



## Timeliness and factors associated with rotavirus vaccine uptake among Australian Aboriginal and non-Aboriginal children: A record linkage cohort study



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### ABSTRACT

**Objectives:** Rotavirus vaccines (RV), included in Australia's National Immunisation Program from mid-July 2007, are unique in strict time limits for administration. Here, we report on timeliness of RV uptake, compare cumulative RV coverage to age 12 months with DTPa, and assess factors associated with receipt of RV among Aboriginal and non-Aboriginal children.

**Methods:** Birth records for 681,456 children born in two Australian states in 2007–2012 were probabilistically linked to national immunisation records. We assessed on-time coverage (defined as receipt of vaccine dose between 4 days prior to scheduled date and the recommended upper limit) for RV and compared this to diphtheria-tetanus-pertussis (DTPa) vaccine. Logistic regression modelling was used to assess independent determinants of receipt of RV.

**Results:** Compared to non-Aboriginal infants, on-time RV coverage was lower for all doses among Aboriginal infants. Post the upper age limit of RV dose2, DTPa dose2 coverage increased by 9–16% to  $\geq 90\%$ , whereas RV coverage remained around 77% (Aboriginal) and 85% (non-Aboriginal). Compared to first-born children, the adjusted odds of receiving  $\geq 1$  RV dose if born to a mother with  $\geq 3$  previous births was 0.30 (95%CI: 0.27–0.34) among Aboriginal, and 0.53 (95%CI: 0.51–0.55) among non-Aboriginal children. Prematurity ( $<33$  weeks), low birthweight ( $<1500$  g), maternal age  $<20$  years, maternal smoking during pregnancy and living in a disadvantaged area were independently associated with decreased vaccine uptake.

**Conclusions:** Aboriginal children are at greater risk of rotavirus disease than non-Aboriginal children and delayed vaccine receipt is substantially higher. Although specific programs targeting groups at risk of delayed vaccination might improve RV coverage, relaxation of upper age restrictions is most readily implementable, and its overall risk-benefit should be evaluated.

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**Abbreviations:** AIR, Australian Immunisation Register; DTPa, diphtheria-tetanus-acellular pertussis vaccine; NICU, neonatal intensive care units; NIP, National Immunisation Program; NSW, New South Wales; RV, Rotavirus vaccine; RV1, monovalent human rotavirus vaccine; RV5, pentavalent bovine-human re-assortment rotavirus vaccine; WA, Western Australia.

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## 1. Introduction

Immunisation is one of the most effective public health measures for prevention of childhood morbidity and mortality [1]. Despite increasing vaccination coverage, there is marked variation in age-appropriate vaccination coverage worldwide, which increases the risk period for infection [2]. Also, delay in vaccination are of special importance in populations at higher risk of vaccine preventable diseases [3,4]. A number of factors (higher birth order, low maternal education, low socio-economic status, parental attitudes/knowledge towards vaccines, cultural preferences and the robustness of the health care system) have been associated with incomplete or delayed vaccination with combined diphtheria-tetanus-acellular pertussis (DTPa) vaccine [3,5]. Also, delayed and/or incomplete vaccination is more common among Indigenous children in high income countries [6–8]. For example, at 12 months of age, 91.3% of Australian non-Aboriginal children but only 79.3% of Australian Aboriginal children had received the third dose (scheduled at 6 months of age) of DTPa vaccine; and of these, on-time vaccination (within 30 days of the due date) was 76.7% among non-Aboriginal children compared to only 61.0% among Aboriginal children [7].

In Australia, two oral live attenuated rotavirus vaccines (RV), RV1 (monovalent human RV, Rotarix® – GlaxoSmithKline Biologicals) and RV5 (pentavalent bovine-human re-assortment vaccine, RotaTeq® – Merck & Co., Inc.) were included in the National Immunisation Program (NIP) in 2007, with all infants born from 1st May 2007 eligible for vaccination. RV1 is administered in a 2-dose schedule at 2 and 4 months of age and RV5 in a 3-dose schedule at 2, 4 and 6 months of age. To minimise the risk of intussusception, it was recommended that the first dose of RV is administered at age 6–14 weeks, with the maximum age for the last dose being 24 weeks for RV1 and 32 weeks for RV5 [9]. Rotavirus immunisation programs differed, with New South Wales (NSW) using only RV1, while Western Australia (WA) initially used RV1 but changed to RV5 in May 2009. From July 2017, only RV1 has been used in all Australian jurisdictions.

Uptake of RV by 12 months of age has been consistently lower than other vaccines with the same administration schedule (e.g. DTPa) [10], but RV coverage by dose prior to 12 months of age has not been assessed. Also, information about the impact of the restricted upper age limit for RV administration on uptake is sparse [11]. Using data from a population-level cohort of children born in NSW and WA with individual-level birth and perinatal data linked to their immunisation records, we aimed to report on timeliness of RV uptake among Aboriginal and non-Aboriginal children, compare cumulative RV coverage to age 12 months with DTPa, and assess factors associated with receipt of RV.

## 2. Methods

### 2.1. Study design and study setting

We conducted a retrospective cohort study using record linkage of administrative health datasets whereby immunisation records for RV were probabilistically linked to birth and perinatal records for a cohort of children born in NSW and WA. This study was conducted as part of a larger study of childhood vaccines administered through the NIP in Australia – the full details of which are provided elsewhere [12].

### 2.2. Study population and data sources

To reflect the introduction of RV in the NIP, the cohort for this study comprised all singleton infants live-born in NSW and WA

between May 2007 and December 2012. The study cohort was identified through the perinatal data collections and the Birth and Death Registries in both states [12]. Along with socio-demographic information, the perinatal dataset also includes maternal medical and obstetric history, details of labour and delivery, characteristics of the child at birth and infant birth outcomes as recorded by the attending midwife or physician. Only those infants who had records in both the perinatal and birth registry datasets were included in the study.

