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Review

Review of the health impact of the oral rotavirus vaccine program in children under 5 years in Australia: 2006 – 2021

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ABSTRACT

Oral rotavirus vaccines were incorporated into the National Immunisation Program (NIP) for all Australian infants in July 2007. Initially each of the eight jurisdictions implemented Rotarix or RotaTeq rotavirus vaccine, however from July 2017 all states and territories have administered Rotarix only. This review evaluates the health impact of the oral rotavirus vaccine program for Australian children less than 5 years old over the first 15 years of the rotavirus vaccine program, observing long-term changes in rotavirus-related health care attendances, public health notifications, and vaccine effectiveness and safety data for both Rotarix and RotaTeq rotavirus vaccines. We searched Medline for studies published between January 2006 and May 2022 using the search terms 'rotavirus', 'rotavirus vaccine' and 'Australia'. Of 491 items identified, 76 items – 36 peer-reviewed articles and 40 reports – were included in the review. We found evidence that the introduction of the oral rotavirus vaccine program in Australia was associated with a prompt reduction in rotavirus-coded and all-cause gastroenteritis hospitalisations of vaccine-eligible children. In the context of less complete coverage, reduced vaccine timeliness and lower vaccine effectiveness, a less substantial and inconsistent reduction in severe rotavirus disease was observed among Aboriginal and Torres Strait Islander children, particularly those living in rural and remote northern Australia. Additional studies report no evidence for the emergence of non-vaccine serotypes and/ or replacement serotypes in Australia during the vaccine era. While the health impact for young children and consequent cost-savings of the oral rotavirus vaccine program have been high, it is important to find strategies to improve rotavirus vaccine impact for Aboriginal and Torres Strait Islander populations to ensure health benefits for all Australian children.

Contents

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1. Introduction

Rotavirus remains a leading cause of dehydrating diarrhoeal disease in young children, with severe disease most common in young children 6 months to 2 years old [1]. Before the availability of rotavirus vaccines, rotavirus was globally responsible for the hospitalisation of more than 2 million children and the death of more than 500,000 children < 5 years old every year [2].

In Australia, before the oral rotavirus vaccine program, rotavirus caused more than 10,000 hospitalisations, 22,000 emergency department (ED) presentations and 115,000 visits to general practitioners for children < 5 years old every year, with an estimated annual cost of A$30 million [3]. The burden of disease was greatest among Aboriginal and Torres Strait Islander children, with the hospitalisation rate more than five times that of non-Indigenous children among those < 12 months old [4]; frequent outbreaks of rotavirus disease occurred in remote communities [5]. However deaths were rare, with just 13 rotavirus-related deaths reported in Australia between 1990 and 2002 and most occurring in the first year of life [4].

In 2006, two oral rotavirus vaccines were licensed for use in Australia – Rotarix™ (GlaxoSmithKline), an attenuated vaccine containing a human G1P [8] rotavirus strain licensed as a two-dose schedule at 2 and 4 months, and RotaTeq™(Merck), containing five human-bovine reassortant vaccine strains (G1, G2, G3, G4 and P1 [8]), licensed as a three-dose schedule at 2, 4 and 6 months [6]. In phase III clinical trials conducted in Europe [7–9], the United States [7], and Latin America [9], both vaccines demonstrated high efficacy (85 – 100 %) against severe rotavirus disease in infants and young children. Due to concerns about an increased risk of intussusception among infants > 3 months old with an earlier tetravalent rhesus-human rotavirus vaccine, the manufacturers recommended upper age limits for administration – second dose of Rotarix by 25 weeks and third dose RotaTeq by 33 weeks [10].

The Northern Territory (NT) introduced a funded rotavirus vaccine program in October 2006, and from July 2007 both vaccines were incorporated into the National Immunisation Program (NIP) for all Australian infants [11]. Initially each of the eight Australian states and territories (jurisdictions) implemented one or other of the two vaccines; from July 2017 all jurisdictions have only administered Rotarix under the NIP [12]. Rotavirus became a nationally notifiable disease in July 2018 [13].

This review evaluates evidence of the health impact of the oral rotavirus vaccine program in Australia for children under 5 years old over the first 15 years of the program. It examines vaccine coverage and timeliness data, including predictors of incomplete or delayed rotavirus vaccine administration, summarises the evidence for decreased rotavirus-related healthcare utilisation and rotavirus laboratory-confirmed infection notifications to jurisdiction-based public health units following implementation of the rotavirus program, and reports the results of vaccine effectiveness studies evaluating rotavirus vaccine protection against gastroenteritis hospitalisations and rotavirus infection notifications. The review also evaluates data on the safety of rotavirus vaccines in the Australian context.

2. Methods

We reviewed the published literature and government reports to identify studies which measured the health impact of the rotavirus vaccine program in Australia. We followed Joanna Briggs Institute methodology and the Preferred Reporting Items for Systematic Reviews and meta-Analysis extension for Scoping Reviews (PRISMA-ScR) guidelines. The protocol is available at Open Science Framework (https://osf.io/mz637).

We searched Medline (via Pubmed) for studies published between January 2006 and May 2022 using the search terms 'rotavirus', 'rotavirus vaccine' and 'Australia'. We also reviewed reports published by the National Centre for Immunisation Research and Surveillance (NCIRS) and the Australian Government Department of Health, and consulted Australian experts in rotavirus and vaccinology to identify articles missed by the above search strategy. Identified items were downloaded and assembled in an Endnote X9 library and imported into Covidence software (covidence.org) where duplicates were removed.

Our initial search identified 491 items (Fig. 1). We screened 458 titles and abstracts, and 157 items progressed to full text review. We excluded 81 items; these were editorials, articles reporting rotavirus burden in the pre-vaccine or the vaccine era only, articles referencing the burden of vaccine preventable disease but which were not specific for rotavirus, reviews of international data, cost-effectiveness studies, rotavirus genotype prevalence studies, and methodological studies evaluating approaches to impact assessment (Supplementary Materials). We included 76 items, comprising thirty-six peer reviewed articles and forty reports. Included items reported data on rotavirus vaccine coverage and timeliness [13–33], compared the number of rotavirus-related health care attendances (hospitalisations, ED presentations, and primary care attendances) [6,34–45] or rotavirus notifications before and after the introduction of the rotavirus vaccine program [34,46–50], and reported vaccine effectiveness in Australian settings [35,51–57]. Items reporting vaccine safety, including rates of intussusception, were also included (Fig. 1, Supplementary Materials) [58–85].

We focused on data for children who were age-eligible for rotavirus vaccination at the time of the study, and where possible ascertained data on both rotavirus-confirmed gastroenteritis and all-cause gastroenteritis.

