Vaccine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

The cost-utility of integrated cervical cancer prevention strategies in the Ontario setting – Can we do better?

Q1 Beate Sander[a,b,c,d,*], William W.L. Wong[b,d], Man Wah Yeung[a], Orges Ormanidhi[d], Karen Atkin[e], Joan Murphy[b,e,f], Murray Krahn[b,c,d,f], Shelley L. Deeks[a,b]

[a] Public Health Ontario, Canada
Q2 [b] University of Toronto, Canada
[c] Institute for Clinical Evaluative Sciences, Toronto, Canada
[d] Toronto Health Economics and Technology Assessment Collaborative, Canada
[e] Cancer Care Ontario, Canada
[f] University Health Network, Toronto, Canada

ARTICLE INFO

Article history:
Received 14 September 2015
Received in revised form 15 January 2016
Accepted 3 February 2016
Available online xxx

Keywords:
Human papilloma virus
Cervical cancer
Vaccination
Screening
Cost-effectiveness analysis

ABSTRACT

Introduction: A universal, publicly funded, school-based human papillomavirus (HPV) vaccination program in grade eight girls was initiated in Ontario in 2007. We present a cost-utility analysis of integrated cervical cancer prevention programs from the healthcare payer perspective.
Methods: Our analysis was based on linked HPV transmission and disease history models. We obtained data from the literature, provincial surveys and Ontario population-based linked health administrative datasets. We modeled combinations of vaccination and screening strategies. We considered vaccination based on the Ontario experience, as well as conservative and optimistic scenarios, varying coverage, vaccine effectiveness and duration of protection. We considered 900 screening scenarios (screening start age: 21–70 years, screening interval: 3–20 years; 1-year time steps). The current schedule screens every 3 years starting at age 21 years. We examined (1) first vaccinated cohort (low herd-immunity), and (2) steady state, i.e. all cohorts were vaccinated (high herd-immunity).
Results: Adding vaccination to the current screening schedule was cost-effective (<C$10,000/quality-adjusted life year (QALY)) across all scenarios. Delaying screening start and/or extending screening intervals increased both expected QALYs and cost, and increased overall NHB for screening schedules with a start age of 25–35 years and 3–10-year intervals for most scenarios.
Conclusion: Delaying screening start age and/or extending screening intervals in vaccinated cohorts is likely to be cost-effective. Consideration should be given to both the short- and long-term implications of health policy decisions, particularly for infectious disease interventions that require long time intervals to reach steady state.

1. Introduction

Worldwide, cervical cancer is the second most common type Q4 of cancer in women. Routine cervical cancer screening programs have significantly reduced cervical cancer incidence. In Ontario, Canada's largest province (population of ~13 million), the incidence of cervical cancer has decreased by 2.1% annually since 1981, with mortality rates falling 3% annually for women aged 35 and over [1]. Provincial guidelines recommend screening every 3 years for all women who are or ever have been sexually active starting at age 21 [2].

Cervical cancer is caused by persistent infection with high-risk (HR) human papillomavirus (HPV), where types 16 and 18 are responsible for approximately 70% of cases prior to routine HPV

Abbreviations: Pap, Papanicolaou; HR, high-risk; HPV, human papillomavirus; LR, low risk; PHU, public health unit; MOHLTC, Ontario Ministry of Health and Long-Term Care; QALY, quality-adjusted life years; HSIL, high-grade cervical squamous intraepithelial lesion; CIN, cervical intraepithelial neoplasia; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; OHR, other high risk; SIRS, susceptible-infectious-recovered-susceptible; NHANES, National Health and Nutrition Examination Survey; ASCCP, American Society for Colposcopy and Cervical Pathology; LBC, liquid based cytology.

Q3 * Corresponding author at: 480 University Avenue, Toronto, ON M5G 1V2, Canada. Tel.: +1 647 260 7425; fax: +1 647 260 7600.
E-mail address: beate.sander@oahpp.ca (B. Sander).

http://dx.doi.org/10.1016/j.vaccine.2016.02.016
0264-410X/

vaccinations [3]. HPV types 16 and 18 are also prevalent in anogenital and oropharyngeal cancers [3]. Low risk (LR) HPV types 6 and 11 are associated with anogenital warts and recurrent respiratory papillomatosis [4,5]. A bivalent vaccine (against types 16 and 18) and a quadrivalent vaccine (against types 6, 11, 16 and 18) are licensed in Canada. Both are highly efficacious against persistent infection with HR HPV types 16 and 18 and precancerous lesions. Ontario implemented a publicly-funded, school-based HPV vaccination program in 2007, targeting grade eight girls (~13 years of age). While falling short of the Canadian Immunization Committee benchmark of 90% of girls aged 14 years [6], vaccination program coverage has increased from 51% (2007/2008) to 80% (2012/2013) [7,8].

Many studies have shown the cost-effectiveness of HPV vaccination plus screening compared to screening only. Despite differences in methodology and setting, studies consistently conclude that HPV vaccination in girls is cost-effective from the health care payer perspective [9]. With the first vaccinated cohort approaching screening age, an assessment of the cost-utility of integrated cervical cancer prevention programs is imperative.

