Evaluating the benefits and costs of using an mRNA versus DNA HR-HPV assay in the National Cervical Screening Programme in the Netherlands

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EUROGIN 2021 THE VIRTUAL EDITION MAY 30 - JUNE 1

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INTRODUCTION

- Persistent infection with high-risk human papillomavirus (HR-HPV) is a leading cause of cervical cancer (1).
- The National Cervical Screening Programme (NCSP) changed to HR-HPV primary screening to detect HR-HPV infections in the Netherlands in 2017.
- The choice of HR-HPV test (mRNA or DNA) used in screening programmes can impact resource use and costs, follow-up testing and referral for colposcopy.
- Both mRNA and DNA tests have similar sensitivity, however, the specificity of mRNA is higher (2), resulting in fewer false-positive results requiring referral for follow-up.

AIM

To explore the impact on costs and number of colposcopies and tests of using an mRNA HR-HPV assay compared to a DNA HR-HPV assay in the National Cervical Cancer Screening Programme (NCSP) in the Netherlands using a modelling approach.

METHOD

- A decision tree model was adapted from a previously published model in England (3) to represent the current cervical screening flowchart in the Netherlands (Figure 1).
- This model estimates the impact on costs, number of colposcopies, HR-HPV and cytology tests of using an mRNA assay compared to a DNA assay for a cohort of women (n= 807,629) aged 30 to 65 years.
- Demographic and screening results published in the 2019 Cervical Screening Programme Monitor (4) and local costs (5,6) were used to parameterise the model.
- Probabilities of progression through the flowchart were sourced from the HORIZON study from Copenhagen (7,8), NCSP (4) and DUSC (9).
- Scenario analyses were conducted to explore parameter uncertainty and provide possible outcomes for a range of values of mRNA and DNA HR-HPV positivity at baseline screen.
- The results from similar analyses from different countries were also compared (Table 2).

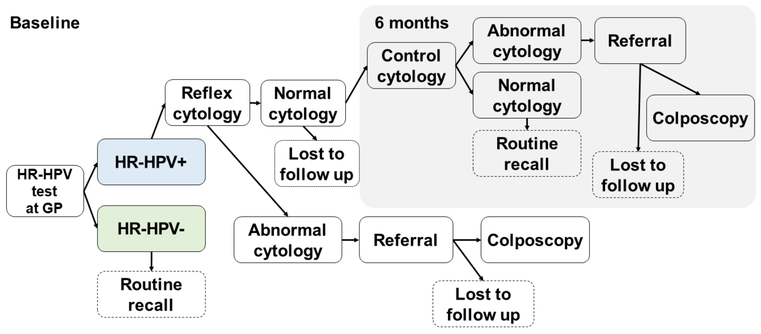

Figure 1: National Cervical Screening Programme flowchart, Netherlands

RESULTS

Adopting an mRNA test rather than a DNA test within the National Cervical Screening Programme in the Netherlands (women aged 30-65) is estimated to save €1.8 million and prevent 855 unnecessary colposcopies and 33,096 cytology tests (Figure3).

As the HORIZON study reported higher DNA HR-HPV positivity than NCSP results, a scenario analysis was conducted in the model to compare the impact of a range of HR-HPV positivity reported in 3 studies using the same DNA HR-HPV test (Table 1). Results show total cost savings with mRNA testing across a range of HR-HPV positivity with and without follow up testing (Figure 2).

Scenarios	A	B	1	2	3
DNA HPV+	10%	16.2%	10%	16.2%	7.5%
mRNA HPV+	5.8%	9.5%	5.8%	9.5%	8.1%
Probability source	NCSP/HORIZON (4, 7, 8)	HORIZON (7, 8)	NCSP/HORIZON (4, 7, 8)	HORIZON (7, 8)	DUSC (9)

Table 1: Probability of HR-HPV positivity at initial screen used in the model for each scenario.

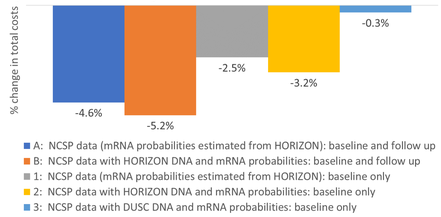

Figure 2: Percentage change in total costs with mRNA compared to DNA for 5 scenarios with varying probability of positive HR-HPV at baseline screen. Negative percentage indicate cost savings with mRNA. Scenarios A and B include baseline and 6 month follow up testing. Scenarios 1, 2 and 3 include costs for baseline screening only.

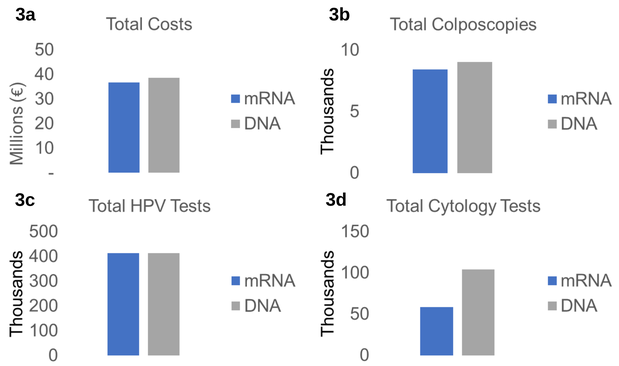

Figure 3: Results reported for one cohort of women participating in cervical screening comparing mRNA HR-HPV assay arm to the DNA HR-HPV assay arm. 3a: Total costs (€) 3b: Total number of colposcopies 3c: Total number of HPV tests 3d: Total number of cytology tests

These results were compared to other international models by converting costs to euros and scaling results per 10,000 women.

A range of outcomes is seen based on the screening algorithm in the country, population characteristics and local costs. In all countries, costs are saved, and unnecessary tests averted (Table 2).

Country	Cost Savings per 10,000 women screened (€)	Number of colposcopies saved per 10,000 women screened	Number of HPV tests saved per 10,000 women screened	Number of cytology tests saved per 10,000 women screened
England	€79,724	125	403	1128
Canada	€11,943	46	65	168
Sweden	€70,026	231	258	369
Denmark	€44,539	242	258	369
France	€30,091	220	178	561
Netherlands	€42,519	21	0	800

Table 2. Cost savings (€) and number of tests and procedures saved per 10,000 women screened using mRNA versus DNA tests.

DISCUSSION

- Adopting an mRNA HR-HPV test instead of a DNA test as part of the National Cervical Screening programme in the Netherlands, gave an estimated €1.8M in total cost savings annually.
- The results from the model in the Netherlands are comparable to results from models for other countries: England (published) and Sweden, Denmark, Canada, and France (unpublished).
- While self-sampling is currently undertaken by <5% of women undergoing cervical screening, self-sampling was excluded from this model. Future studies may explore the impact of self-sampling on the performance of the NCSP.
- The higher specificity of the mRNA compared to DNA (2) can reduce unnecessary referrals to colposcopy. Given the similarity in the sensitivity between mRNA and DNA tests, this will not lead to true positives being missed.
- The choice of HR-HPV assay could make a difference to costs and resource use and is important to consider when making decisions at the national level in the Netherlands.

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