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Impact and effectiveness of childhood varicella vaccine program in Queensland, Australia

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ABSTRACT

Background: In November 2005, Australia introduced a publicly funded single dose of varicella vaccine for children aged 18-months. We describe the impact of this program on varicella hospitalisations in Queensland and provide the first assessment of single-dose varicella vaccine effectiveness in Australia since the program commenced.
Methods: Age-standardised varicella hospitalisation rates were calculated for 2000–2014 and pre- and post-public funding period rates compared. Case-control studies were conducted to investigate the association between vaccine receipt and both varicella hospitalisations and uncomplicated varicella emergency department presentations. Cases were matched to controls from a population-based register by date of birth and state of residence. Vaccine effectiveness was calculated as (1 – odds ratio) × 100%.
Results: Compared to the pre-funded period (2000–2003), age-standardised varicella hospitalisation rates declined by more than 70% in 2011–2014 with varicella principal diagnosis rates declining from 5.7 to 1.6 per 100,000 population per year. Varicella vaccine effectiveness at preventing hospitalisation with a principal diagnosis of varicella among children aged 19-months to 6-years was 81.9% (95% confidence interval: 61.8–91.4%), while for emergency department presentations among children aged 19-months to 8-years it was 57.9% (95% confidence interval: 48.5–65.5%).
Conclusions: In Australia, the single-dose varicella vaccination program has substantially reduced varicella morbidity. The single-dose varicella vaccine schedule is moderately-to-highly effective against hospitalisation, but appears less effective against emergency department presentations.

1. Introduction

Australia began public funding of varicella vaccine (VV), as part of the National Immunisation Program in November 2005, with the inclusion of a single-dose at 18-months of age [1]. The program also included a time-limited, catch-up dose for 10–13 year olds in Queensland who were unvaccinated or had no previous history of varicella disease [1]. Previous ecological studies have described the impact of the publicly funded varicella program in Australia, with significant reductions in national varicella hospitalisations in both vaccine age-eligible children and vaccine age-ineligible adults [2], and on national neonatal varicella incidence [3], suggesting direct and indirect protection. To date, there have been

Abbreviations: ACIR, Australian Childhood Immunisation Register; CI, confidence intervals; ED, emergency department; EDIS, Emergency Department Information System; ICD-10-AM, International Statistical Classification of Diseases, 10th Revision, Australian Modification; IRR, incidence rate ratios; MMRV, measles, mumps, rubella and varicella vaccine; OR, odds ratio; VE, vaccine-effectiveness; VIVAS, Vaccination Information and Vaccination Administration System; VV, varicella vaccine.

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no vaccine-effectiveness (VE) estimates of VV in Australia during the public funding era.

The monovalent VVs, Varivax (Merck & Co., Inc, Whitehouse Station, NJ, USA) and Varilrix (GlaxoSmithKline, Rixensart, Belgium), became available in Australia in 2000. In late 2003 a single-dose of VV was recommended, but not publicly funded, at 18-months of age [4]. With the commencement of public funding, Queensland initially used both Varivax and Varilirix between November 2005 and June 2006. Subsequently, only Varilrix was used in the public program until July 2013, when the quadrivalent measles, mumps, rubella, and varicella vaccine (MMRV), Priorix-Tetra (GlaxoSmithKline, Rixensart, Belgium), replaced VV at age 18-months [5]. In Queensland, the adolescent catch-up dose was undertaken through school-based immunisation of 13-year olds from 2007 [6].

Before VV was recommended in late 2003, national coverage of children at age 24-months was 9.7%, reaching 20.9% by the end of the pre-funding period in 2005 [2]. VV coverage among children aged 24-months in Queensland increased steadily from 81.8% in 2007 to 87.1% in 2012 for monovalent VV, and to 91.4% for MMRV in 2014 [7–11]. The uptake of the school-based immunisation program targeting 13-year olds also increased from 32% in 2007 to 52% in 2014 [12]. Information is not available on the proportion of adolescents who due to prior vaccination or varicella infection were ineligible for VV through the school-based program. The coverage reported through the school-based program is likely to underestimate the true coverage achieved as adolescents were also able to receive the catch-up VV from their family doctor [12].

The aim of this study is to describe the impact of the single-dose program on varicella hospitalisations in Queensland between January 2000 and December 2014 and, for the first time, investigate the VE of a single dose of VV against hospitalisation and emergency department (ED) presentation in Queensland among children aged from 19-months to 8-years of age.