3. Results

3.1. Vaccine coverage & timeliness

We identified 5 articles [14–18] and 16 reports [12,19–33] reporting rotavirus vaccine coverage and timeliness in an Aus-

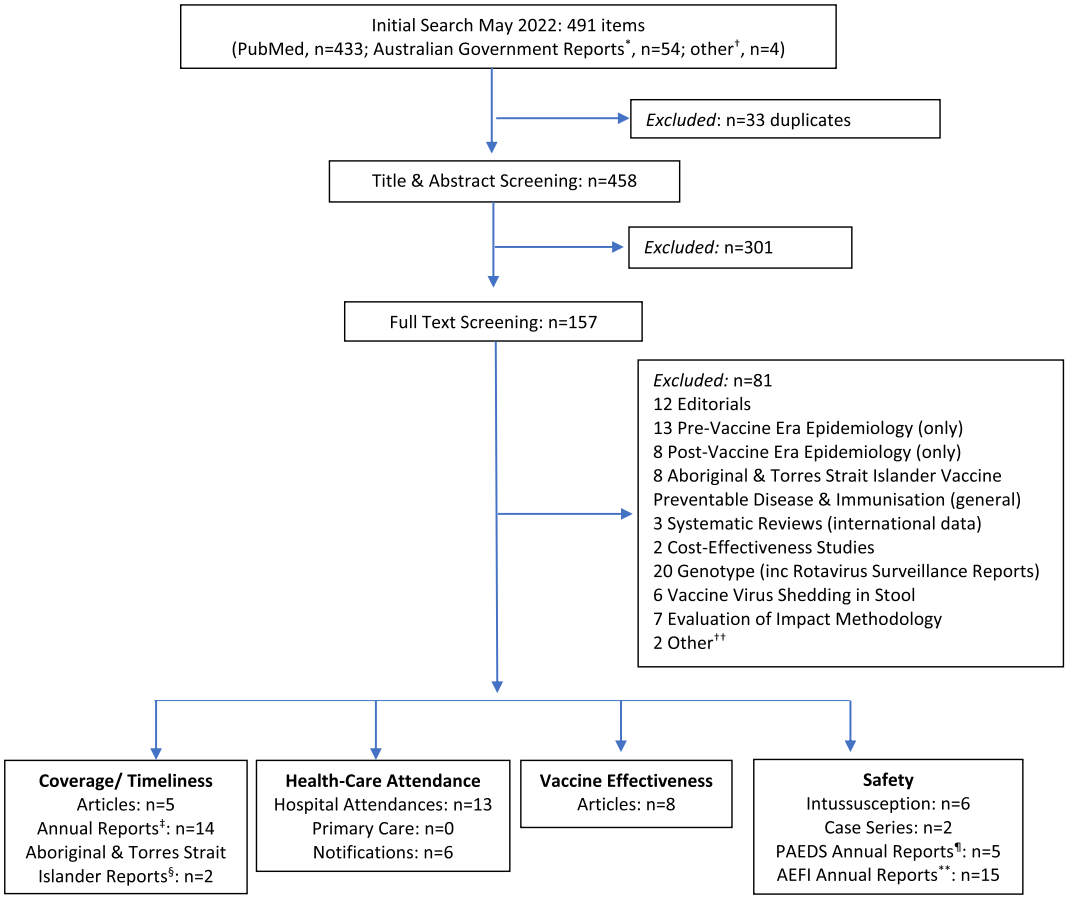

Fig. 1. PRISMA-ScR Flow Chart– Health impact of the oral rotavirus vaccine program in Australia, 2006 – 2021.*Australian Government Reports include Immunisation Coverage Annual Report n = 14; Vaccine Preventable Diseases and Vaccination Coverage in Aboriginal and Torres Strait Islander People n = 2; Paediatric Active Enhanced Disease Surveillance Annual Report n = 5; Surveillance of Adverse Events Following Immunisation Annual Report n = 13; Australian Rotavirus Surveillance Program Annual Report n = 16; Rotavirus Surveillance in Australia n = 1; Effect of COVID-19 public health measures on nationally notifiable diseases in Australia: preliminary analysis n = 3.† Other; articles located from reference list of included studies.‡ Immunisation Coverage Annual Report.§ Vaccine Preventable Diseases and Vaccination Coverage in Aboriginal and Torres Strait Islander People.¶ Paediatric Active Enhanced Disease Surveillance Annual Report.** Surveillance of Adverse Events Following Immunisation Annual Report ††Association between introduction of rotavirus vaccine program and decline in incidence of type 1 diabetes.

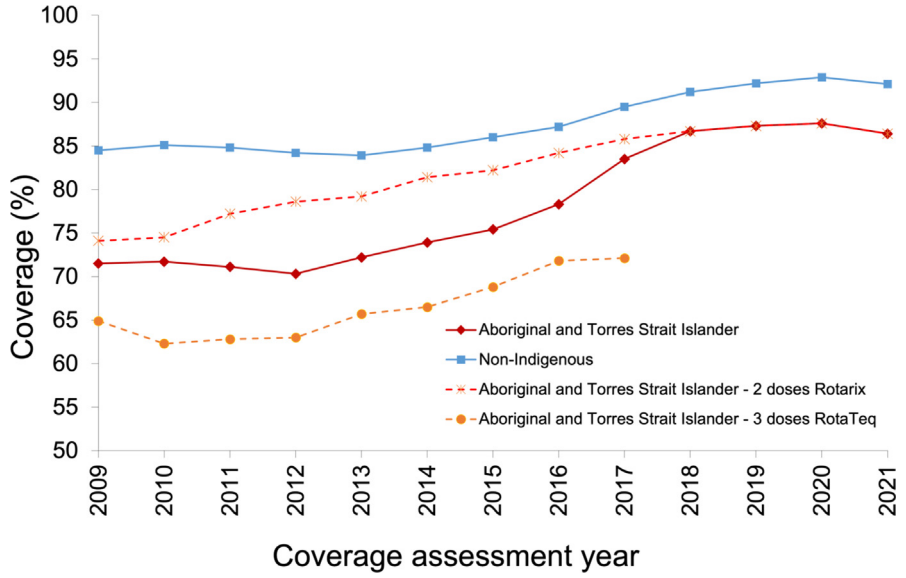

Fig. 2. Trends in rotavirus vaccination coverage at 12 months of age, by Indigenous status and vaccine brand, Australia, 2009 to 2021*. Source: Australian Immunisation Register.*2nd dose of Rotarix or 3rd dose of RotaTeq, assessed for preceding year-wide birth cohort (eg 2009 data points represent coverage for 2008 birth cohort). Analyses of coverage by brand assessed for those states/ territories where Rotarix/ RotaTeq in use at time (RotaTeq used only in Queensland, South Australia and Victoria from program inception to mid-2017, and in Western Australia from mid-2009 to mid-2017).

tralian context. All reported > 80 % rotavirus vaccine coverage rates for non-Indigenous children in the early rotavirus vaccine program era. However, reported coverage was consistently lower for Aboriginal and Torres Strait Islander children, particularly in jurisdictions recommending 3-dose RotaTeq (Fig. 2), and low compared to other vaccines in the NIP schedule [12,19–31]. Implementation of the 2-dose Rotarix schedule in all jurisdictions from mid-2017 was associated with an immediate increase in the proportion of Australian children who were fully vaccinated for rotavirus, with 88 % Aboriginal and Torres Strait Islander and 93 % non-Indigenous children fully vaccinated by 12-months old in 2020 [12].

