Limitations of simulation models for cervical cancer screening

Authors' reply

We are happy that Anne Hammer and colleagues have found our Article on cervical cancer screening to be of interest. They raise the important point that cervical cancer incidence is influenced by period and cohort effects.[1] We argue that our results are more generalisable than Hammer and colleagues suggest because we conditioned the model predictions on a woman's human papillomavirus (HPV) positivity, cytology test result, and whether she had a hysterectomy. As Hammer and colleagues point out, the cervical cancer risk for the average woman differs between countries or between racial groups in the USA, most likely because of differences in HPV acquisition, screening practices, and incidence of hysterectomy over time.[1,2] As such, these differences in cancer risk are expected to substantially diminish once we consider whether a woman is HPV negative, cytology negative, and has a cervix, because these are the factors that drive differences in cervical cancer risk between periods, cohorts, and populations. Although the work done for the US Preventive Services Task Force by Kulasingam and colleagues[3] (and cited by Hammer and colleagues) corrected for hysterectomy, it did indeed only focus on risk based on cumulative cytology test results, and did not include the detailed conditioning as described in our Article. Therefore, although our predictions for the so-called typical woman reflect the risk for the average Canadian woman, our predictions for women with negative screen test results are more widely generalisable across populations. This finding is supported by observational data, which show that the cumulative incidence of CIN3+ becomes very similar across developed countries after stratification by cytology and HPV test result.[4]

We agree with Hammer and colleagues that it is important to acknowledge that the validity of any modelling result is always dependent on model assumptions. We are fortunate that the natural history of oncogenic progression from HPV infection to cervical cancer on which we based our model is the most well studied of any cancer.[5] Because we calibrated the model assuming a stable participation rate in cervical cancer screening, we emphasise that our results are most applicable to developed countries with long-standing screening programmes. It is important to realise that risk estimates from observational studies are also affected by period and cohort effects. Even if there existed a registry with sufficient quality data to calculate the lifetime risk of cervical cancer after stopping screening, it would reflect the risk for a woman who stopped screening 30–40 years ago, and not the risk for a woman who stops screening today. Because we wished to project the future long-term risks for women in a current epidemiological context, simulation modelling based on tenable assumptions was an appropriate strategy.

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