The Australian Immunisation Register (AIR), formerly known as the Australian Childhood Immunisation Register, is a national register that records immunisation data, including immunisation date, type and dose of vaccine given to any individual; this is sent to the AIR by the immunisation provider. Further details on how the AIR records were probabilistically linked to the cohort (by the Australian Institute of Health and Welfare) and cleaned have been provided elsewhere [12]. We identified immunisation records, up to December 2013, for RV (RV1 and RV5) and DTPa vaccines included in the NIP. Immunisation records that did not link to the infants in the birth cohort and infants whose immunisation date preceded their date of birth were excluded (Fig. 1).

### 2.3. Time windows for on-time vaccine receipt

The time window for each on-time receipt of the vaccine dose was based on the recommended immunisation schedule [9]. While the recommended upper age limit was adhered to in each dose window, a '4-day grace period' [13] was incorporated into the start date of each dose window. Thus, for RV1, the first on-time dose window was from 39 days to 104 days and the second was from 67 days to 174 days. For RV5, the first on-time dose window was from 39 days to 90 days, the second from 67 days to 230 days and the third was from 95 days to 230 days. Vaccination coverage by 12 months of age was assessed based on the 'last dose assumption', whereby if the last dose of a vaccine that requires more than one dose to complete the series is recorded then the child is deemed to be fully immunised for that vaccine irrespective of whether or not the previous dose(s) were recorded [14].

### 2.4. Variables of interest

Parental and infant demographic factors and perinatal factors considered to be associated with poor adherence with immunisation schedules and with rotavirus infection were examined [3,15–17]. Parental risk factors included maternal age, paternal age, mother's place of birth, maternal smoking during pregnancy, number of previous pregnancies (as proxy for parity), mode of delivery, socio-economic status and remoteness of residence (see [Supplementary Table 1](#)).

Infant risk factors included Aboriginal and/or Torres Strait Islander (hereafter referred to as Aboriginal) status of the infant; this was identified using an algorithm that combined the recorded Aboriginal status for the infant on all the available linked datasets in the study, as described previously [18]. Other infant-related risk factors included sex, state of birth, gestational age, birth weight, Apgar score at 5 min, year of birth, season of birth and whether hospitalized <6 weeks after birth.

### 2.5. Statistical analysis

For each scheduled dose, the proportion of infants with an on-time vaccine was calculated using the number of infants with a vaccine dose recorded within the dose window (as described above) as the numerator, and the total number of infants in the

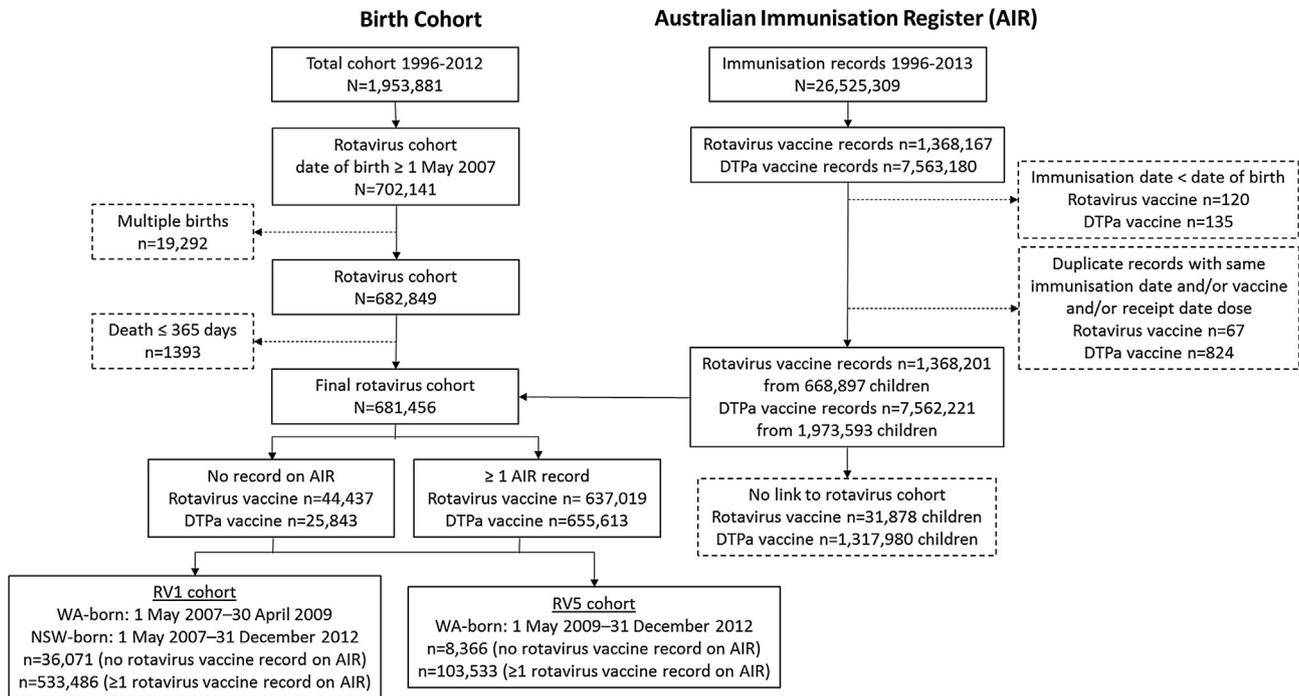


Fig. 1. Flow chart showing the derivation of the study cohort and their immunisation records.

cohort eligible for vaccination at the end of that dose window as the denominator. Infants who died before the end of the dose window for each dose were excluded. Since coverage was also assessed at 12 months of age, infants who had a record for death before their first birthday were excluded for all analyses. Coverage estimates by population sub-group for each scheduled dose were calculated separately for Aboriginal and non-Aboriginal infants. For all analyses relating to RV5 dose 3 including coverage estimates, the cohort was restricted to only WA births from 1st Jan 2010 onwards (Fig. 1).