Predictors of incomplete or delayed rotavirus vaccine coverage during the early vaccine program were examined in a study of 680,000 non-Indigenous and Aboriginal and Torres Strait Islander children born in New South Wales and Western Australia between 2007 and 2012. This study reported that incomplete vaccination was independently associated with prematurity (<33 weeks gestation), low birth weight (<1500 g), maternal age (<20 years old), maternal smoking during pregnancy, higher birth order, mode of delivery, children born to overseas born mothers and living in an area of relative socio-economic disadvantage [18].

Two studies reported that the introduction of rotavirus vaccines into the NIP in 2007 coincided with improvements in the timeliness of other NIP vaccines, with the improvement greatest for doses administered at 6-months old [15,16].

3.2. Hospital attendances

Our search identified 13 studies comparing hospital attendances for rotavirus and all-cause gastroenteritis in the pre-vaccine and the rotavirus vaccine program era. Of these, 10 studies reported on hospitalisations only [6,35–38,40,41,43–45], two studies reported on ED presentations only [34,42] and one study reported on both hospitalisations and ED presentations [39]. Data was reported for both Rotarix and RotaTeq, both nationally and in select states and territories.

All studies compared hospital attendances – hospitalisations and ED presentations in the years immediately pre- and post-introduction of the national vaccine program (pre- and post-2007). In the context of rapid vaccine uptake [16], there was a > 64 % decrease in rotavirus-coded hospitalisations in the first three years of the program among vaccine eligible children (those born on or after May1, 2007) (Table 1). Several studies also observed a decrease in rotavirus-coded hospitalisations and ED presentations among children too old to have been vaccinated (typically children > 2 years old), mostly in the order of 40 – 60 % (range 0 % – 100 %) (Table 2) [6,34–42,45]. A single site study reported an 87 % decline in nosocomial rotavirus infections [38].

Four studies reported length-of-stay as an indicator of rotavirus disease severity and found no evidence of a difference in the pre-vaccine vs rotavirus vaccine program era, typically 1 to 2 days [37,39,41,44]. One study used the Vesikari Score [86] to evaluate gastroenteritis severity and classified 88 % and 84 % of rotavirus admissions as severe (Vesikari Score $\geq$ 11) in the pre- and vaccine period, respectively. This study observed that most children hospitalised in the vaccine era were unvaccinated, with evidence that cases among vaccinated children were less severe than cases among unvaccinated children (mean Vesikari Score 12.3 (95 %CI, 10·8 – 13·7) vs 14·0 (95 %CI, 13·2 – 14·9)) [44].

The largest reduction in hospital attendances was observed among vaccine-eligible children, although one study reported a slight increase in rotavirus-coded hospitalisations among Victorian infants who were too young to be fully vaccinated, almost exclusively in children 0 to 3 months old [36]. A slight increase in rotavirus coded hospitalisations for the 0 to 5 months old age group was also observed in New South Wales, although the number of cases was few [36]. An increase in the median age of children admitted to hospital with rotavirus gastroenteritis was described in two studies, from approximately 13 to 31 months in Victoria and from approximately 18 to 29 months in South Australia (with data analysed for 331 and 312 admitted children, respectively) [39,44], but not in a third study from the Australian Capital Territory, mean age at admission pre-vaccine 21 months vs post vaccine 20 months (data analysed for 289 admitted children) [41].

In the first three years of the rotavirus vaccine program declines in ED presentations, short-stay admissions, and hospitalisations for all-cause gastroenteritis were observed mostly in the order of 30 % to 50 % (range 7 to 78 %) (Table 1). Several authors noted that the decrease in hospital attendances for both rotavirus-coded and all-cause gastroenteritis was largely accounted for by the attenuation of the usual winter/ spring peak in rotavirus infections [6,34,36–39,41].

Two studies reported data for Aboriginal and Torres Strait Islander children [6,45]. Both studies reported a higher baseline hospitalisation rate of rotavirus-coded gastroenteritis among Aboriginal and Torres Strait Islander children in the pre-vaccine era and both observed that the relative decline in hospitalisations in the vaccine era (as a proportion of the baseline rate) was less substantial than for other children (Table 3), with 825 – 1045 per 100,000 Aboriginal and Torres Strait Islander children < 12 months old hospitalised with severe rotavirus gastroenteritis in the vaccine era, compared to 100 – 135 per 100,000 non-Indigenous children < 12 months old (2007 – 2010) [6]. Similar results were also observed in studies reporting data for the NT – a jurisdiction with a high proportion of Aboriginal and Torres Strait Islander children [6,40] In the NT, the decline in hospitalisations for rotavirus coded gastroenteritis and all-cause gastroenteritis was 52 % to 57 % and 32 to 35 %, respectively (Table 3). No decrease in hospitalisations was observed for Aboriginal and Torres Strait Islander children too old to have been vaccinated (>3 years) [6].

3.3. Primary healthcare presentations

Our search identified no studies comparing data on primary care attendances with rotavirus gastroenteritis or all-cause gastroenteritis in the rotavirus vaccine compared to the pre-vaccine era.

3.4. Rotavirus notifications

Two articles evaluated rotavirus positive laboratory results and notification of laboratory-confirmed rotavirus infections to jurisdiction-based public health units in the years immediately before and after initiation of the rotavirus vaccine program. The first reported laboratory-confirmed rotavirus infections from two large public pathology providers in Sydney, New South Wales [34], and the second reported state-wide laboratory-confirmed rotavirus infections and public health notifications to the Queensland Health Notification Data database. The studies reported a 43 % to 87 % decrease in rotavirus positive laboratory test results for children < 12 months old and a 65 % decrease in public health notifications for children $\geq$ 12mths old, in the rotavirus vaccine program era (Table 1). A decrease in rotavirus notifications among children who were too old to be vaccinated was also observed (Table 2) [34,46]. A third report compared rotavirus notifications in the context of G2P[4] rotavirus epidemics in the pre-vaccine era (2004) and in the vaccine era (2009) in the Northern Territory [47]. This study observed little difference in the number of cases notified or the duration of the outbreaks, or in the proportion of cases who were Aboriginal and Torres Strait Islander children, however it did note a trend towards older age in the 2009 epidemic

Table 1
Health-care attendance and notifications for laboratory-confirmed rotavirus gastroenteritis and all-cause gastroenteritis pre- and post- introduction of the rotavirus vaccine program.

