Estimating the costs and benefits of HR-HPV assay choice in a theoretical HPV primary cervical screening algorithm in Ontario, Canada

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INTRODUCTION

- Current cervical screening program guidelines for Ontario recommend cytology testing every 3 years for ages 25-70 (1).
- High-risk human papillomavirus (HR-HPV) types cause nearly all cervical cancer cases (2).
- Several provinces in Canada are moving towards implementing primary HR-HPV screening in their cervical screening programs.
- Primary HR-HPV screening has been found to be more sensitive than primary cytology in detecting high grade disease of the cervix (3).
- Canadian provinces and territories will need to consider how cervical screening is organized and implemented, including the choice of HR-HPV assay, as choice of test influences costs and resource use.

AIM

To explore the impact of choosing either a DNA or mRNA HR-HPV assay in a theoretical primary HPV screening algorithm in Ontario, Canada for a population of women aged 30-65 years using a decision tree model.

METHOD

- A published decision tree model based on the Cervical Screening Programme (CSP) in England (4) was adapted to the primary HPV algorithm proposed by the Cervical Screening Guideline Working Group in Ontario. (Figure 1)
- The outcomes were total costs, and number of colposcopies, HPV tests and cytology tests.
- Screening coverage and population data from the Ontario Screening Program (5) and Statistic Canada (6) and local 2020 costs (7,8) informed model input values.
- Probability data was taken from the FOCAL study (9), a randomised trial comparing screening using HPV and liquid based cytology (LBC), using both DNA (HC2) and mRNA in the larger Vancouver area.
- The FOCAL authors provided an unpublished breakdown of cytology results in year one and two for women who tested HR-HPV positive with the mRNA and DNA tests which were used to parameterise the model.
- The uncertainty in results was explored using deterministic sensitivity analysis and scenario analyses.

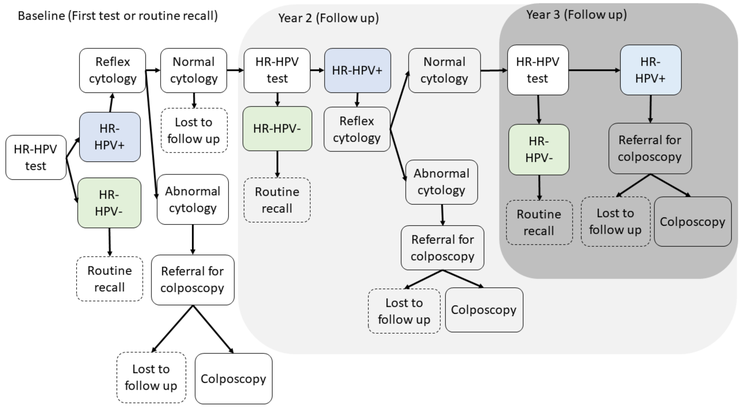

Figure 1: Primary HR-HPV cervical screening algorithm

RESULTS

- If an mRNA assay were used rather than a DNA assay, an estimated cost savings of CAD $4.01 million annually (95% credibility interval (CI): -$7,866,251 to $8,035) could be realized, with 10,639 unnecessary colposcopies averted (95% CI: 10,170 to 11,092) among 2.3 million women screened (Figure 2, Figure 3, Figure 4).
- The results were robust to parameter uncertainty and across a range of plausible scenarios, including extending screening to younger women.
- In a scenario including women under the age of 30 in the HPV primary screening algorithm (256,143 aged 21-24 years and 330,859 aged 25-29) using mRNA testing compared to DNA testing resulted in increased cost saving of $6.75 million and 23,179 unnecessary colposcopies avoided.
- The cost of the HR-HPV test and probability of positive test at year 1 had the largest impact on the difference in cost and number of colposcopies between the mRNA and DNA arms in deterministic sensitivity analysis (Figure 2).

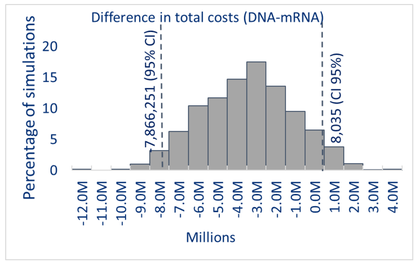

Figure 2: Distribution of the difference between the mRNA and DNA arms in total costs (CAD $) as a result of varying input parameters as a probability distribution around the base case input value in the PSA. Negative results indicate cost savings with mRNA.

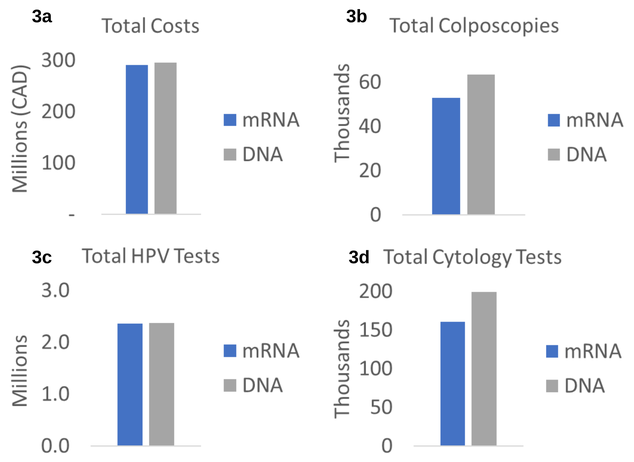

Figure 3: Results reported for one cohort of women participating in cervical screening over 3 years in the mRNA HR-HPV assay arm compared to the DNA HR-HPV assay arm. 3a: Total costs (CAD) 3b: Total number of colposcopies 3c: Total number of HPV tests 3d: Total number of cytology tests

	Total Colposcopies	Total HPV Tests	Total Cytology Tests
mRNA	52,865	2,355,741	160,854
DNA	63,504	2,370,766	199,513
Difference (mRNA-DNA)	**-10,639**	**-15,025**	**-38,659**

Table 1: Number of tests and procedures in the mRNA HR-HPV test arm compared to the DNA HR-HPV test arm. A negative number denotes savings with mRNA testing.

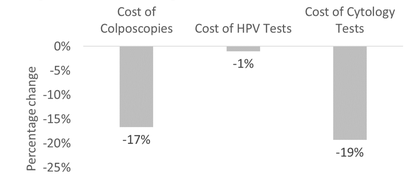

Figure 4: Percentage change in costs in the mRNA HR-HPV test arm compared to the DNA HR-HPV test arm. A negative number denotes savings with mRNA testing.

DISCUSSION

- All provinces in Canada currently employ cytology primary cervical cancer screening. Ontario is one of the first regions to consider HPV primary screening.
- Whilst the Ontario algorithm has not yet been agreed upon, this study shows that the choice of HPV assay is an important consideration within an HPV primary cervical screening program.
- Using mRNA tests instead of DNA tests could save over CAD $4 million annually, and avoid approximately 11,000 unnecessary colposcopies, 15,000 HPV tests and 40,000 cytology tests.
- Given the non-inferior sensitivity of mRNA compared to DNA according to the Meijer criteria (10), no difference in the longer-term outcomes such as disease and pre-cancerous states are anticipated by the choice of test.
- Further work could explore screening intervals, age ranges included in HPV primary screening, the inclusion of genotyping in the algorithm and the impact of a vaccinated population entering the screening program.

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