource utilisation volumes, including the number of HPV tests, cytology tests, colposcopy evaluations, biopsies, and pre-cancer treatments.

Cost-effectiveness was assessed considering the incremental cost-effectiveness ratio (ICER) and Net Monetary Benefit at an indicative willingness to pay threshold of £20,000 or £30,000 per QALY gained, as per UK National Institute of Clinical Excellence (NICE) guidelines on value-for-money. Univariate sensitivity analyses (summarised in **Table 6** in the report) assessed the impact of uncertainty relating to costs, QALY weights, background screening attendance, HPV vaccination and hysterectomy rates on overall costs, QALYS and the cost-effectiveness ratio. Uncertainty around costs, QALY weights and Net Monetary Benefit were also explored using probabilistic sensitivity analysis (as recommended by NICE) for each strategy in 3,000 simulations. **Table 3** in the report itemises the programme costs and **Table 4** the utility weights contributing to the calculation of the ICER and univariate sensitivity analyses. **Table 5** outlines the assumptions used in the probabilistic sensitivity analysis.

These scenarios and outcomes were simulated for a hypothetical cohort of unvaccinated women who turned 26 in 2021. This cohort was chosen as it represents the youngest cohort of women who would have received the YouScreen self-sampling offer, and who would potentially benefit from YouScreen for the entire screening age range (25-64 years) or their screening lifetime. By “unvaccinated” we mean that neither these 100,000 women nor any other person in the population had received HPV vaccination. This is a fiction as over 80% of females turning 26 in 2021 received HPV vaccination in 2009/10. The impact of HPV vaccination is considered in a sensitivity analysis.

Results were additionally scaled to the England female population in 2021 thereby allowing an estimate of outcomes that could have occurred in that year if the various scenarios (including the No YouScreen scenario of offering HPV screening from age 25) had been operating in their steady state by then (i.e. for the lifetime duration of all females in the population) and if the population offered YouScreen were representative of England as a whole. The findings scaled to England should be interpreted with caution since the current screen-eligible population primarily consists of women with a lifetime of screening under primary cytology (which is less effective than HPV screening) and so even the No YouScreen scenario will have lower levels of disease than are currently observed in England.

Results

Lifetime cohort modelling results

All three self-sampling models for under-screened women were predicted to reduce cancer cases and deaths when compared to the current practice of no self-sampling.

Over the lifetime of a population of 100,000 women who turned 26 in 2021, when compared to current practice without self-sampling:

- Offering self-sampling to under-screened women with **direct mail-out only** is predicted to prevent an additional 10 cervical cancer cases (a relative reduction of 2.7%) and 4 cervical cancer deaths (a relative reduction of 0.9%);
- Self-sampling with the **GP opportunistic only** is predicted to prevent an additional 11 cervical cancer cases (relative reduction of 2.9%) and 4 cervical cancer deaths (relative reduction of 1.0%),
- **YouScreen as it occurred** (combined approach) is predicted to prevent 17 cervical cancer cases and 4 cervical cancer deaths (relative reductions in cervical cancer cases and deaths 4.5% and 1.1% respectively).

Had self-sampling for under-screened women been operating in England in 2021 and reached steady state, then, compared with the current practice without self-sampling, there would have been

- 2.1% fewer cervical cancer cases and 2.5% fewer cervical cancer deaths in the context of direct mail-out only;
- 2.9% fewer cervical cancer cases and 2.6% fewer cervical cancer deaths in the context of GP opportunistic only;
- and **5.1% fewer cervical cancer cases and 4.1% fewer cervical cancer deaths** in the context of YouScreen as it occurred (combined mail-out and GP opportunistic offers).

Assuming total HPV test delivery costs (which includes clinical, laboratory and delivery cost) of £38.80 for clinician-collected, £25.51 for YouScreen direct mail-out, £19.65 for YouScreen GP opportunistic, offering self-sampling to never- and under-screened women as per YouScreen found that:

- The YouScreen GP opportunistic only pathway would be cost-effective for a cohort of unvaccinated women, ICER = £2,284 per QALY gained. Range cost saving to £22,250
 - Mean ICER from PSA on costs and QALYs only £597
- The combined model of GP opportunistic and mail-out (YouScreen as it occurred) was also effective, and potentially cost-effective relative to YouScreen GP opportunistic alone (ICER = £24,562 per QALY gained). Range £12,169-£76,828
 - Mean ICER from PSA of £19,580
- Self-sampling under the YouScreen direct mail-out only pathway was also effective and had a cost-effectiveness ratio of £9,392 per QALY gained relative to the status quo of screening without self-sampling. However direct mail-out *on its own* was predicted to be both less effective and more costly than the GP opportunistic model.
- The PSA suggests that providing self-sampling in the form of GP Opportunistic only is cost-effective compared with no self-sampling when the willingness-to-pay (WTP) threshold is between £597 and £19,580 per QALY gained as it has the highest Net Monetary Benefit.
- The PSA suggests that at a WTP threshold between £20,000 and £30,000 per QALY, the combined YouScreen as it occurred approach most often provides the greatest Net Monetary Benefit of the four options (do nothing/ status quo, direct mail-out only, opportunistic only, YouScreen as it occurred) with probability of 47% for combined and 39% for opportunistic only at the £30,000 per QALY WTP threshold.