Rotavirus Gastroenteritis					
Hospitalisations				% Decrease	
Author	Jurisdiction	Vaccine	Results	Age < 12mths	Age ≥ 12mths
Field 2010 [35]	Qld[†]	RotaTeq	*Hospitalisations < 12 months:*		
			375 (2000–2006) vs 124 (2008) per 100,000; RR 0.3 (95%CI, 0·3–0·4)	−67%	
Buttery 2011 [36]	VIC[‡]	RotaTeq	*Hospitalisations < 12 months;* (2003–2006) vs (2007–2009)	−68%	
			Hospitalisations 13 to 24 months; (2003–2006) vs (2007–2009)		−68%
Clarke 2011 [37]	SA[§]	RotaTeq	*Hospitalisations < 24 months;* 933 (2005–2007) vs 88 (2008–2010) per 100,000		−90%
Macartney 2011 [38]	NSW[¶]	Rotarix	*Hospitalisations < 12 months*; (2001-2006) vs (2008-2009)	−93%	
			*Nosocomial Transmission (all ages);** (2001–2006) vs (2008–2009)		−87%
Dey 2012 [6]	National [**]	Rotarix	*Hospitalisations < 12 months;*		
		RotaTeq	388 (2001–2006) vs 135 (2009–2010) per 100,000; IRR 0·35 (95%CI, 0·31-0·39)	−65%	
			Hospitalisations 12 to 23 months;		
			484 (2001–2006) vs 67 (2009–2010) per 100,000; IRR 0·14 (95%CI, 0·12-0·16)		−86%
Pendleton 2013 [40]	NSW[**]	Rotarix	*Hospitalisations NSW 0 to 11 months;*		
			34 (95%CI, 32-35) (1998–2006) vs 4 (95%CI, 2·7-5·4) (2008–2009) per 10,000	−88%	
			Hospitalisations NSW 12 to 23 months;		
			56 (95%CI, 54-57) (1998–2006) vs 8 (95%CI, 6·6-10·5) (2008–2009) per 10,000		−86%
			Hospitalisations ACT 0 to 11 months;		
	ACT[**]		43 (95%CI, 36-51) (1998–2006) vs 8 (95%CI, 2·3-21·5) (2008–2009) per 10,000	−81%	
			Hospitalisations ACT 12 to 23 months;		
			83 (95%CI, 73-93) (1998–2006) vs 9 (95%CI, 2·4-22·3) (2008–2009) per 10,000		−89%
David 2014 [41]	ACT[††]	Rotarix	*Hospitalisations < 12 months;* 14 (2004–2006) vs 5 (2008–2012) per year	−64%	
			Hospitalisations 12 to 23 months; (2004–2006) vs (2008–2012)		−81%
			Hospitalisation 24 to 35 months; (2004–2006) vs (2008–2012)		−88%
Clarke 2020 [44]	SA[‡‡]	RotaTeq	*Hospitalisations < 5 years;** 233 (2005–2007) vs 79 (2009–2013) per year		−66%
Emergency Department Presentations				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12mths**	**Age ≥ 12mths**
Davey 2015 [42]	NSW[§§]	Rotarix	*ED Presentations < 5 years;** 995 (2003 –2006) vs 340 (2008–2011) per 100,000		−66%
Public Health Notifications				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12mths**	**Age ≥ 12mths**
Lambert 2009 [46]	Qld[¶¶]	RotaTeq	*Public Health Notifications < 2 years;** (2006) vs (2008)		−65%
Laboratory Isolates				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12mths**	**Age ≥ 12mths**
Belshaw 2009 [34]	NSW[***]	Rotarix	*Laboratory Isolates < 15 months;* 102 –285 (2001–2006) vs 36 (2008) per year	− 65% to − 87%	
Lambert 2009 [46]	Qld[†††]	RotaTeq	*Laboratory Isolates < 2 years;** (2000–2006) vs (2008)	−43%	
All-Cause Gastroenteritis					

Hospitalisations				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12mths**	**Age ≥12mths**
Buttery 2011 [36]	VIC‡	RotaTeq	*Shot Stay Unit Admissions (all ages);** 739 (2006) vs 166 (2009) per year		−78%
Clarke 2011 [37]	SA§	RotaTeq	*Hospitalisations < 24 months;* 3616 (2005–2007) vs 1676 (2008–2010) per 100,000		−54%
Akikusa 2013 [39]	VIC‡	RotaTeq	*Hospitalisations (all ages);** 1000 (2005) vs 506 (2009) per year		−49%
			*Short Stay Unit Admissions (all ages);** 531 (2005) vs 166 (2009) per year		−69%
Pendleton 2013 [40]	NSW**	Rotarix	*Hospitalisations NSW 0–11 months;*		
			203 (95%CI, 200-207)(1998–2006) vs 128 (95%CI, 121-136)(2008–2009) per 10,000	−37%	
			Hospitalisations NSW 12–23 months;		
			256 (95%CI, 252-260)(1998–2006) vs 117 (95%CI, 110-124)(2008–2009) per 10,000		−54%
			Hospitalisations ACT 0–11 months;		
	ACT**		154 (95%CI, 141-168) (1998–2006) vs 63 (95%CI, 42-90) (2008–2009) per 10,000	−59%	
			Hospitalisations ACT 12–23 months;		
			219 (95%CI, 203-236) (1998–2006) vs 50 (95%CI, 32-75) (2008–2009) per 10,000		−77%
Fathima 2021 [45]	WA*‡‡‡	Rotarix+	*Hospitalisations < 12 months;* (2004–2007) vs (2007–2012) (95%CI, 29–71%)	54%	
		RotaTeq+	*Hospitalisations 12–23 months;* (2004–2007) vs (2007–2012) (95%CI, −10 to 63%)		36%
			Hospitalisations 2 years; (2004–2007) vs (2007–2012) (95%CI, 3 to 66%)		43%
ED Presentations				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12mths**	**Age ≥ 12mths**
Belshaw 2009 [34]	NSW§§	Rotarix	*ED Presentations < 15 months;* 81–131 (2001–2007) vs 75 (2008) per 1,000		− 7% to − 43%
Akikusa 2013 [39]	VIC‡	RotaTeq	*ED Presentations (all ages);** 53-77 (2004-2007) vs 34 (2009) per 1000 children		− 36% to − 56%
Davey 2015 [42]	NSW§§	Rotarix	*ED presentations < 5 years;** 3750 (2003–2006) vs 2780 (2008–2011) per 100,000		−26%

*not all children in the cohort were age-eligible for rotavirus vaccination.
†Queensland Hospital Admitted Patient Data Collection.
‡Royal Children's Hospital, Victoria.
§ South Australian Hospitals.
¶The Children's Hospital at Westmead, New South Wales.
**National Hospital Morbidity Database, Australian Institute of Health and Welfare.
††The Canberra Hospital, Australian Capital Territory.
‡‡Women's & Children's Hospital, South Australia.
§§New South Wales Emergency Department Data Collection.
¶¶Communicable Disease Branch, Queensland Health.
***South Eastern Sydney Laboratory Surveillance Program.
†††Queensland Health Laboratories.
‡‡‡Western Australian Hospital Morbidity Data Collection.

Table 2
Health-care attendance and notifications for laboratory-confirmed rotavirus gastroenteritis pre- and post- introduction of the rotavirus vaccine program among children too old to have received rotavirus vaccination.