To compare the timing of DTPa and RV, the cumulative vaccination coverage up to 365 days after birth was calculated for the 2nd and 3rd doses of each vaccine. Multivariable logistic regression modelling was used to obtain adjusted odds ratios (aOR) with 95% confidence intervals (CI) for the association between the parental/ infant factors and (a) receipt of at least one dose of any RV  $\geq$  39 days of age (not restricted to on-time doses) and (b) receipt of all doses (considered to be fully immunised) of the vaccine assessed at 12 months. Only variables (potential risk factors) with a p-value  $\leq$  0.2 in univariate analyses were included in the multivariable model. Aboriginal and non-Aboriginal infants were assessed separately. All analyses were conducted using Stata (version 13.1).

## 2.6. Ethical approvals

Ethical approvals were received from the State and National Health Ethics Committees, WA and NSW Aboriginal Health Ethics Committees and the Australian Institute of Health and Welfare Ethics Committee. The assembled linked dataset was accessed through the Secure Unified Research Environment [19].

## 3. Results

The cohort for RV coverage analysis consisted of 681,456 births, (Fig. 1) of whom 34,450 (5.1%) were recorded as being Aboriginal. Of the cohort, 637,019 (93.4%) had at least one record for RV on the

AIR and 636,718 of these infants had received  $\geq$  1 dose of RV by 12 months of age (Table 1). Less than 1% ( $n = 2,596$ ) of the vaccinated infants received RV before the recommended age of 39 days (Table 1). Of the 484,302 infants who had a record for RV1 as their second dose, 10,831 (1.8%) received their dose beyond the recommended upper age limit of 174 days; and of the 115,223 infants who had a record for RV5 as their second or third dose, 4969 (5.0%) received it beyond the recommended upper age limit of 230 days (Table 1). Approximately 89% of the 515,070 infants who received only RV1 and 81% of the 108,456 infants who received only RV5 had completed the full vaccine series.

### 3.1. On-time dose uptake

Among non-Aboriginal infants, on-time RV uptake has remained consistent since 2008 (around 89% for dose 1 and 86% for dose 2). Among Aboriginal infants on-time coverage showed a steady increase over the study period to 86% for dose 1 and 80% for dose 2 in 2012 (Fig. 2; Table 2). Vaccine uptake for the first dose was higher than subsequent doses among both Aboriginal and non-Aboriginal infants. Vaccine uptake among Aboriginal infants was lower than among non-Aboriginal infants for all doses of the vaccine and there was an increase in this disparity for each subsequent dose of the vaccine – the absolute difference in the proportion vaccinated between non-Aboriginal and Aboriginal infants was 5.9% (95% CI: 4.9–6.9) for dose 1, 10.7% (95% CI: 9.7–11.6) for dose 2 and 24.0% (95% CI: 22.0–26.1) for dose 3 (Table 2).

Infants with a birthweight of  $<$ 1500 g, followed by pre-term infants with gestational age of  $<$ 33 weeks, had the lowest on-time vaccine uptake for all doses among both Aboriginal and non-Aboriginal infants (Table 3). Varying levels of on-time vaccine uptake were observed within each population sub-group and the level of variation differed between Aboriginal and non-Aboriginal infants. For example, among Aboriginal infants, 82.1% of first-born infants had an on-time dose 2 recorded compared to only 63.2% of infants born to mothers who had 3 or more previous pregnancies; only 66.0% of infants with gestational age  $<$ 33 weeks had

**Table 1**  
Characteristics of children who received  $\geq 1$  dose of rotavirus vaccine (2007–2012).

	Aboriginal N = 34,450 n (%)	Non-Aboriginal N = 647,004 n (%)	Total population N = 681,456 n (%)
Received $\geq 1$ dose of any rotavirus vaccine (by 12 months of age)	30,705 (89.1)	606,013 (93.7)	636,718 (93.4)
Total number of doses received			
Only RV1	<b>N = 24,063</b>	<b>N = 491,007</b>	<b>N = 515,070</b>
1	3,959 (16.5)	54,643 (11.1)	58,602 (11.4)
2	20,079 (83.4)	435,776 (88.8)	455,855 (88.5)
>2 doses	25 (0.1)	588 (0.1)	613 (0.1)
Only RV5	<b>N = 5,807</b>	<b>N = 102,649</b>	<b>N = 108,456</b>
1	749 (12.9)	4,504 (4.4)	5,253 (4.8)
2	1,324 (22.8)	13,564 (13.2)	14,888 (13.7)
3	3,734 (64.3)	84,580 (82.4)	88,314 (81.4)
>3 doses	–	<5 (<0.1)	<5 (<0.1)
Mixed series	<b>N = 873</b>	<b>N = 12,620</b>	<b>N = 13,493</b>
1	–	–	–
2	410 (47.0)	5,427 (43.0)	5,837 (43.3)
3	463 (53.0)	7,178 (56.9)	7,641 (56.63)
>3 doses	0	15 (0.1%)	15 (0.1)
Age < 39 days at dose 1	106 (0.3)	2,490 (0.4)	2,596 (0.4)
Age > 174 days for RV1*	840 (3.1)	9,991 (1.8)	10,831 (1.8)
Age > 230 days for RV5#	435 (9.8)	4534 (4.8)	4,969 (5.0)
Median age in days (IQR)			
RV1			
Dose 1	57 (47–65)	56 (46–62)	56 (46–62)
Dose 2	126 (120–138)	124 (120–132)	125 (120–132)
RV5			
Dose 1	63 (58–72)	60 (56–64)	60 (56–65)
Dose 2	130 (122–145)	125 (120–133)	125 (120–133)
Dose 3	193 (184–208)	189 (183–201)	189 (183–201)

Note: Numbers for RV1 and RV5 include children born in both New South Wales and Western Australia (2007–2012).

\* Denominator: total population = 592,737, Aboriginal = 26816, non-Aboriginal = 565,921.

