**Appendix to the article:**

***Could HPV testing on self-collected samples be routinely used in an organised cervical screening program? A modelled analysis***

Contents

[Background to Policy1-Cervix model 2](#_Toc52377955)

[Detailed model parameters 2](#_Toc52377956)

[Test performance 2](#_Toc52377957)

[Screening behaviour 3](#_Toc52377958)

[Vaccination assumptions 5](#_Toc52377959)

[References 5](#_Toc52377960)

# Background to Policy1-Cervix model

Policy1-Cervix is a well-established model of HPV transmission, natural history, vaccination, cervical screening, and treatment of precancer and cancer, that has previously been described in detail, and validated against age-specific rates of HPV prevalence, screening participation, cytology test results, detected high grade abnormalities, invasive cancer and mortality [1-4]. The model platform has been used to undertake large number of policy evaluations in England, the United States, Australia, New Zealand, China, Vietnam, and at the global scale [2 5-20]. A detailed model description is available online at [www.policy1.org](http://www.policy1.org) [4].

The analysis in this article forms part of a program of evaluation work across the cervical cancer spectrum, *Pathways Cervix* [21]. Model parameters for the base case (for example, relating to natural history, screening participation, adherence to follow-up, test characteristics, cancer survival) and the specific cohort selected for evaluation were set to be consistent across *Pathways Cervix* evaluations of a wide range of cancer control options, in order to systematically compare these and produce a list of ‘best buys’ for future decision-making in cervical cancer control.

# Detailed model parameters

## Screening behaviour

Hypothetical scenarios in the first component of our analysis explored the population-level impact of offering self-collection, if it was successful in increasing screening participation (scenarios 1-6). In these scenarios, it was assumed that self-collection would increase initiation of screening in previously unscreened women aged 30 years or more (Supplementary Figure 1), and also boost participation either specifically in under-screened women (those whose most recent HPV test was seven or more years ago), or in all women (five or more years since last HPV test). Participation was boosted by assuming that a proportion of women (15%, 50%, or 80%) who would not otherwise have attended for screening at a given timepoint did attend due to the option of self-collection (population coverage in base case and for scenarios with boosted participation is shown in Supplementary Figure 2).

Supplementary Figure 1 - Proportion of women who have ever been screened, by age

Supplementary Figure 2 - Percentage of women screened within the previous five years, under varying assumptions of boosted participation due to self-collection, by age

Boosted participation refers to the percentage of women who would not otherwise attend for screening at a given time point, but do so as a result of the option of self-collection. Scenarios S1, S2, S5, S6 as described in Table 2 of the main text.

## Vaccination assumptions

All scenarios assume that quadrivalent vaccine is used from 2007 on.

Supplementary Table 1 – Proportion of unvaccinated females who complete a full vaccine course, by age and calendar year

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Age** | **2007** | **2008** | **2009** | **2010** | **2011** | **2012 onwards** |
| 12 | 0 | 0.77 | 0.76 | 0.763 | 0.783 | 0.824 |
| 13 | 0 | 0.77 | 0 | 0 | 0 | 0 |
| 14 | 0 | 0.765 | 0 | 0 | 0 | 0 |
| 15 | 0.765 | 0.76 | 0 | 0 | 0 | 0 |
| 16 | 0.735 | 0 | 0 | 0 | 0 | 0 |
| 17 | 0.675 | 0 | 0 | 0 | 0 | 0 |
| 18 | 0.209 | 0 | 0 | 0 | 0 | 0 |
| 19 | 0.174 | 0.232 | 0 | 0 | 0 | 0 |
| 20 | 0.174 | 0.209 | 0.278 | 0 | 0 | 0 |
| 21 | 0.162 | 0.197 | 0.244 | 0 | 0 | 0 |
| 22 | 0.162 | 0.186 | 0.22 | 0 | 0 | 0 |
| 23 | 0.162 | 0.186 | 0.22 | 0 | 0 | 0 |
| 24 | 0.139 | 0.186 | 0.209 | 0 | 0 | 0 |
| 25 | 0.145 | 0.186 | 0.209 | 0 | 0 | 0 |
| 26 | 0.237 | 0.29 | 0.209 | 0 | 0 | 0 |

