Vaccine 34 (2016) 4678–4683

Contents lists available at ScienceDirect

Vaccine

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

Early impact of Ontario's human papillomavirus (HPV) vaccination program on anogenital warts (AGWs): A population-based assessment

Fiona M. Guerra [a], Laura C. Rosella [a,b,c], Sheila Dunn [d,e], Sarah E. Wilson [a,b,c], Cynthia Chen [a], Shelley L. Deeks [a,b,*]

[a] Public Health Ontario, 480 University Avenue, Suite 300, Toronto, ON M5G 1V2, Canada
[b] Dalla Lana School of Public Health, University of Toronto, 155 College St, Toronto, ON M5T 3M7, Canada
[c] Institute for Clinical Evaluative Sciences, Veterans Hill Trail, 2075 Bayview Avenue G106, Toronto, ON M4N 3M5, Canada
[d] Department of Family and Community Medicine, University of Toronto, 500 University Ave, Toronto, ON M5G 1V7, Canada
[e] Women's College Hospital and Women's College Research Institute, 790 Bay St, Toronto, ON M5G 1N8, Canada

ARTICLE INFO

Article history:
Received 15 April 2016
Received in revised form 3 August 2016
Accepted 4 August 2016
Available online 12 August 2016

Keywords:
Human papillomavirus
HPV
Genital warts
Vaccine
Epidemiology
STI
Health services research

ABSTRACT

Introduction: This study aimed to evaluate the early population impact of Ontario's school-based human papillomavirus (HPV) vaccination program, implemented in September 2007 for grade 8 females, by comparing anogenital wart (AGW) health care utilization before and after vaccine program implementation, in program-eligible and program-ineligible cohorts, focusing on 15–26 year olds.
Methods: Using a retrospective longitudinal population-based study design, health administrative data were used to identify incident AGWs and total health service utilization (HSU) for AGWs for Ontario residents 15 years and older between April 1 2004 and March 31 2014. The study period was divided into two eras: the pre-vaccine program era and the vaccine program era. Negative binomial models were generated to analyze trends across time by age group and sex. We adjusted female rates for routine Papanicolaou (Pap) testing to address spillover effects of Pap smear policy changes on AGW diagnosis.
Results: Between fiscal years 2004 and 2013, AGW incidence decreased 2.6% on average per year in 15–17 year old females, and total HSU for AGWs decreased an average of 4.8% and 2.2% per year in 15–17 and 18–20 year old females. Comparing the vaccine era to the pre-vaccine era, AGW incidence decreased 6.5% in 18–20 year old females, and AGW HSU decreased 13.8%, 11.1%, and 10.0% in 15–17, 18–20, and 21–23 year old females respectively. In contrast, male AGW incidence rates increased an average of 4.1%, 2.8%, and 0.9% per year in 15–17, 21–23, and 24–26 year old males respectively. AGW incidence rates increased 12.2% in 15–17 year old males from the pre-vaccine to vaccine era.
Conclusion: The decline in AGW incidence and HSU in program-eligible females suggests the school-based HPV vaccination program has had an early population impact in Ontario. The increasing AGW incidence in males suggests no early evidence of herd effects in males.

1. Introduction

In September 2007, Ontario, Canada's most populated province with approximately 13.3 million residents in 2011 [1], implemented a voluntary, publicly-funded school-based human papillomavirus (HPV) vaccination program for grade 8 girls, using the HPV4 vaccine, Gardasil® [2]. Initially a three-dose schedule was used, but this was modified in the 2015/16 school year to a two-dose schedule. Evaluating the impact of the program on population-level cervical cancer incidence in Ontario will require the passage of substantial time due to the latency period from HPV infection to cervical cancer; however, health care utilization

Abbreviations: OHIP, Ontario Health Insurance Program; RPDB, Registered Persons Database; ICES, Institute for Clinical Evaluative Sciences; MOHLTC, Ministry of Health and Long-Term Care; CIHI, Canadian Institute of Health Information; HSU, health service utilization.

* Corresponding author at: Immunization and Vaccine-Preventable Diseases, Public Health Ontario, 480 University Ave., Suite 300, Toronto, ON M5G 1V2, Canada.

E-mail addresses: fiona.guerra@gmail.com (F.M. Guerra), laura.rosella@utoronto.ca (L.C. Rosella), sheila.dunn@wchospital.ca (S. Dunn), sarah.wilson@oahpp.ca (S.E. Wilson), Cynthia.Chen@oahpp.ca (C. Chen), shelley.deeks@oahpp.ca (S.L. Deeks).

http://dx.doi.org/10.1016/j.vaccine.2016.08.020
0264-410X/

for anogenital warts (AGWs) provides an early indication of the program's impact in preventing HPV-induced lesions, while also providing valuable information on the change in the AGW burden. Researchers from other countries with HPV vaccination programs, including Australia, the United States (US), Sweden, and Denmark, have begun reporting significant decreases in the incidence of AGWs among females, with the greatest reductions in settings with high vaccine uptake; however, the indirect impact on males has varied ([3–9], and reviewed by [10–13]).