# denominator: total population = 99973, Aboriginal = 4430, non-Aboriginal = 9554.

received dose 2 on time compared to 75.8% in infants born full-term. Among non-Aboriginal infants, on-time vaccine uptake for dose 2 was 88.0% in first-born infants and only 77.9% in infants born to mothers with 3 or more previous births; and on-time dose 2 vaccine uptake was only 77.0% in infants born <33 weeks gestation compared to 85.6% coverage in infants born full-term. Also, similar to the overall estimates, vaccine uptake in the different population sub-groups for both Aboriginal and non-Aboriginal infants showed decreasing trends with each subsequent dose of the vaccine – for example, among Aboriginal infants born to mothers who have had 3 or more previous births, there was a 10% point difference between those receiving dose 1 and dose 2 (Table 3). The only exception to this was infants with gestational age <33 weeks or birthweight <1500 g whose on-time vaccine uptake was similar or higher for the second dose than the first dose.

### 3.2. Comparison of dose timing for DTPa and RV vaccines

Among infants who had a record for receipt of the 2nd dose of DTPa and/or RV, approximately 75% of Aboriginal and 85% of non-Aboriginal infants had received their second dose by 174 days (recommended upper age limit for RV1; Fig. 3). DTPa coverage reached 91% in Aboriginal (increase of 16%) and 94% in non-Aboriginal infants (increase of 9%) for dose 2 by 12 months of age whereas for RV, only an additional 3% of both Aboriginal and non-Aboriginal infants received dose 2 between 174 days and 12 months of age (Fig. 3).

There were similar findings for dose 3 among WA-born infants, where RV5 was used, with 54% Aboriginal and 78% non-Aboriginal infants receiving dose 3 of DTPa and/or RV by 230 days, the recommended upper age limit for RV5. From 230 days to 12 months, an

additional 2% of Aboriginal and non-Aboriginal infants received a third dose of RV5, while 21% Aboriginal) and 9% non-Aboriginal infants received a third dose of DTPa (Fig. 3).

### 3.3. Determinants of vaccine uptake

Adjusting for all factors, Aboriginal infants had a 36% (95% CI: 34–39) lower odds of receiving at least one dose of any RV ( $\geq 39$  days after birth but not restricted to on-time doses) compared to non-Aboriginal infants (data not shown). In the adjusted model for Aboriginal infants, vaccine uptake steadily increased over time with an aOR of 2.22 (95% CI: 1.94–2.53) among infants born in 2012 as compared to those born in 2007 (Table 4). The strongest association with vaccine uptake was birth order; infants born to mothers with 3 or more previous pregnancies had 70% (95% CI: 66–73%) lower odds of receiving at least 1 dose compared to first-born infants. Infants born to teenage parents had an approximately 30% lower odds of receiving at least 1 dose compared to infants born to parents aged  $\geq 35$  years, and infants born with a birthweight of <1500 g had 54% lower odds of receiving at least 1 dose than infants of normal birthweight. Aboriginal infants living in WA were less likely to receive at least 1 dose of RV than infants living in NSW (aOR 0.63; 95% CI: 0.58–0.68).

Vaccine uptake increased over the study period among non-Aboriginal infants, with the greatest increase occurring in the 2 years (2008–2009) after vaccine introduction (Table 4). Non-Aboriginal infants living in WA had lower odds of receiving at least 1 dose than those living in NSW (aOR 0.85; 95% CI: 0.83, 0.87). Among non-Aboriginal infants, birthweight had the strongest association with vaccine uptake; infants with birthweight <1500 g had 64% lower odds of receiving at least 1 dose than those of normal

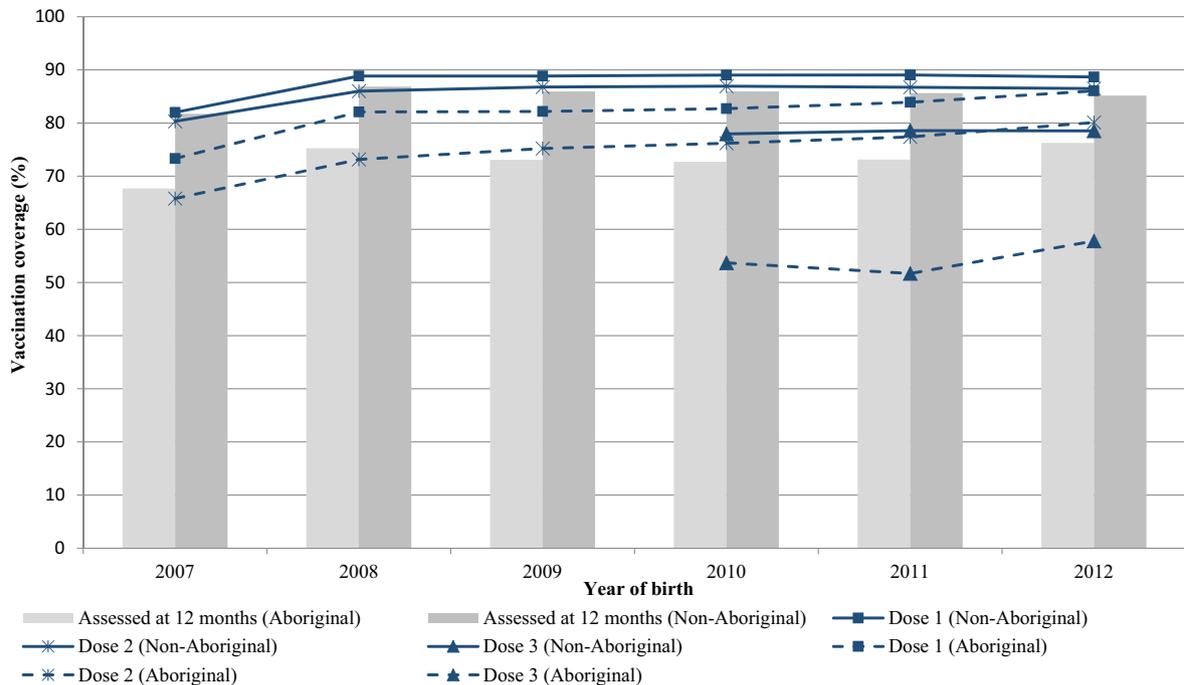


Fig. 2. Proportion of Aboriginal and non-Aboriginal infants with on-time receipt of rotavirus vaccine by dose and year and coverage\* assessed at 12 months.