Supplementary Table 2 – Proportion of unvaccinated males who complete a full vaccine course, by age and calendar year

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age** | **2013** | **2014** | **2015** | **2016 onwards** |
| 12 | 0.750 | 0.755 | 0.755 | 0.755 |
| 13 | 0 | 0 | 0 | 0 |
| 14 | 0.664 | 0.715 | 0 | 0 |
| 15 | 0.316 | 0 | 0 | 0 |
| 16 | 0.01325 | 0 | 0 | 0 |

## Test performance

The modelled accuracy of HPV-testing was adjusted so that test performance on self-collected samples, relative clinician-collected samples was consistent with data from a meta-analysis [22]. The relative performance of PCR-based tests was used, as Australian pathology standards require that PCR-based HPV tests must be used on self-collected samples [23]. Relative sensitivity and specificity using PCR-based tests were only reported for the CIN2+ endpoint, not for CIN3+. Therefore the relative performance at the CIN3+ threshold was set to be similar to (but not better than) that for CIN2+, based on the meta-analysis reporting similar relative performance at both CIN2+ and CIN3+ thresholds when data were pooled across all HPV test types (including both signal-based and PCR-based tests) [24].

Supplementary Table 3 – Test performance of HPV testing on a self-collected sample, relative to a clinician-collected sample

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test performance** | **Model** | **Range for sensitivity analysis** | **Target (95% CI)** | **Reference** |
| Relative sensitivity |  |  |  |  |
| CIN2+ | 0.98 | (0.94 - 1.02) | 0.98 (0.95 - 1.02) | [22 25] |
| CIN3+ | 0.95 | (0.92 – 1.00) | - |  |
| Relative specificity |  |  |  |  |
| CIN2+ | 1.02 | (0.94 - 1.05) | 1.02 (0.94 - 1.09) | [22 25] |
| CIN3+ | 1.02 | (0.94 - 1.04) | - |  |

Based on the performance of PCR-based HPV tests only [22]; Australian pathology standards require that PCR-based HPV tests must be used on self-collected samples [24].

# References

1. Lew JB, Simms K, Smith MA, et al. National Cervical Screening Program Renewal: Effectiveness modelling and economic evaluation in the Australian setting (Assessment Report). MSAC application number 1276. Report to the Medical Services Advisory Committee (MSAC), Department of Health Australia. Canberra: Department of Health 2014.

2. Lew J-B, Simms K, Smith MA, et al. Primary HPV testing versus cytology-based cervical screening in women in Australia vaccinated for HPV and unvaccinated: effectiveness and economic assessment for the National Cervical Screening Program. Lancet Public Health 2017;**2**:96-107.

3. Hall MT, Simms KT, Lew J-B, et al. Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017-2035: Example from Australia. PLoS One 2018;**13**(2):e0185332 doi: 10.1371/journal.pone.0185332

4. Cancer Council NSW. Policy1-Cervix Documentation. 2019 (accessed 14th February 2020). <https://www.policy1.org/models/cervix/documentation/policy1-cervix-v1_0.pdf>.

5. Kitchener HC, Canfell K, Gilham C, et al. The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. Health Technol Assess 2014;**18**(23):1-196.

6. Legood R, Smith M, Lew J-B, et al. Cost effectiveness of human papillomavirus test of cure after treatment for cervical intraepithelial neoplasia in England: economic analysis from NHS Sentinel Sites Study. BMJ 2012;**345**:e7086 doi: 10.1136/bmj.e7086.

7. Canfell K, Lew JB, Smith M, et al. Cost-effectiveness modelling beyond MAVARIC study end-points. In: Kitchener HC, Blanks R, Cubie H, et al., eds. MAVARIC - a comparison of automation-assisted and manual cervical screening: a randomised controlled trial. Health Technology Assessment ; Vol. 15: No. 3, 2011.

8. Burger EA, Smith MA, Killen J, et al. Projected time to elimination of cervical cancer in the USA: a comparative modelling study. The Lancet Public Health 2020 doi: 10.1016/S2468-2667(20)30006-2.