Hospitalisations				
Author	Jurisdiction	Vaccine	Results	% Decrease
Field 2010 [35]	Qld[†]	RotaTeq	*Hospitalisations 5–19 years* 7.9 (2000–2006) vs 3.3 (2008) per 100,000; RR 0.4 (95%CI, 0·3–0·6)	−58%
Buttery 2011 [36]	VIC[‡]	RotaTeq	*Hospitalisations 25 to 36 months;* (2003–2006) vs (2007–2009)	−53%
Clarke 2011 [37]	SA[§]	RotaTeq	*Hospitalisations 3 to < 6 years;* 106 (2005–2007) vs 36 (2008–2010) per 100,000	−66%
Macartney 2011 [38]	NSW[¶]	Rotarix	*Hospitalisations 24 to 59 months*; (2001–2006) vs (2009)	−35%
			Hospitalisations > 60 months; (2001–2006) vs (2009)	−50%
Dey 2012 [6]	National [**]	Rotarix	*Hospitalisations 3 years;*	
		RotaTeq	122 (2001–2006) vs 65 (2009–2010) per 100,000; IRR 0·53 (95%CI, 0·46–0·62)	−47%
			Hospitalisations 4 years; 67 (2001–2006) vs 32 (2009–2010) per 100,000; IRR 0·48 (95%CI, 0·39–0·59)	−52%
			Hospitalisations 5–19 years; 7 (2001–2006) vs 3 (2009–2010) per 100,000; IRR 0·51 (95%CI, 0·43–0·60)	57%
Pendleton 2013 [40]	NSW[**]	Rotarix	*Hospitalisations NSW 24 to 35 months;* 33 (95%CI, 32–35) (1998–2006) vs 10 (95%CI, 7.7–11.9) (2008–2009) per 10,000	−70%
			Hospitalisations NSW 36 to 47 months; 16 (95%CI, 15–17) (1998–2006) vs 4 (95%CI, 2·9–5·8) (2008–2009) per 10,000	−75%
			Hospitalisations NSW 48 to 59 months; 9 (95%CI,8.1–9.5) (1998–2006) vs 2.6 (95%CI, 1.7–3.9) (2008–2009) per 10,000	−71%
	ACT[**]		*Hospitalisations ACT 24 to 35 months;* 40 (95%CI, 33–47) (1998–2006) vs 0 (95%CI, 0–8.0) (2008–2009) per 10,000	−100%
			Hospitalisations ACT 36 to 47 months; 18 (95%CI, 14–24) (1998–2006) vs 4 (95%CI, 0.5–16.2) (2008–2009) per 10,000	−78%
			Hospitalisations ACT 48 to 59 months; 9.2 (95%CI, 6.3–13.1) (1998–2006) vs 0 (95%CI, 0–8.6) (2008–2009) per 10,000	−100%
David 2014 [41]	ACT[††]	Rotarix	*Hospitalisation 24 to 35 months*; (2004–2006) vs (2007)	−85%
			Hospitalisation 36 to 47 months; (2004–2006) vs (2007)	−43%
Public Health Notifications				
Author	**Jurisdiction**	**Vaccine**	**Results**	**% Decrease**
Lambert 2009 [46]	Qld[¶¶]	RotaTeq	*Public Health Notifications 2–4 years;* (2006) vs (2008)	−56%
Laboratory Isolates				
Author	**Jurisdiction**	**Vaccine**	**Results**	**% Decrease**
Belshaw 2009 [34]	NSW[***]	Rotarix	*Laboratory Isolates 15 months to 5 years;* 76–281 (2001–2006) vs 81 (2008) per year	+7 % to −71%

[†]Queensland Hospital Admitted Patient Data Collection.
[‡]Royal Children's Hospital, Victoria.
[§] South Australian Hospitals.
[¶]The Children's Hospital at Westmead, New South Wales.
[**]National Hospital Morbidity Database, Australian Institute of Health and Welfare.
[††]The Canberra Hospital, Australian Capital Territory.
[¶¶]Communicable Disease Branch, Queensland Health.
[***]South Eastern Sydney Laboratory Surveillance Program.

(median age 12 months (IQR 5 to 22 months) in 2009 vs 9 months (IQR 6 to 16 months) in 2004), and a decrease in the proportion of notified rotavirus cases who were hospitalised (76 % in 2009 vs 94 % 2004).

A substantial reduction in national rotavirus notifications was observed during the 2020 COVID-19 pandemic, 18 % fewer notifications than 2019 and 27 % fewer notifications than the 5-year (2015–2019) average [48]. The Northern Territory Centre for Disease Control and Central Queensland Public Health Unit similarly reported a decrease in rotavirus notifications in early – mid 2020, when compared to the 5-year average [49,50].

3.5. Vaccine effectiveness

Seven studies evaluated the direct protective effect of rotavirus vaccine in Australia (Table 4). Three studies evaluated vaccine effectiveness against gastroenteritis-coded hospitalisations [35,52,53] and four studies evaluated vaccine effectiveness against notified rotavirus infection [51,54–56].

Among children < 12 months old, vaccine protection against rotavirus-coded hospitalisations was observed to be high in Queensland (3-dose RotaTeq VE 94 %), and against notified rotavirus infection of any severity in Western Australia (2-dose Rotarix VE 78 % & 3-dose RotaTeq VE 95 %) and in New South Wales (2-dose Rotarix VE 79 %) (Table 4). High vaccine effectiveness (2-dose Rotarix VE 88 %) was also observed among children < 12 months old in New South Wales in 2017 (a year with a 3,1-fold increase in rotavirus notifications compared to 2016) and high levels of circulating heterotypic G3 rotavirus strains [55]. From the second year of life, vaccine protection against notified rotavirus infection was observed to be lower in both Western Australia and New South Wales (Table 4).

Four studies reported vaccine effectiveness in the context of three genotype specific rotavirus epidemics. All three epidemics occurred in rural and remote NT and/ or Western Australia, and all study populations had a high proportion of Aboriginal and Torres Strait Islander children (80 – 98 %) [51–53,56]. Vaccine protection against notified rotavirus infection and rotavirus-coded hospitalisations was observed to be high among young children during an epidemic caused by a partially homotypic G9P[8] rotavirus in 2007, VE 81 % and VE 85 % respectively [51,52]. However, lower levels of vaccine protection were observed against notified rotavirus infection and severe rotavirus gastroenteritis requiring hospitalisation during epidemics of heterotypic G2P[4] in 2009 and 2017, particularly in the second year of life (Table 4) [53,56].

Table 3
Health-care attendance for laboratory-confirmed rotavirus gastroenteritis and all-cause gastroenteritis pre- and post- introduction of the rotavirus vaccine program for Aboriginal and Torres Strait Islander children.