In combination, these probabilities suggest that there is a reasonably high certainty that a strategy involving an opportunistic GP offer would be cost-effective (86% probability at WTP £30,000 per QALY), but less certainty regarding whether a GP opportunistic offer should be used on its own or in combination with direct mail-out.

Trial-based modelling results – screening participation

The model predicted that, over a full 12-month period, YouScreen as it occurred (combined approach) would have the effect of increasing screening participation by the end of 2021 by 2.5 percentage points, from 60.0% to 62.5%. Projected over a 5-year period, it was predicted that direct mail-out, YouScreen GP opportunistic only, and YouScreen as it occurred (direct mail-out and GP opportunistic combined) would increase the number of women screened at least once in that timeframe by 2.9%, 4.2%, and 6.8%, respectively.

Trial-based modelling results – CIN2+ detection

It was also reported that YouScreen direct mail-out, YouScreen GP opportunistic only, and YouScreen as it occurred would increase detection of CIN2+ (and CIN3+) over a 5-year period by:

- YouScreen direct mail-out only CIN2+ ↑ 8.51%; CIN3+ ↑ 7.02%
- YouScreen GP opportunistic only CIN2+ ↑ 10.56%; CIN3+ ↑ 9.65%
- YouScreen as it occurred CIN2+ ↑ 17.70%; CIN3+ ↑ 15.40%

Lifetime cohort modelling results – screening participation

Considering screening participation among women aged 25-64 years in terms of those who are up to date with screening (screened in the last 3.5 years for ages 25-49; screened in the last 5.5 years for ages 50-64) **coverage** is 68.1% (66.6% 25-49 years; 70.8% 50-64 years) for no YouScreen. In a population where overdue women had all been offered self-sampling from the age of 26 coverage would be increased as shown in Table 8 below.

Table 8 Summary of the screening participation outputs lifetime cohort modelling:

Scenarios	Screening coverage
No YouScreen	68.12% 66.6% 25 – 49 years 70.8% 50 – 64 years
YouScreen direct mail-out:	72.76% 69.8% 25-49 years 77.7% 50-64 years
YouScreen (GP opportunistic):	72.96% 70.0% 25-49 years 77.9% 50-64 years
YouScreen as it occurred: (combined mail-out and GP opportunistic)	74.35% 71.5% 25 – 49 years 79.1% 50 – 64 years

Limitations:

1. This CEA may be underestimating the overall risk of HPV disease in women in England. However, this would have the effect of the findings underestimating the effectiveness and cost-effectiveness of the YouScreen protocols.
2. It is likely that the findings for older birth cohorts are further underestimating risks of cervical disease in the near term but nonetheless found that self-sampling would represent very good value for money in older cohorts.
3. Other factors such as offer acceptance rates, impact of COVID pandemic, laboratory handling of samples via manual process, and trial restrictions on how the offer could be made may impact acceptance and return rates in a real-world screening programme. The authors consider that these factors are more likely to show an underestimation of the acceptance rate of the offer in which a national programme could control and automate the management of the offer and sample analysis. Thus, the absolute benefit of self-sampling in this analysis may have been underestimated.

4. There was a lot of uncertainty surrounding costs of delivering the routine cervical screening programme including HPV testing and reflex cytology testing. Costs were modelled based on public contract awards for laboratory services and estimate of the YouScreen costs. Cost assumptions were varied in all uncertainty analyses (although over a wider range for HPV test costs in univariate sensitivity analysis than PSA). The cost of HPV testing directly influences the cost effectiveness, with upper bound costs resulting in YouScreen scenarios being less cost effective than at the baseline costs. At the very high end of costs explored in univariate analyses, YouScreen as it occurred (combined GP opportunistic and direct mail-out) may no longer be cost-effective (ICER: £76,828).

Nevertheless, even though the cost-effectiveness ratios were less favourable in these two cases when the upper bound costs were assumed, they remained below £30,000 per QALY gained for the direct mail-out only and the opportunistic GP offer only (but not for the combined scenario).

Conclusions:

1. **Offering self-sampling to never screened and under-screened women in England across a range of ages as part of the National Cervical Screening Programme, particularly when offered in a GP setting, is both effective and cost-effective.**
2. **An approach which entirely relies on direct mail-out is predicted to be both more costly and less effective than offering self-sampling in a GP setting. However, direct mail-out could supplement a GP-based approach to self-sampling provided test costs are low enough. Additionally, direct mail-out only is cost effect relative to the status quo and could be considered whether opportunistic offering in a GP setting is not possible.**
3. **Introducing self-sampling for under-screened women even at relatively older ages (41 or 56) would be cost saving and increase QALYs overall (see page 58 of report and Tables 13, 14 in Appendix). This underscores the importance of a rapid roll-out to capture as many under-screened women as possible.**
4. **A GP opportunistic offer was cost effective in all sensitivity analyses and may be a good place to start a roll out for under and unscreened women.**