9. Smith MA, Lew JB, Walker RJ, et al. The predicted impact of HPV vaccination on male infections and male HPV-related cancers in Australia. Vaccine 2011;**29**(48):9112-22 doi: 10.1016/j.vaccine.2011.02.091.

10. Smith MA, Canfell K, Brotherton JM, et al. The predicted impact of vaccination on human papillomavirus infections in Australia. Int J Cancer 2008;**123**(8):1854-63.

11. Simms KT, Hall M, Smith MA, et al. Optimal Management Strategies for Primary HPV Testing for Cervical Screening: Cost-Effectiveness Evaluation for the National Cervical Screening Program in Australia. PLoS One 2017;**12**(1):e0163509 doi: 10.1371/journal.pone.0163509.

12. Smith MA, Gertig D, Hall M, et al. Transitioning from cytology-based screening to HPV-based screening at longer intervals: implications for resource use. BMC Health Services Research 2016;**16**(1):1.

13. Simms KT, Smith MA, Lew JB, et al. Will cervical screening remain cost-effective in women offered the next generation nonavalent HPV vaccine? Results for four developed countries. Int J Cancer 2016;**139**(12):2771-80 doi: 10.1002/ijc.30392.

14. Simms KT, Laprise J-F, Smith MA, et al. Cost-effectiveness of the next generation nonavalent human papillomavirus vaccine in the context of primary human papillomavirus screening in Australia: a comparative modelling analysis. Lancet Public Health 2016;**1**(2):e66-e75 doi: 10.1016/s2468-2667(16)30019-6.

15. Smith MA, Hall M, Lew JB, et al. Potential for HPV vaccination and primary HPV screening to reduce cervical cancer disparities: Example from New Zealand. Vaccine 2018;**36**(42):6314-24 doi: 10.1016/j.vaccine.2018.08.063.

16. Lew J-B, Simms K, Smith M, et al. Effectiveness Modelling and Economic Evaluation of Primary HPV Screening for Cervical Cancer Prevention in New Zealand. PLoS ONE 2016;**11**(5):e0151619 doi: 10.1371/journal.pone.0151619.

17. Canfell K, Shi JF, Lew JB, et al. Prevention of cervical cancer in rural China: Evaluation of HPV vaccination and primary HPV screening strategies. Vaccine 2011;**29**(13):2487-94 doi: 10.1016/j.vaccine.2010.12.085.

18. Canfell K, Kim JJ, Brisson M, et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet 2020;**395**(10224):591-603 doi: 10.1016/s0140-6736(20)30157-4.

19. Brisson M, Kim JJ, Canfell K, et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet 2020;**395**(10224):575-90 doi: 10.1016/s0140-6736(20)30068-4.

20. Simms KT, Steinberg J, Caruana M, et al. Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020-99: a modelling study. Lancet Oncol 2019;**20**(3):394-407 doi: 10.1016/S1470-2045(18)30836-2.

21. Velentzis LS, Smith MA, Simms KT, et al. Pathways to a cancer-free future: A protocol for modelled evaluations to maximize the future impact of interventions on cervical cancer in Australia. Gynecologic Oncology 2019;**152**(3):465-71 doi: <https://doi.org/10.1016/j.ygyno.2018.12.019>.

22. Arbyn M, Castle PE. Offering self-sampling kits for HPV testing to reach women who do not attend in the regular cervical cancer screening program. Cancer Epidemiology Biomarkers & Prevention 2015 doi: 10.1158/1055-9965.epi-14-1417.

23. National Pathology Accreditation Advisory Council. Requirements for Laboratories Reporting Tests for the National Cervical Screening Program (First Edition). First ed. Canberra: Commonwealth Department of Health,, 2017.

24. National Pathology Accreditation Advisory Council. Requirements for Laboratories Reporting Tests for the National Cervical Screening Program (Second Edition). Canberra, 2019.

25. Arbyn M, Verdoodt F, Snijders PJ, et al. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. Lancet Oncol 2014;**15**(2):172-83 doi: 10.1016/S1470-2045(13)70570-9

S1470-2045(13)70570-9 [pii].