Rotavirus Gastroenteritis					
Hospitalisations – Aboriginal and Torres Strait Islander Children				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12 months**	**Age ≥ 12mths**
Dey 2012 [6]	National[§]	Rotarix RotaTeq	*Hospitalisations < 12 months;* 1465 (2004–2006) vs 1045 (2009–2010) per 100,000; IRR 0·71(95%CI,0·58–0·87) *Hospitalisations 1 to 4 years;** 280 (2004–2006) vs 257 (2009–2010) per 100,000; IRR 0·92 (95%CI, 0·74–1·14)	−29%	−8%
Pendleton 2013 [40]	NT[§]	Rotarix	*Hospitalisation NT 0 to 11 months;*† 289 (95%CI,269–309)(1998–2006) vs 123 (95%CI, 90–163)(2008–2009) per 10,000 *Hospitalisations NT 12 to 23 months;* † 181 (95%CI, 166–198)(1998–2006) vs 87 (2008–2009)(95%CI, 60–122) per 10,000	−57%	−52%
Fathima 2021 [45]	WA[¶]	Rotarix[‡¶] RotaTeq[‡]	*Hospitalisations < 12 months;* 15·5 (2004–2007) vs 5·3 (2007–2012) per 1,000; IRR 0·34 (0·23–0·51) *Hospitalisations 12 to 23 months;* 6·6 (2004–2007) vs 2·9 (2007–2012) per 1,000; IRR 0·43 (0·24–0·76) *Hospitalisations 2 to 4 years;** 0·6 (2004–2007) vs 0·4 (2007–2012) per 1,000; IRR 0·68 (0·26–1·79)	−66%	−56% −33%
All-Cause Gastroenteritis					
Hospitalisations – Aboriginal and Torres Strait Islander Children				**% Decrease**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12 months**	**Age ≥ 12mths**
Pendleton 2013 [40]	NT[§]	Rotarix	*Hospitalisations NT 0 to 11 months;*† 960 (95%CI, 924–997) (1998–2006) vs 624 (95%CI, 548–709) (2008–2009) per 10,000 *Hospitalisations NT 12 to 23 months;*† 862 (95%CI, 828–897) (1998–2006) vs 589 (95%CI, 514–671) (2008–2009) per 10,000	−35%	−32%

*not all children in the cohort were age-eligible for rotavirus vaccination.
†NT – jurisdiction with high proportion of Aboriginal and Torres Strait Islander children.
‡Western Australian Rotavirus Program; Rotarix from July 2007 & RotaTeq from July 2009.
§National Hospital Morbidity Database, Australian Institute of Health and Welfare.
¶Western Australian Hospital Morbidity Data Collection.

In the Western Australian study estimates of vaccine effectiveness against notified rotavirus infection were observed to be no lower for Aboriginal and Torres Strait Islander children than for non-Indigenous children, or for children living in non-metropolitan than for children in metropolitan areas [54]. The results were at odds with the persistently high rates of rotavirus hospitalisation observed for Aboriginal and Torres Strait Islander children living in regional/ remote areas, which the authors suggested might be better explained by lower rotavirus vaccine coverage rather than high rates of vaccine failure.

Our search identified one study that reported a 3-dose RotaTeq protective effect against ED presentations and subsequent hospitalisations with febrile seizures (VE 36 % and 38 % respectively) [57].

3.6. Vaccine safety

Several articles examined intussusception in Australia in the rotavirus vaccine era. Four studies compared rates of intussusception in the years immediately before and after the introduction of the vaccine program [58,60–62]. Two studies evaluated multi-jurisdictional data from the national sentinel Paediatric Active Enhanced Disease Surveillance (PAEDS) Network and the Australian Paediatric Surveillance Unit and observed a 3- to 7-fold increased risk of intussusception in the first 7 days following dose 1 of Rotarix and a 5- to 10- fold increased risk in the first 7 days following dose 1 of RotaTeq, though events remained rare (Table 5). A smaller relative increase in risk was also observed up to 21 days following the first and second doses of both vaccines. There was no observed increase in risk following the third dose of RotaTeq [58,60]. One of these studies summarised the mid-range estimate of attributable risk for both vaccines to be 5·6 additional cases per 100,000 vaccinated Australian infants, or 14 additional cases annually [60]. A retrospective analysis of hospitalisations and ED presentations in New South Wales between 2007 and 2010 also found comparable increase in the relative risk of intussusception following the first dose of Rotarix [61].

A study of ICD discharge codes from the WA Hospital Morbidity Data Collection from January 2000 to December 2012, reported a 70 % increase in intussusception-coded hospitalisations in the rotavirus vaccine era which was no greater among 2-month to 7-month old vaccine-eligible children (40 %) than among children 12-months to 23– months old (55 %) or children 2- years to 4- years old (84 %) [62]. This study also observed no significant change in the rates of intussusception-coded hospitalisations associated with a procedure code between the pre- and post- rotavirus vaccine era. The authors proposed that the increase in intussusception coded hospitalisations in the vaccine era may be better explained by increased awareness of intussusception or changes in coding practices over time than by vaccine-related effects.

Data from the PAEDS network was used to assess the severity of rotavirus vaccine-associated intussusception [63]. After adjusting for age and sex, the study found no evidence of a difference in severity between vaccine-associated and non-vaccine associated intussusception cases. Two additional studies reported similar rates of surgical intervention in vaccine-associated and non-vaccine associated intussusception cases [58] and no apparent difference in severity as measured by length of stay, successful reduction by air enema, or need for surgery [61].

Table 4
. Rotavirus Vaccine Effectiveness Studies.

Vaccine Effectiveness					
Hospitalisations				**Vaccine Effectiveness (95%CI)**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12 months**	**Age ≥ 12mths**
Snelling 2009 [52]	NT[†]	Rotarix	(2-dose) 2007 G9P[8] Rotavirus GE hospitalisation < 12mths	85% (23 to 97%)	
Field 2010 [35]	Qld[‡]	RotaTeq	(3-dose) 2008 Rotavirus GE hospitalisation < 12mths	94% (83 to 98%)	
Snelling 2011 [53]	NT[§]	Rotarix	(2-dose) 2009 G2P[4] Rotavirus GE hospitalisation < 12mths	51% (−92% to 88%)	
			(2-dose) 2009 G2P[4] Rotavirus GE hospitalisation ≥ 12mths		9% (−186% to 66%)
Notified Rotavirus Infection				**Vaccine Effectiveness (95%CI)**	
Author	**Jurisdiction**	**Vaccine**	**Results**	**Age < 12 months**	**Age ≥ 12mths**
Graham 2008 [51]	NT[¶]	Rotarix	(2-dose) 2007 G9P[8] Rotavirus Notified Rotavirus Infection	81% (95%CI, 27–95%)	
Fathima 2019 [54]	WA[**]	Rotarix*	(2-dose) 2009–2011 Notified Rotavirus Infection 6–11mths	78% (2 to 95%)	
			(2-dose) 2009–2011 Notified Rotavirus Infection 12–24mths		54% (2 to 79%)
		RotaTeq*	(3-dose) 2009–2011 Notified Rotavirus Infection 6–11mths	95% (71 to 99%)	
			(3-dose) 2009–2011 Notified Rotavirus Infection 12–24mths		51% (−99 to 88%)
Maguire 2019 [55]	NSW	Rotarix	(2-dose) 2010–2016 Notified Rotavirus Infection 6–11mths	79% (74 to 84%)	
			(2-dose) 2010–2016 Notified Rotavirus Infection 1–3yrs		68% (64 to 72%)
			(2-dose) 2017 Notified Rotavirus Infection 6–11mths	88% (79 to 94%)	
			(2-dose) 2017 Notified Rotavirus Infection 1–3yrs		84% (80 to 87%)
Middleton 2020 [56]	NT[††]	Rotarix/ RotaTeq	(Any-Dose) 2017 G2P[4] Notified Rotavirus Infection < 12mths	52% (−2% to 78%)	
	WA[§§]		(Any-Dose) 2017 G2P[4] Notified Rotavirus Infection ≥ 12mths		−22% (−173% to 45%)