2. Methods

A cost-utility analysis evaluating integrated primary (HPV vaccination, assuming the bivalent and quadrivalent vaccines to have a similar profile in all important aspects) and secondary (screening) cervical cancer prevention strategies in Ontario was performed from the health care payer perspective (Ontario Ministry of Health and Long-Term Care (MOHLTC)). Health outcomes included HPV infection by age over time, cervical cancer cases, deaths and quality-adjusted life years (QALYs). Health care costs included intervention costs for immunization and screening programs and treatment costs for high-grade cervical squamous intraepithelial lesion (HSIL), cervical intraepithelial neoplasia (CIN 2–3), and invasive cervical cancer.

Primary outcomes were QALYs, costs in 2012 Canadian dollars, incremental cost-effectiveness ratio (ICER), and net health benefit (NHB), calculated as QALYs – (cost/λ), where λ was the cost-effectiveness threshold of $50,000 per QALY. NHB represents the difference between incremental effectiveness (in QALYs) and the health equivalent of the costs using a specific cost-effectiveness threshold (in QALYs). Hence, NHB greater than zero QALYs is considered cost-effective. NHB allows for strategies to be ranked from least to most cost-effective [10]. Multiple cohorts were simulated over 100 years. At the individual level, a lifetime time horizon was adopted. Future costs and QALYs were discounted at 5% [11].

2.1. Model

The analysis was based on linked HPV transmission and disease history models. The heterosexual network model of HPV transmission predicted age-specific incidence of infection over time by HPV type. The disease history model simulated the cervical cancer disease pathway from HPV infection to invasive cervical cancer and predicted HPV-related health outcomes.

2.2. HPV transmission model

The dynamic HPV transmission model was a pair model [12] that simulated sexual partnerships within a sexual network of 50,000 people. Multiple cohorts were simulated in 1 month time steps, accounting for overlapping partnerships, multiple age and sexual risk groups, partnership type (casual versus steady) and safe sex practices (condom usage). Males and females entered the population at age 15 years and exited upon death.

Infection with types 16, 18, other high risk (OHR), or LR types was transmitted in a partnership at a constant rate per unit time that varied according to infection type and age of the partners. The model assumed a Susceptible-Infectious-Recovered-Susceptible (SIRS) natural history (i.e. infection often clears spontaneously and the individual is susceptible to reinfection). Infections persisted for 1 year on average before clearing. Natural immunity lasted a few years on average. The duration of partnerships, infection, natural immunity, and vaccine immunity were sampled from an Erlang distribution for each individual, varying by age.

The sexual behavior parameters were calibrated with US National Health and Nutrition Examination Survey (NHANES) 2009–2010 data on number of lifetime partners by age and number of partners in the last 12 months by age [13]. The natural history parameters were calibrated with Canadian data on prevalence of type 16, type 18, OHR and LR infections by age [11,12].

2.3. Disease history model

The Ontario-specific cervical cancer model is an extension and update of the validated Canadian Cervical Cancer model [14] which only accounted for HR or LR persistent HPV infection. The pathway was restructured to accommodate the specific HPV types 16, 18, OHR and LR types, describing lifetime events of the Ontario

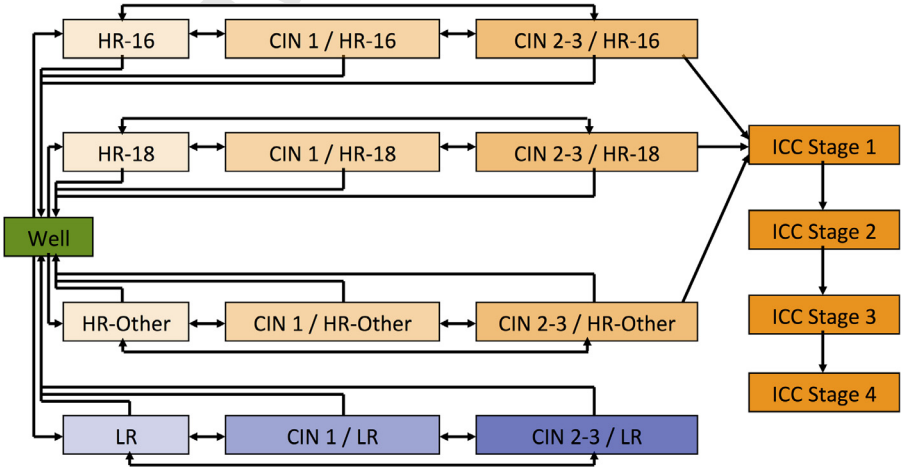

Fig. 1. Disease history model for cervical outcomes.
CIN 1, CIN 2, CIN 3, cervical intraepithelial neoplasia, stage 1, stage 2, stage 3; LR, low risk; HR, high risk; ICC, invasive cervical cancer.

Please cite this article in press as: Sander B, et al. The cost-utility of integrated cervical cancer prevention strategies in the Ontario setting – Can we do better? Vaccine (2016), http://dx.doi.org/10.1016/j.vaccine.2016.02.016