Table 2  
Number and proportion of children who received rotavirus vaccine by dose number and assessed at 12 months.

Scheduled dose	Aboriginal N = 34,450		Non-Aboriginal N = 647,004		Total population N = 681,454	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
<b>On-time doses</b>						
Dose 1	28,318	82.2 (81.8, 82.6)	569,847	88.1 (88.0, 88.2)	598,165	87.8 (87.7, 87.9)
Dose 2	25,893	75.2 (74.7, 75.6)	555,440	85.9 (85.8, 85.9)	581,333	85.3 (85.2, 85.4)
Dose 3*	2,998	54.3 (53.0, 55.7)	67,917	78.4 (78.1, 78.6)	70,915	76.9 (76.6, 77.2)
<b>Assessed at 12 months<sup>‡</sup></b>	25,259	73.3 (72.9, 73.8)	552,532	85.4 (85.3, 85.5)	577,791	84.8 (84.7, 84.9)

\* For Dose 3 – cohort is only births in WA (2010–2012). Denominators: non-Aboriginal N = 86,678; Aboriginal N = 5518; total population N = 92,196.  
<sup>‡</sup> Deemed to be fully vaccinated (2nd dose of RV1 or 3rd dose of RV5) as assessed at 12 months of age.

birthweight. A trend of decreasing odds of receiving at least 1 dose was observed with increased birth order and decreasing parental age (Table 4). Non-Aboriginal infants born at <33 weeks gestation had 27% lower odds of receiving at least 1 dose than infants born at ≥37 weeks. Non-Aboriginal infants of overseas-born mothers had a 43% (95% CI: 42–45%) lower odds of receiving at least 1 dose than infants of Australian-born mothers.

Using the last dose assumption, the proportion of infants deemed ‘fully immunised’ by 12 months for RV was 73.3% among Aboriginal infants and 85.4% among non-Aboriginal infants (Table 2). Factors associated with being fully immunised at 12 months (versus no doses) were broadly similar to the factors associated with receipt of at least one dose of RV (Supplementary Table 2).

#### 4. Discussion

Rotavirus is the most common pathogen associated with severe gastroenteritis and is a leading cause of childhood morbidity and mortality worldwide [20,21]. Our estimates for any (93.5%) and full (85.4% among non-Aboriginal children and 73.3% among Aboriginal children) immunisation coverage are comparable to previous Australian estimates and to estimates from other countries with universally funded immunisation programs, and substantially

higher than in countries without funded programs [10,22,23]. Although initiation and completion of rotavirus vaccination in Aboriginal children increased over the course of the study period, there still exists a significant disparity in their coverage compared to non-Aboriginal children. Considering that receipt of the full dose series of the RV has been shown to afford the highest protection against severe rotavirus infection, this disparity is of concern and may contribute to persistently higher burden of gastroenteritis-related hospitalisation among Aboriginal children [17,24].

The upper age restriction for RV is the main driver of lower coverage than other vaccines with a similar infant schedule, such as DTPa (>90% at age 12 months) as observed elsewhere [11,22]. In our study, post the upper age limit of RV1 vaccine, 2-dose DTPa coverage increased a further 9–16%, while 2-dose RV coverage only increased by 3%. The differential between DTPa and RV coverage was most evident among Aboriginal children. This underlines the importance of improving the timeliness of all vaccines through appropriate promotional strategies and/or vaccine reminders. Strict age restrictions have been imposed for initiating and completing rotavirus vaccination because of concerns about vaccine-associated intussusception; post-marketing studies have confirmed a small increase in risk of intussusception following RV administration [25,26]. In Australia, the incidence of intussusception among children aged <2 years was estimated to be 0.54

**Table 3**  
Proportion of Aboriginal and non-Aboriginal infants with receipt of on-time rotavirus vaccine by dose and population sub-groups.