*Western Australian Rotavirus Program; Rotarix from July 2007 & RotaTeq from July 2009.
[†]Alice Springs Hospital, Northern Territory; March 2007 – July 2007.
[‡]Queensland Hospital Admitted Patient Data Collection; January 2008 – December 2008.
[§]Alice Springs Hospital, Northern Territory; February 2009 – May 2009.
[¶]Northern Territory Notifiable Disease System; March 2007 – May 2007.
[**]Western Australia Notifiable Infections Disease Database; January 2009 – December 2011.
[††]New South Wales Notifiable Conditions Information Management System; January 2010 - December 2017.
[‡‡]Northern Territory Notifiable Disease System: March 2017 to June 2017.
[§§]Western Australia Notifiable Infectious Disease Database; March – June 2017.

In the pre-vaccine era, Aboriginal and Torres Strait Islander children were reported to have lower rates of intussusception than non-Indigenous children [87]. The Western Australian birth cohort study spanning both the pre-vaccine and the vaccine era (2000 – 2012) also observed a lower rate of intussusception-coded hospitalisation among Aboriginal children < 5 years old (IRR 0·33, 95 % CI 0·18 – 0·62) [62].

Our search identified one case report [84] and a small case series commenting on the administration of oral rotavirus vaccines among nine premature infants with short gut syndrome and high output ileostomies, and found that oral RotaTeq was tolerated in most cases [85].

4. Discussion

Our review found strong evidence that shortly after the introduction of the rotavirus vaccine program in Australia, moderately high vaccine coverage was achieved rapidly and was followed by a prompt reduction in rotavirus-coded and all-cause gastroenteritis hospitalisations for young children who were eligible for vaccination (those born mid-2007). A reduction in hospitalisations among older vaccine-ineligible children was also observed in the early years of the vaccine program, suggesting an indirect protective effect due to decreased circulation of rotavirus in the community. In most settings, measured vaccine effectiveness against rotavirus-coded hospitalisations and notified rotavirus infections was high for children < 12 months old, although there was some evidence of decreased protection, including against severe infection, from the second year of life. There was no evidence of an appreciable difference in health impact in jurisdictions using Rotarix rotavirus vaccine compared to RotaTeq rotavirus vaccine, noting both vaccines were used contemporaneously in different state-based programs initially, but only Rotarix has been used since July 2017.

Very high rates of rotavirus hospitalisation were observed among Aboriginal and Torres Strait Islander children before the rotavirus vaccine program [4,5]. While appreciable absolute reductions in notifications and hospitalisations for this population were observed in the early years of the vaccine program [6,45], the relative reductions were smaller and the residual rate of hospitalisation with severe rotavirus gastroenteritis remains much higher than for non-Indigenous children [6]. This high residual hospitalisation and notification rate is potentially related to lower vaccine coverage – particularly for jurisdictions recommending 3-dose RotaTeq, less timely vaccine administration, as well as reduced rotavirus vaccine effectiveness compared to non-Indigenous children, observed to be as low as 51 to 52 % among children < 12 months old during heterotypic G2P[4] rotavirus epidemics in rural and remote locations [53,56]. Lower vaccine efficacy and effectiveness has also been observed among children in high rotavirus burden and low resource settings in Africa and South-East Asia [88] and for candidate rotavirus vaccines among Native American populations in North America [89,90]. A recent systematic review of the performance rotavirus vaccines in high mortality settings in Asia and Africa reported vaccine efficacy of 48 to 57 % in the first year following vaccination, and 29 to 54 % in the second year [88]. The reduced effectiveness in those settings has been attributed to a variety of host and/ or environmental factors, including high levels of maternally-derived, vaccine-neutralising anti-rotavirus antibodies, poor infant nutrition, environmental enteropathy and intestinal dysbiosis, comorbid infection, and a high diversity of circulating rotavirus strains [91].

In contrast to the high vaccine effectiveness observed against severe rotavirus gastroenteritis requiring hospitalisation in Phase

Table 5
Vaccine Attributable Risk of Intussusception.

Vaccine Attributable Risk of Intussusception				
Author	**Jurisdiction**	**Vaccine**	**Results**	**Relative Risk/Incidence (95%CI)**
Buttery 2011 [58]	VIC†		*Intussusception 1 to < 3 months‡*	
	SA†	RotaTeq	1–7 days post Dose 1 RotaTeq	5·3 (1·1 to 15·4)
	NSW†		1–21 days post Dose 1 RotaTeq	3·5 (1·3 to 7·6)
	WA*	Rotarix	1–7 days post Dose 1 Rotarix	3·5 (0·7 to 10·1)
			1–21 days post Dose 1 Rotarix	1·5 (0·4 to 3·9)
Carlin 2013 [60]	VIC‡		*Intussusception 1 to < 12 months*	
	SA‡	RotaTeq	1–7 days post Dose 1 RotaTeq	9·9 (3·7 to 26·4)
	Qld‡		8–21 days post Dose 1 RotaTeq	6·3 (2·8 to 14·4)
	WA‡	Rotarix	1–7 days post Dose 1 Rotarix	6·8 (2·4 to 19·0)
	NSW‡		8–21 days post Dose 1 Rotarix	3·5 (1·3 to 8·9)
	NT‡			
Quinn 2014 [61]	NSW§		*Intussusception< 12 months*	
		Rotarix	1–7 days post Dose 1 Rotarix	11·1 (2·6 to 48·0)
			1–21 days post Dose 1 Rotarix	5·5 (1·7 to 17·8)
Fathima 2020 [62]	WA¶	Rotarix	*Post Vaccine (2008–2012) vs Pre Vaccine (2000–2006)*	
		RotaTeq	*Intussusception 2 to 7 months*	
			All-Intussusception-Coded hospitalisations	1·4 (0·9 to 2·2)
			Intussusception 8 to 11 months	
			All-Intussusception-Coded hospitalisations	1·02 (0·7 to 1·6)
			Intussusception 12 to 23 months	
			All-Intussusception-Coded hospitalisations	1·55 (1·1 to 2·3)
			Intussusception 2 to 4 years	
			All-Intussusception-Coded hospitalisations	1·84 (1·2 to 2·8)
			Intussusception 2 to 7 months	
			Intussusception-Coded hospitalisations with intussusception treatment-related procedure codes	1·07 (0·6 to 1·8)

*Western Australian Rotavirus Program; Rotarix from July 2007 & RotaTeq from July 2009.
†Australian Paediatric Surveillance Unit (APSU) and Paediatric Active Enhanced Disease Surveillance (PAEDS); July 2007 – December 2008; historical controls from Australian Institute of Health and Welfare July 2000 – June 2006.
‡ Australian Paediatric Surveillance Unit (APSU) and Paediatric Active Enhanced Disease Surveillance (PAEDS); July 2007 – June 2010; self-controlled case series from Australian Childhood Immunisation Register July 2007 – June 2010.
§Admitted Patient Data Collection and Emergency Department Data Collection, New South Wales; July 2007 – June 2010; self-controlled case series.
§§ Hospital Morbidity Data Collection, Western Australia; 2008–2012; historical controls from the Hospital Morbidity Data Collection 2000 – 2006.

