Evaluating the choice of HPV assay in the French cervical screening programme with a decision tree model

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INTRODUCTION

- Persistent infection with high-risk human papillomavirus (HR-HPV) has been linked to precancerous lesions (cervical intraepithelial neoplasia (CIN)) which may progress to cervical cancer (1).
- Countries around the world have, or are considering, implementing HR-HPV testing in cervical screening.
- Guidance was issued in 2020 to include the use of assays to detect HR-HPV infections in a national cervical screening programme in France.
- To achieve efficient resource use in cervical screening, the type of HR-HPV assay should be considered.

AIM

To evaluate the impact of using an mRNA vs DNA HR-HPV assay in the new French cervical screening programme, using a modelling approach.

METHOD

- A decision tree model was developed to evaluate using a similarly sensitive, but more specific, mRNA HR-HPV assay (Aptima HR-HPV assay) (2) compared to a DNA HR-HPV test (cobas 4800 HPV assay) in the proposed cervical screening algorithm in France.
- This model was adapted from an analysis of HPV primary screening in England (3).
- In the proposed cervical screening algorithm in France the following were modelled:
  - Figure 1A) Ages 25-29 have primary cytology screening (4).
  - Figure 1B) Ages 30-65 have HPV primary screening (5).
- The model follows a hypothetical cohort from baseline screen for two years through recall visits exiting at discharge to routine recall, colposcopy, or loss to follow up.
- The outcomes were the total costs and total colposcopies, HPV and cytology tests in the DNA and mRNA arms.
- HPV and cytology positivity probability inputs were taken from HORIZON, a head-to-head study of mRNA and DNA assays with follow-up (5,6) with similar HPV positivity to France (FASE (7)).
- Population and local costs were taken from published French sources and confirmed with experts.
- Sensitivity analysis explored the robustness of results to parameter and structural uncertainty.

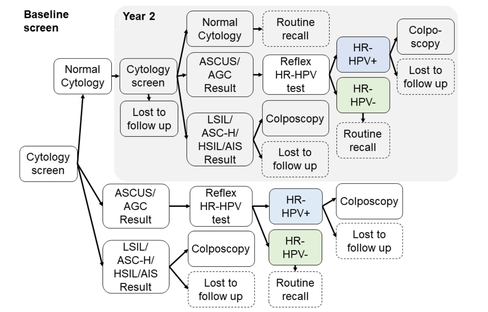

Figure 1A: Cytology primary cervical screening algorithm for women aged 25-29

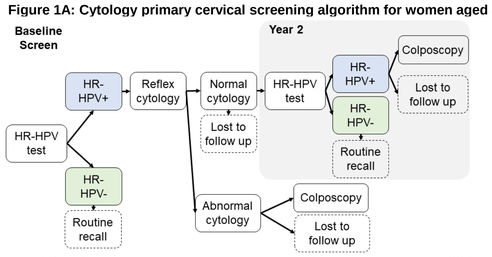

Figure 1B: HPV primary cervical screening algorithm for women aged 30-65

RESULTS

Using an mRNA HR-HPV test instead of a DNA test is estimated to save €6.5 million (95% CI €-13.8 million – 712,623) and prevent 47,795 (95% CI 47,287 - 48,314) unnecessary colposcopies over two years for a cohort of 2,168,806 million women aged 25-65 participating in the proposed national cervical screening programme in France (Figure 2, Figure 3, Table 1).

Costs and number of colposcopies were most sensitive to the probability of a positivity DNA HR-HPV test in year 1 in the deterministic sensitivity analysis.

In 93.5% of iterations in the probabilistic sensitivity analysis (PSA), the mRNA arm was cost saving compared to the DNA arm (Figure 4).

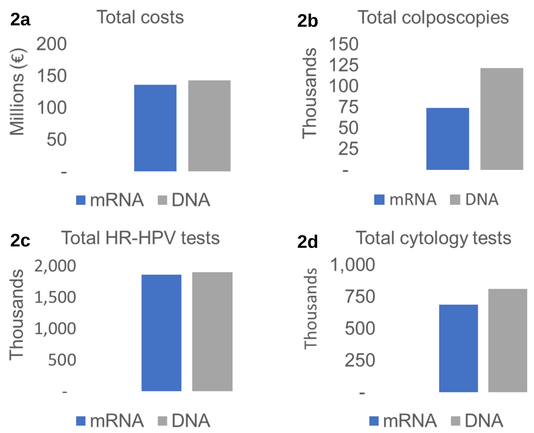

Figure 2: Baseline outcomes for cohort of women participating in cervical screening over 2 years in the mRNA HR-HPV assay arm compared to the DNA HR-HPV assay arm. 2a: Total costs (€) 2b: Total number of colposcopies 2c: Total number of HPV tests 2d: Total number of cytology tests

	Total colposcopies	Total HPV tests	Total cytology tests
mRNA	74,208	1,861,925	690,150
DNA	122,003	1,900,590	811,820
Difference (mRNA-DNA)	-47,795	-38,666	-121,670

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.

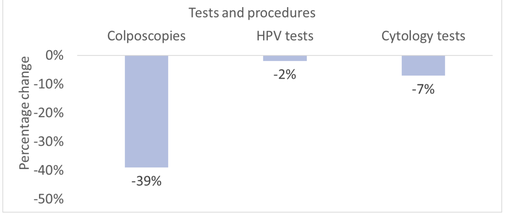

Figure 3: Percentage change in number of tests and procedures in the mRNA HR-HPV assay arm compared to the DNA HR-HPV assay arm

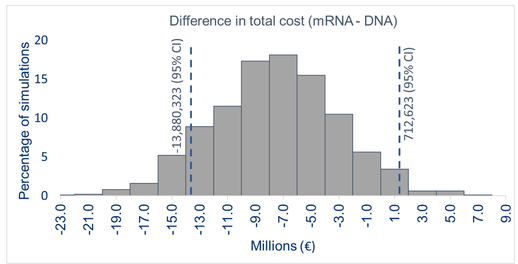

Figure 4: Distribution of the difference between the mRNA and DNA arms in total costs (€) as a result of varying input parameters as a probability distribution around the base case input value in the PSA. Negative results indicate cost savings with mRNA.

DISCUSSION

- Using an mRNA rather than DNA test could yield an estimated annual cost saving of €6.5 million and reduces the total colposcopies, HPV and cytology tests required.
- Reducing unnecessary testing reduces mental health burden associated with further testing.
- Uncertainty analyses indicate robust results across a range of inputs.
- As mRNA and DNA tests have similar test sensitivity, true positives will not be missed, and total costs are reduced by eliminating unnecessary colposcopy referrals, HR-HPV and cytology tests.
- These results are in line with studies in the UK (3) and Canada that showed that using an mRNA assay results in cost savings and reduced unnecessary tests across different population and screening algorithms.
- Future work will evaluate the introduction of self-sampling into the screening algorithm.
- These results can inform the implementation of the national cervical screening programme in France.

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