Subgroup	ABORIGINAL						NON-ABORIGINAL					
	Dose 1		Dose 2		Dose 3 (only RV5)		Dose 1		Dose 2		Dose 3 (only RV5)	
	n	%	n	%	n	%	n	%	n	%	n	%
<b>Mother's age (years)</b>												
≥35	2,633	80.3	2,417	73.7	251	55.5	135,229	88.0	132,083	86.0	14,679	78.1
30–34	4,297	82.1	3,929	75.1	430	54.8	190,793	88.8	187,137	87.1	22,848	80.4
25–29	6,929	82.1	6,389	75.7	733	54.3	157,333	88.1	153,411	85.9	19,745	78.8
20–24	9,139	82.9	8,348	75.8	960	54.2	71,338	86.7	68,370	83.1	8,795	74.4
<20	5,320	82.1	4,810	74.2	624	53.8	15,154	85.6	14,439	81.6	1,850	71.2
<b>Father's age (years)</b>												
≥35	4,905	82.7	4,516	76.2	487	58.4	220,747	88.2	215,787	86.2	25,063	78.7
30–34	4,817	82.9	4,445	76.5	448	54.9	181,248	88.8	177,674	87.0	21,940	80.3
25–29	6,721	84.2	6,213	77.9	724	58.4	112,371	88.0	109,101	85.4	14,162	77.9
20–24	6,692	82.6	6,084	75.1	766	54.2	38,216	86.8	36,472	82.9	4,994	74.2
<20	2,489	81.7	2,268	74.5	285	51.7	5,155	85.0	4,929	81.3	638	69.4
<b>Delivery method</b>												
Vaginal	18,971	81.3	17,229	73.8	1,894	52.3	317,333	87.2	307,105	84.4	32,494	74.8
Instrumental	2,247	85.6	2,125	81.0	287	59.5	72,471	89.4	71,769	88.6	11,332	84.4
Caesarean	7,091	83.7	6,531	77.1	817	57.8	179,943	89.0	176,472	87.3	24,091	80.8
<b>Maternal smoking during pregnancy</b>												
No	16,762	85.0	15,686	79.5	1,989	60.3	515,505	88.4	504,432	86.5	62,494	79.5
Yes	11,535	78.5	10,187	69.3	1,009	45.5	53,545	85.5	50,213	80.2	5,423	67.2
<b>Number of previous pregnancies</b>												
0	10,326	86.7	9,776	82.1	941	63.5	232,114	88.7	230,328	88.0	23,544	85.2
1	7,267	84.2	6,721	77.9	760	56.3	191,725	89.0	186,470	86.6	21,743	79.6
2	4,591	82.4	4,120	73.9	474	55.8	88,565	87.6	84,969	84.0	12,158	75.3
3 or more	6,115	73.5	5,258	63.2	823	44.8	57,043	83.4	53,283	77.9	10,472	67.2
<b>Birth Season</b>												
Spring	7,262	82.2	6,798	77.0	732	55.6	152,257	88.4	148,802	86.4	17,084	78.9
Winter	7,595	81.3	6,839	73.2	757	54.5	152,483	87.8	148,081	85.3	16,981	78.5
Autumn	6,945	82.6	6,300	74.9	759	51.7	136,848	87.5	133,865	85.6	17,592	78.3
Summer	6,516	82.9	5,956	75.7	750	55.8	128,259	88.7	124,692	86.2	16,260	77.7
<b>Birthweight group (gms)</b>												
<1500	220	60.4	222	61.0	36	44.4	1910	60.0	2,358	74.1	308	66.2
1500–2499	2,004	75.7	1,768	66.8	203	43.5	19,423	86.1	18,926	83.9	2,360	74.8
2500–3499	15,072	81.6	13,680	74.1	1616	52.7	295,853	88.2	288,373	86.0	36,186	78.8
3500–4499	10,522	84.9	9,773	78.9	1106	60.2	242,969	88.4	236,435	86.1	28,173	78.4
≥4500	496	85.8	447	77.3	37	53.6	9,578	87.7	9,232	84.5	890	73.6
<b>Gestational age (weeks)</b>												
<33	415	66.5	412	66.0	58	45.0	3,789	69.3	4,208	77.0	526	70.0
33–34	504	74.5	455	67.2	50	43.5	5,802	86.6	5,680	84.8	776	76.2
35–36	1,573	78.7	1,407	70.4	188	47.0	20,518	87.9	19,882	85.2	2,850	75.6
≥37	25,817	82.9	23,613	75.8	2,702	55.5	539,687	88.3	525,623	86.0	63,761	78.6
<b>Socio-economic index*</b>												
91–100% (least disadv)	343	88.6	317	81.9	36	65.5	53,543	88.2	52,660	86.8	5,361	79.1
76–90%	1,217	85.8	1,138	80.3	158	65.0	91,304	88.9	89,695	87.3	11,526	81.3
26–75%	10,471	84.3	9,740	78.4	958	56.8	275,294	88.3	268,553	86.2	32,702	78.2
11–25%	6,459	82.0	5,894	74.8	683	52.9	83,224	87.6	80,539	84.8	9,602	76.5
0–10% (most disadv)	8,600	80.0	7,665	71.3	846	50.4	49,614	87.1	47,360	83.1	4,166	74.4
<b>Remoteness index</b>												
Major Cities	11,932	82.0	10,964	75.4	1080	52.2	434,733	88.0	424,378	85.9	47,152	78.6
Inner Regional	7,787	84.5	7,047	76.4	304	61.3	82,286	89.0	79,570	86.1	8,381	77.6
Outer Regional	4,650	83.9	4,219	76.1	486	54.4	29,641	87.6	28,641	84.7	4,807	76.1
Remote	1,888	78.8	1,733	72.3	488	57.5	5,981	89.8	5,893	88.5	2,343	81.3
Very Remote	972	73.3	908	68.4	323	50.1	1,529	88.9	1,507	87.6	674	75.4
<b>Mother Country of Birth</b>												
Australia	27,553	82.2	25,185	75.2	2,886	54.0	379,262	89.4	369,344	87.1	42,868	79.0
Overseas	742	81.3	686	75.1	112	63.3	188,844	85.5	184,362	83.4	25,045	77.2
<b>Infant State of birth</b>												
WA	7,952	75.2	7329	69.3	2,998	54.3	138,808	87.2	136,871	85.9	67,917	78.4
NSW	20,366	85.3	18,564	77.8	–	–	431,039	88.4	418,569	85.8	–	–

Note: 95% confidence intervals were very tight/narrow and hence not reported.

per 100,000 child-years before the immunisation program [27]. An additional 5.6 cases of intussusception are estimated to occur per 100,000 vaccinated infants, with the severity of intussusception episodes among vaccinated infants no different from that among

unvaccinated infants [25,28]. In light of the minimal increased risk of intussusception following vaccination and the fact that intussusception is rarely fatal in Australia, relaxing the upper age restrictions for RV, as recommended by WHO for countries with high