3 clinical trials, vaccine protection against milder disease (any-severity rotavirus gastroenteritis) was observed to be lower [7,92]. No Australian studies have directly evaluated the impact of rotavirus vaccination on primary care utilisation. However, two studies reported a decrease in laboratory and public health notification data [34,46]. This suggests the vaccine program resulted in reduced medical attendances across healthcare settings, including primary care. However, rotavirus infection was only notifiable in three jurisdictions – Queensland, Western Australia and the Northern Territory – prior to the introduction of the rotavirus vaccine program, making it difficult to generalise the findings beyond the sites reported in this review. The substantial reduction in rotavirus notifications observed during the 2020 COVID-19 pandemic likely reflects altered healthcare-seeking behaviour as well as a decrease in spread of common infectious diseases within the community, associated with lockdowns, school and day-care centre closures and increased compliance with hand hygiene [93].

Rotashield, the first licensed oral rotavirus vaccine, was withdrawn in the late 1990 s when post licensure surveillance studies suggested an attributable risk of intussusception, a serious and potentially fatal involution of the intestine causing gut obstruction, of approximately 1 in 10,000 vaccine recipients [10]. However, the pathogenic mechanisms involved in intussusception following rotavirus vaccination remain uncertain and the incidence, case ascertainment and fatality rate varies widely between populations [10]. We found studies reporting a small absolute increased risk of intussusception following the first dose of both vaccines, and a lesser increase after the second dose, although intussusception attributed to vaccination remained rare. These results are consistent with early post-licensure evaluations in several high- and middle-income countries, which report a low risk of 1 – 6 excess cases per 100 000 vaccinated infants for both Rotarix and RotaTeq [94]. A more recent systematic review and *meta*-analysis of 25 randomised clinical trials with more than 200 000 participants from 33 countries, including low-income countries, found no evidence of an increased risk of intussusception following rotavirus vaccination [95].

While vaccine coverage was moderately high, coverage statistics may not capture delayed vaccination and resultant delayed protection [15]. Vaccine delay is particularly relevant for oral rotavirus vaccines because of restrictions on the upper age limit of vaccination (second dose Rotarix by 25 weeks and third dose RotaTeq by 33wks) prevents catch up of missed doses. A reduction in the gap in rotavirus vaccine coverage for Aboriginal and non-Indigenous children occurred following the nationwide switch to exclusively use the 2-dose Rotarix vaccine in 2017 [12], However, ensuring high coverage and timeliness of vaccination remains important for all vulnerable and at-risk children, including Aboriginal and Torres Strait Islander children. Early identification of at-risk groups, including premature and low birth-weight infants, is important, as is working with at-risk communities to identify culturally appropriate, effective, and sustainable strategies to improve timely immunisation uptake [17].

Considering the persistently high rates of severe rotavirus disease and all-cause gastroenteritis for Aboriginal and Torres Strait Islander children, additional strategies are needed. A neonatal RV3-BB vaccine, developed in Australia, has been observed to confer vaccine protection (VE 75 % at 18 months old) when administered in a 3-dose schedule starting at birth in Indonesia [96], and may provide both earlier and extended protection against severe rotavirus disease for Aboriginal and Torres Strait Islander children.

In the ORVAC study – Optimising Rotavirus Vaccine for Aboriginal Children, we are exploring the immunological and clinical impact of scheduling a third (booster) dose of oral Rotarix rotavirus vaccine for Northern Territory Aboriginal infants who are 6 to < 12 months old [97]. Later dosing of rotavirus vaccines is consistent with current recommendations from the World Health Organisation which recommends that in high burden settings that doses can be given to children up to 24 months old [10].

There were several limitations to our review. We were unable to account for variation in rotavirus testing threshold and rotavirus/ intussusception discharge coding practices between different jurisdictions. Rotavirus vaccine shedding in stool has been observed in infants following rotavirus vaccine administration [98], and thus it is possible some studies have over-estimated the residual burden of rotavirus disease in young infants. Conversely, poor sensitivity of the rotavirus-specific hospital discharge codes has also been documented [99], and it is likely that included studies underestimate the true incidence of rotavirus hospitalisations.

We did not evaluate the impact of the oral rotavirus vaccine program among older children (>5 years old), although some studies observed indirect protective effects for this age group. In general, rotavirus disease in children > 5 years old is less likely to be severe and/or require health care attendance.

Two decades of Australian rotavirus surveillance data has been recently summarised elsewhere, finding evidence of greater genotype diversity and fluctuating genotype dominance in the vaccine era, and differences in genotype dominance and diversity between jurisdictions using RotaTeq vs Rotarix vaccines [100]. There has been no evidence of emergence of non-vaccine serotypes and/ or replacement serotypes, though ongoing surveillance and the use of phylogenetic analysis will be important to provide further insight on the impact of rotavirus vaccines on strain diversity [100].

Our review did not attempt to quantify additional benefits of the rotavirus vaccine program resulting from improved coverage or timeliness of other concomitantly scheduled infant vaccines. Nor was it within the scope of our review to evaluate the impact of the program on health care centres in the form of reductions in economic cost, overworked clinic staff, and reduced capacity for routine primary healthcare duties which have previously been observed in rotavirus outbreaks, especially in rural and remote Australia [101], though we note the results of a retrospective economic evaluation which estimated total healthcare cost savings in Australia to be A$65 million in excess of the total cost of the program between 2007 and 2012 [102].

5. Conclusions

The rotavirus vaccine program has resulted in a significant decrease in the burden of rotavirus disease for most Australian children. However, ongoing observation of the health impact of rotavirus vaccines is important, especially in rural and remote locations where early program data indicated a high residual burden of rotavirus disease for Aboriginal and Torres Strait Islander children. It is essential to find strategies to improve vaccine impact for this population and ensure the health benefits of vaccination are realised for all Australian children.

6. Contributors

BFM wrote the first draft of the report with input from TLS, MD, KM, PF, JEB. BFM, TLS and MD conceived the study. BFM, TLS, MD, JEB and KM contributed to the study protocol. BFM screened all titles and abstracts and extracted data. BFM tabulated the data with the assistance of TLS, MD and KM. All authors had full access to the data in the study, contributed to the manuscript and had final responsibility for the decision to submit for publication. All authors attest they meet the ICMJE criteria for authorship and have seen and approved the final version of the manuscript.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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