Our objective was to evaluate the early population impact of Ontario's HPV school-based vaccination program on AGWs by comparing health care utilization for AGWs before and after program introduction using health administrative data. We aimed to estimate the benefits of the program at the population level by age group and sex.

2. Methods

2.1. Population and study period

The population included all Ontario residents 15 years and older with a valid health card number in Ontario's health care system (described below). Average annual incidence was reported for individuals 15 years and older, but our analysis of pre-vaccine and vaccine eras focused on 15–26 year olds as this is the age group where we would likely see the earliest and greatest population impact on AGWs given the age eligibility of the vaccine program. In our analysis, the year started on April 1 and ended March 31 in keeping with the fiscal calendar, and the study period was April 1 2003 to March 31 2014 (years 2003–2013). The first year of the study period was used as a wash-out year to exclude prevalent cases (see Outcome Definition). The study period was divided into two eras: the pre-vaccine program era (2004–2007), and the vaccine program era (2008–2013). Although Ontario's program was implemented in September 2007, the full first series of HPV4 vaccination would have been completed between March and May 2008, hence April 1 2008 was designated as the start of the vaccine program era. Grade 8 girls are eligible for the program, most of whom are 13 years of age by December 31 of the calendar year in which they are in grade 8. For the purposes of this study we defined the program eligible cohort during the vaccine program era as females born between January 1 1994 and December 31 2000 (aged 14–20 years in 2013). We did not have individual-level data on HPV4 vaccination status.

2.2. Data sources

Health administrative data has been used to estimate AGW burden in other studies [6,7,14–18]. Health care encounters captured by the provincial insurance plan data were used to measure AGW-related health care utilization. Ontario provides health care coverage to all residents through the Ontario Health Insurance Program (OHIP). Eligibility requires that an individual be a Canadian citizen, landed immigrant, or refugee, has Ontario as their primary or permanent home, and resides in Ontario for at least 153 days over a 12-month period. There is no parallel system of private services for routine medical care and hospitalizations. Individual-level outpatient physician visits for AGWs were captured within the OHIP database, which represents approximately 90% of AGW health service visits captured by the provincial health insurance administrative databases [16]. The Registered Persons Database (RPDB) contains information on all Ontario residents who are eligible for health care coverage and was used to determine population size, sex, and date of birth. These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES).

2.3. Outcome definitions

Consistent with previous health services studies on AGWs, an episode of AGWs was deemed incident if it was preceded by a 12-month window without any AGW-related care utilization [9,15–18]. In addition to AGW incidence, we report total AGW HSU rates, which counted every health care encounter that fulfilled the AGW outcome definition in the numerator. As described further elsewhere, the OHIP database provides diagnostic and procedural codes from physician office visits that can be combined into algorithms to generate a probable outcome definition for AGWs [16,19]. A physician office visit was counted as an AGW visit if any of the following ten code combinations were billed: 099 only if billed with Z117; or, 079 only if billed with Z117; or, 629 only if billed with Z117; or, Z549; or, Z758; or, Z733, Z736, or Z769 only in females; or, Z767 or Z701 only in males [16].

2.4. Statistical analysis

We analyzed annual AGW HSU rates and incidence per 1000 population across the study period stratified by sex and age group among 15–26 year olds. The crude rates were calculated by dividing the numerator (number of prevalent AGW cases stratified by fiscal year, gender, and age group) by the denominator (size of the Ontario population in the same fiscal year, gender and age group). We then modeled the numerator count as the outcome and fiscal year as the independent continuous variable in the negative binomial regression models with the log link function and log (population) as the offset. Average annual rates are reported by era and are the average of the annual HSU or incidence rates for each year in a given era. A negative binomial regression model was also used to model incidence or HSU rates by year. Considering that some AGWs diagnosed at the time of routine Papanicolaou (Pap) testing might not otherwise be diagnosed, we adjusted for the impact of changes in Pap testing rates resulting from revisions to Ontario's cervical screening guidelines in 2011 and associated changes to OHIP Pap testing reimbursement for physicians in 2012. As we are examining changes over time, we wanted to ensure this potential change in outcome identification was adjusted for. We used established billing codes to identify Pap tests (Supplemental Table S1) [19,20]. Visits meeting the Pap test outcome definition occurring 12 months or more apart were considered as routine screening visits. After we calculated the Pap testing rates, they were adjusted in the negative binomial model as a continuous variable for females, with unadjusted rates explored in a sensitivity analysis. Reported percent changes were the average annual change between 2004 and 2013, relative to 2004, or between the pre-vaccine and vaccine eras (Supplemental Table S2). The threshold for statistical significance was set at $p < 0.05$. Analyses were performed using SAS, 9.3 (The SAS Institute, Cary, NC) and Microsoft Excel 2010.

This study was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre and the Ethics Review Board at Public Health Ontario.

3. Results

3.1. AGW counts, AGW sex and age distribution

Between April 1 2004 and March 31 2014, 113 029 individuals 15 years and older made 286 609 health care visits for AGWs through physician offices. In the pre-vaccine and vaccine eras the