2. Methods

We analysed hospitalisation data (2000–2014) and conducted a matched case-control study. The case-control study included children aged up to 8-years who were eligible for publicly funded VV between January 2006 and June 2013 in Queensland, Australia.

2.1. Data sources

The ACIR is a near-complete population register with 99% of children included on the register by age 12-months regardless of vaccination status [13]. ACIR data were used to identify controls and their vaccination status in the case-control study.

Queensland public and private hospitalisation episodes coded for varicella or its complications (International Statistical Classification of Diseases, 10th Revision, Australian Modification [ICD-10-AM] codes B01.0-B01.9) in any diagnostic field between January 2000 and December 2014, were retrieved from the Queensland Hospital Admitted Patient Database [14]. Mid-year Queensland population estimates between 2000 and 2014, were obtained from the Australian Bureau of Statistics [15] in order to calculate hospitalisation rates.

Paediatric ED presentations with the ICD-10-AM code B01.9 (varicella without complication) were obtained from the Emergency Department Information System (EDIS). EDIS operates in 25 Queensland public hospitals, which in 2010/2011 were responsible for 80% of all non-admitted (ED and outpatient) hospital presentations for any cause, in Queensland public hospitals.

Vaccination records of hospitalised and ED cases were retrieved from the Queensland vaccination register (Vaccination Information and Vaccination Administration System; VIVAS). VIVAS is not a population-based vaccination register and only records vaccination encounters, meaning it was not inclusive of wholly unvaccinated children.

2.2. Hospitalisation patterns

Average annual age-specific varicella hospitalisation rates, directly age standardised to the 2014 population, and 95% confidence intervals (CIs) were calculated for time-periods corresponding to when VV was licensed, but not recommended (2000–2003); when VV was recommended, but not publicly funded (2004–2005); and two periods when VV was publicly funded (early: 2007–2010; late: 2011–2014). To allow time for initial program implementation, the first-year of the funded program was not included in the analysis.

Crude and age-specific incidence rates were calculated for hospitalisations where varicella was recorded as the principal diagnosis or in any diagnostic field using Poisson regression. Directly age-standardised rates were calculated using the 2014 population. Incidence rate ratios (IRRs) and 95% CIs were calculated, comparing age-specific and age-standardised rates in the vaccine-funded period to those in the vaccine-licensed period.

2.3. Vaccine effectiveness case-control study

We calculated the VE of VV in preventing hospitalisation with varicella in the principal diagnostic and any diagnostic field, and in preventing ED presentation for varicella in Queensland using a matched case-control method. This method was used previously to assess VE of pertussis vaccine in Australia [16].

We included cases born after 01 July 2004, and therefore eligible for funded VV, and who were at least 19-months old at hospitalisation or ED presentation. Only children attending hospital between January 2006 and June 2013 with their first varicella hospitalisation or ED presentation during the study period were included.

To determine the vaccination status of cases, the Queensland Health Data Linkage Unit linked vaccination records from VIVAS to ED presentation and hospitalisation data using LinkageWiz probabilistic data matching software, v5.3 (LinkageWiz Inc, Adelaide, South Australia). Weighting scores were assigned to matching variables, including surname, first name, date of birth, and address. Middle- and lower-weighted pairs were individually assessed, and higher-weighted pairs checked for false matching related to multiple births.

Twenty controls and their VV records from the ACIR were matched to each case by date of birth (either the same day, or one day on either side of the case's date of birth), sex, and residential jurisdiction. As cases were de-identified, we could not exclude the possibility of a case also being selected as one of their own controls.

Vaccination was considered valid if it was received at least 42-days before illness onset among cases and 14-days before the case's disease onset for controls. Cases were excluded if their symptoms began within 42-days of being vaccinated to ensure VV-associated rashes were not misclassified as varicella cases in our study.

We used conditional logistic regression to estimate the odds ratio (OR) for VE in preventing hospitalisation and ED presentations among children aged 19-months to 6-years and 19-months to 8-years, respectively. VE in preventing hospitalisation was calculated for children aged to 6-years as there were no vaccine eligible hospitalised cases older than this. We also undertook analysis stratified by the age-groups: 19 months-2 years, 3–4 years, and 5–6 years for hospitalisation; and 19 months-2 years, 3–4 years,