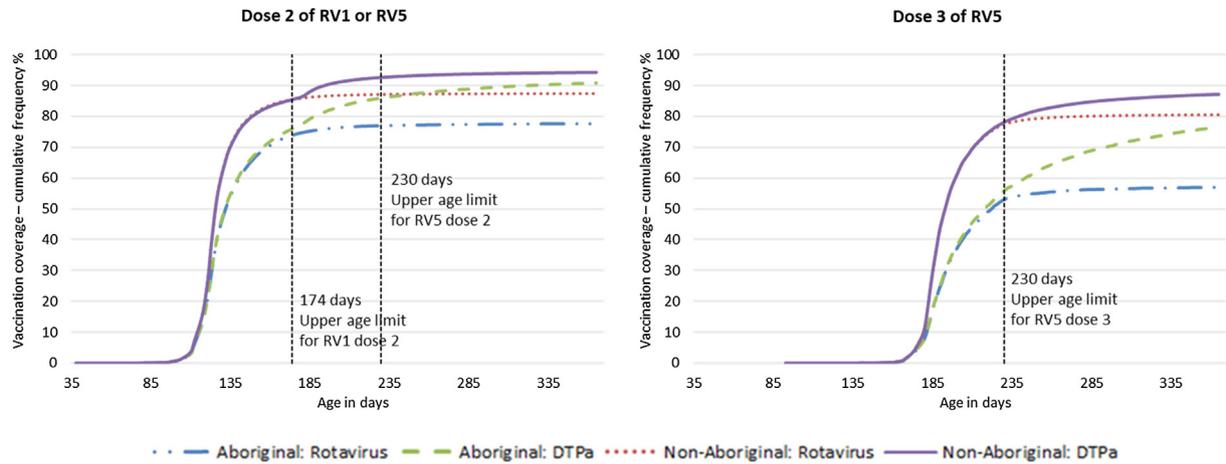


Fig. 3. Cumulative vaccine dose coverage by age in days for dose 2 and dose 3 of rotavirus\* and DTPa vaccines.

Table 4

Adjusted odds ratios (aOR) of receipt of  $\geq 1$  dose of rotavirus vaccine\* among Aboriginal and non-Aboriginal infants (2007–2012).

Characteristics	Aboriginal			Non-aboriginal		
	n (%)	Univariate OR	Adjusted aOR	n (%)	Univariate OR	Adjusted aOR
<b>Year of birth</b>						
2007	3,119 (78.5)	Ref	Ref	66,855 (87.9)	Ref	Ref
2008	5,166 (85.3)	1.59	1.61	105,465 (92.7)	1.74	1.84
2009	5,330 (86.6)	1.77	1.83	106,932 (93.3)	1.90	2.02
2010	5,449 (87.3)	1.88	1.78	106,624 (93.2)	1.89	2.00
2011	5,425 (88.0)	2.01	1.99	107,663 (93.2)	1.88	1.92
2012	5,256 (89.7)	2.39	2.22	104,783 (93.0)	1.82	1.90
<b>Mother's age (years)</b>						
$\geq 35$	2,778 (84.7)	Ref	Ref	141,773 (92.3)	Ref	Ref
30–34	4,513 (86.3)	1.13	1.07	200,177 (93.2)	1.14	1.08
25–29	7,295 (86.5)	1.16	1.04	165,235 (92.5)	1.03	0.99
20–24	9,582 (86.9)	1.20	0.92	75,092 (91.2)	0.87	0.88
<20	5,577 (86.1)	1.11	0.71	16,045 (90.7)	0.81	0.84
<b>Father's age (years)</b>						
$\geq 35$	5,141 (86.7)	Ref	Ref	231,644 (92.6)	Ref	Ref
30–34	5,077 (87.4)	1.06	0.93	190,242 (93.2)	1.10	1.00
25–29	7,030 (88.1)	1.13	0.92	117,956 (92.4)	0.97	0.90
20–24	7,015 (86.6)	0.99	0.75	40,186 (91.3)	0.85	0.82
<20	2,620 (86.0)	0.94	0.70	5471 (90.2)	0.74	0.70
<b>Delivery method</b>						
Caesarean	7,441 (87.8)	Ref	Ref	188,898 (93.5)	Ref	Ref
Instrumentation	2,359 (89.9)	1.23	0.92	75,934 (93.7)	1.04	0.99
Vaginal	19,935 (85.4)	0.81	0.88	333,384 (91.7)	0.77	0.81
<b>Maternal smoking during pregnancy</b>						
No	17,562 (89.1)	Ref	Ref	540,983 (92.7)	Ref	Ref
Yes	12,161 (82.7)	0.59	0.71	56,484 (90.2)	0.72	0.82
<b>Number of previous pregnancies</b>						
0	10,795 (90.7)	Ref	Ref	243,862 (93.2)	Ref	Ref
1	7,637 (88.5)	0.79	0.72	200,991 (93.3)	1.02	0.99
2	4,809 (86.3)	0.65	0.54	92,953 (91.9)	0.83	0.80
3 or more	6,485 (78.0)	0.37	0.30	60,097 (87.9)	0.53	0.53
<b>Birth Season</b>						
Spring	7,671 (86.9)	Ref	Ref	159,806 (92.7)	Ref	Ref
Winter	7,965 (85.3)	0.88	0.85	160,045 (92.2)	0.92	0.92
Autumn	7,282 (86.6)	0.98	0.88	144,152 (92.1)	0.92	0.84
Summer	6,827 (86.8)	1.00	0.94	134,319 (92.9)	1.02	0.95
<b>Birthweight group (gms)</b>						
<1500	268 (73.6)	0.35	0.46	2,590 (81.4)	0.34	0.46
1500–2499	2,130 (80.4)	0.51	0.70	20,556 (91.1)	0.80	0.90
2500–3499	15,804 (85.6)	0.74	0.86	310,355 (92.5)	0.97	1.02
3500–4499	11,023 (89.0)	Ref	Ref	254,662 (92.7)	Ref	Ref
$\geq 4500$	516 (89.3)	1.03	0.88	10,035 (91.9)	0.89	0.88

(continued on next page)

Table 4 (continued)

Characteristics	Aboriginal					Non-aboriginal				
	n (%)	Univariate		Adjusted		n (%)	Univariate		Adjusted	
		OR	95% CI	aOR	95% CI		OR	95% CI	aOR	95% CI
<b>Gestational age (weeks)</b>										
≥37	27,058 (86.9)	Ref		Ref		565,943 (92.6)	Ref		Ref	
35–36	1,667 (83.4)	0.76	0.67, 0.85	1.04	0.89, 1.22	21,578 (92.4)	0.98	0.93, 1.03	1.04	0.98, 1.10
33–34	534 (78.9)	0.56	0.47, 0.68	0.89	0.69, 1.15	6,123 (91.4)	0.86	0.79, 0.93	0.96	0.86, 1.06
<33	486 (77.9)	0.53	0.44, 0.64	0.89	0.63, 1.25	4,622 (84.6)	0.44	0.41, 0.47	0.73	0.64, 0.84
<b>Socio-economic index*</b>										
91–100% (least disadv)	355 (91.7)	Ref		Ref		56,409 (93.0)	Ref		Ref	
76–90%	1,276 (90.0)	0.81	0.54, 1.21	0.83	0.53, 1.30	95,917 (93.4)	1.07	1.03, 1.11	1.09	1.04, 1.13
26–75%	11,029 (88.7)	0.71	0.49, 1.02	0.81	0.54, 1.22	288,898 (92.7)	0.96	0.93, 0.99	1.07	1.03, 1.10
11–25%	6,758 (85.8)	0.54	0.38, 0.78	0.70	0.46, 1.06	87,393 (92.0)	0.87	0.84, 0.91	1.09	1.04, 1.13
0–10% (most disadv)	9,028 (84.0)	0.47	0.33, 0.68	0.66	0.43, 0.99	52,076 (91.4)	0.81	0.77, 0.84	1.09	1.04, 1.14
<b>Remoteness index</b>										
Major Cities	12,623 (86.8)	Ref		Ref		457,644 (92.7)	Ref		Ref	
Inner Regional	8,085 (87.7)	1.09	1.00, 1.16	0.99	0.91, 1.08	85,726 (92.8)	1.01	0.98, 1.04	0.94	0.91, 0.97
Outer Regional	4,855 (87.6)	1.08	0.98, 1.19	1.27	1.14, 1.41	30,799 (91.1)	0.80	0.77, 0.83	0.79	0.76, 0.82
Remote	1,988 (82.9)	0.74	0.66, 0.83	1.05	0.92, 1.20	6,207 (93.2)	1.09	0.99, 1.20	1.14	1.03, 1.26
Very Remote	1,044 (78.7)	0.56	0.49, 0.65	1.03	0.86, 1.22	1,592 (92.6)	0.98	0.82, 1.18	1.07	0.89, 1.29
<b>Mother Country of Birth</b>										
Australia	28,939 (86.4)	Ref		Ref		397,134 (93.7)	Ref		Ref	
Overseas	781 (85.5)	0.93	0.77, 1.13	0.65	0.53, 0.80	199,336 (90.2)	0.62	0.61, 0.64	0.57	0.55, 0.58
<b>Infant State of birth</b>										
NSW	21,249 (89.0)	Ref		Ref		453,022 (92.9)	Ref		Ref	
WA	8,496 (80.4)	0.51	0.48, 0.54	0.63	0.58, 0.68	145,300 (91.2)	0.80	0.78, 0.81	0.85	0.83, 0.87

\* Receipt of at least one dose of rotavirus vaccine (RV1 or RV5) ≥ 39 days after birth but not restricted to on-time doses.

burden, should be considered as a strategy for improving vaccine uptake [29].

Along with uptake, timeliness is recognised as a key measure of the impact of childhood vaccination programs since the aim of these programs is to not only afford protection to all children against vaccine-preventable infections but also to minimise the time when they are more vulnerable to these infections. To our knowledge, this is the first study to look at RV coverage at recommended time points among various population sub-groups and identify patterns and predictors of uptake of RV available through a nation-wide funded immunisation program. Although 95% of those immunised with RV received their dose within the recommended upper/lower age limit, on-time vaccine uptake estimates were as low as 45% in some population subgroups in our study with uptake being lower for Aboriginal infants across all of the population subgroups.

The key population subgroups associated with the lowest on-time vaccine uptake and the lowest odds of receiving the RV in our study were very preterm and with very low birthweight infants who are at increased risk of rotavirus gastroenteritis and its ensuing complications [15,17]. Though the safety and effectiveness of RV have been demonstrated in preterm and low birthweight infants, age-eligible infants in neonatal intensive care units (NICUs) may not be vaccinated due to residual concerns over safety or due to potential transmission of live vaccine strains in the NICU [30]. As these infants are typically inpatients for at least two months, they are often no longer age-eligible at hospital discharge [31]. Relaxation of upper age restrictions for RV and earlier administration of rotavirus vaccine in nurseries would improve uptake in this vulnerable group.

Higher birth order, younger maternal age, maternal smoking during pregnancy, mode of delivery and birth in WA were other factors associated with low vaccine uptake in both Aboriginal and non-Aboriginal children, factors previously identified as associated with decreased and/or delayed vaccine uptake [3,6,7,32].

Lower socio-economic status was associated with increased vaccine uptake among non-Aboriginal children, but this association was not significant in Aboriginal children after adjusting for other factors. Implementation of appropriately targeted vaccination strategies like active 'precall' and 'recall' among the groups we identified merits further evaluation.

The strength of our study is the use of a large comprehensive population-based cohort, with near complete demographic data, linked to an immunisation register that captures the individual immunisation records of 99% of the target population [33]. Also, since we have reliable data on Aboriginal status, we were able to compare coverage and determinants of coverage between Aboriginal and non-Aboriginal children. Our study, however, does have some limitations. We lacked information on other factors associated with immunisation uptake, including religious beliefs, breastfeeding and parental attitudes. Our vaccination coverage estimates could be underestimated by about 3%, because records have not been transmitted to the immunisation register by providers for a number of reasons including technical problems with the automated software packages [34].

In conclusion, we have identified several population subgroups with suboptimal RV uptake among whom measures including recall and reminders as well as changes in practice among neonatal nurseries could be beneficial. However, relaxation of the upper age restriction for rotavirus vaccine doses is the most readily implementable initiative and evaluating the impact of this change on disease prevention and adverse outcomes such as intussusception is essential.

#### 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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## Author contributions

Dr Fathima carried out the analysis and drafted the initial manuscript. Drs Gidding, Snelling, Blyth, Liu, Moore and Profs de Klerk and McIntyre conceptualized and designed the study, contributed to the interpretation of the results and critically reviewed and revised the manuscript. Dr Sheridan assisted with data cleaning and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2019.08.013>.

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