



**Australian Government**  
**Department of Health**

# COMMUNICABLE DISEASES INTELLIGENCE

2019 Volume 43

<https://doi.org/10.33321/cdi.2019.43.49>

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# Communicable Diseases Intelligence

ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

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# Gaps in maternal influenza vaccine uptake in Northern Territory: A need for a year-round influenza vaccination campaign

Priya Darshene Janagaraj, Pari Shanmuga Raman Gurusamy and Rosalind Webby

## Abstract

### Introduction

Maternal influenza vaccination was introduced in 2010 due to the high morbidity and mortality associated with influenza in pregnancy. The aim of this study was to assess the maternal influenza vaccination uptake in Northern Territory public hospitals and identify gaps to improve uptake.

### Methods

Birth data from Northern Territory (NT) public hospitals obtained from the Perinatal Register for deliveries in 2016 were merged with vaccination records from the NT immunisation register.

### Results

There were 3,392 viable pregnancies in NT public hospitals in 2016 with 45.6% vaccination coverage against influenza. There was a statistically significant difference in coverage with 68.5% in Indigenous vs 31.7% in non-Indigenous deliveries ( $p < 0.001$ ), yielding an odds ratio of 4.67 (95% CI 4.02, 5.42) for maternal influenza vaccination across Indigenous status. Influenza vaccination coverage for preterm births (<37 weeks) was low especially in non-Indigenous mothers at 27.2% vs 65.05% in Indigenous mothers ( $p < 0.001$ ). A distinct immunisation administration pattern was noted for 2016 with 58.9% of vaccinations occurring between April and June regardless of Indigenous status and maternal gestational age. This correlated with the annual influenza immunisation campaign by the NT and Commonwealth.

### Conclusion

A year-round maternal influenza vaccination campaign is crucial to avoid missed opportunities and increase vaccination protection for mother and baby. Antenatal influenza vaccination campaign with health care workers education and increasing patient awareness should continue throughout the year.

Keywords: Maternal, pregnancy, influenza, Aboriginal, vaccination, Northern Territory, uptake, gaps

## Introduction

Maternal immunisation has a crucial role in protecting mothers and their newborn infants from influenza infection.<sup>1-3</sup> Influenza is a viral illness causing millions of hospitalisations and deaths globally.<sup>4</sup> Influenza infection in pregnancy, especially in the 3rd trimester, is associated with increased morbidity and mortality.<sup>5-7</sup> Pregnant women are at increased risk of influenza complications due to the physiological changes of pregnancy, including immune suppression.<sup>8,9</sup> The only protection against influenza is the yearly seasonal influenza vaccine. In addition to protecting the mothers, the vaccine protects their newborn infants via antenatal in-utero-transplacental transfer of antibodies.<sup>2,10,11</sup>

The World Health Organization (WHO) designated pregnant women as a priority group for influenza vaccination after the 2009 influenza pandemic, which resulted in severe influenza in pregnant women.<sup>12</sup> Maternal influenza vaccination was introduced in Australia in 2010 on the National Immunisation Program (NIP).<sup>13</sup> Vaccination is currently available to pregnant women at any gestational age (GA) and is endorsed by The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).<sup>13</sup> Additionally, the NIP provides an annual influenza vaccination for all Indigenous people 15 years and above.<sup>13</sup> However, despite well-founded recommendations and a good safety profile, the uptake of influenza vaccination in pregnancy remains sub-optimal.<sup>i</sup>

The aim of this study is to assess the coverage of maternal influenza vaccination in the Northern Territory (NT) and identify factors impacting coverage.

## Methods

### Population and Setting

NT has a population of 244,048, with the highest proportion of Indigenous residents in any Australian state at 25%.<sup>14</sup> There are approximately 4,000 births annually in NT.<sup>15</sup>

### Data Collection

We retrospectively reviewed the influenza immunisation coverage rates for all births in NT public hospitals in 2016. Birth data was obtained from the Northern Territory Perinatal Register (NTPR), which records all births in the NT. Influenza immunisation records were obtained from January 2015 to December 2017 for women aged between 13 to 55 years old from the NT immunisation register (NTIR), a state-based immunisation register. Data on postpartum vaccination up to 6 months post-delivery were also collected to analyse timing of vaccination. The mother's name, age, hospital record number (HRN), Indigenous status, suburb of residency, date of delivery, place of delivery and GA at delivery were obtained from the perinatal register. These data were linked to the NTIR using a unique identifier (HRN) and cross checked manually to ensure data integrity. This allowed us to determine the vaccination status and timing of vaccine administration during pregnancy for each woman.

### Ethics Approval

The study design and access to registry data was approved by and registered with the Human Research Ethics Committee (HREC) of the NT Department of Health and Menzies School of Health Research (reference number 2015/2485). The proposal was also approved by the Central Australian HREC (reference number HREC-16-436).

### Definition for valid immunisation

As per the current RANZCOG and Australian Immunisation guidelines, a valid influenza

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i Since April 2019, influenza vaccine is funded for all Indigenous Australians above the age of 6 months under the National Immunisation Program

vaccination status in pregnancy was defined as receiving 1 dose of inactivated influenza vaccine at any GA. Influenza vaccine was available in 2016 from April. Mothers who delivered from January to May 2016 were considered to have had a valid immunisation if they had received an influenza vaccine for the 2015 flu season, even if it was prior to their conception. Current guidelines do not recommend a second dose of influenza vaccination in pregnancy and therefore mothers who received 2015 influenza vaccine whilst pregnant were included. Post-partum vaccination was defined as an immunisation during the first 180 days following delivery, for women who did not receive a valid antenatal or pre-conception immunisation. Post-partum vaccination was not included in the coverage data but was used to assess trend in uptake, as there has been increasing evidence on the benefit of maternal vaccination in protecting infants up to 6 months of age via immunoglobulin A (IgA) transfer through breastmilk.<sup>ii</sup>

## Statistical Analysis

Data were entered into SPSS v.25 and Microsoft Excel, and both were used to perform the statistical analysis.

Vaccinations received were coded into three categories based on time of vaccination related to pregnancy: pre-conception, during pregnancy and postpartum. Pre-conception vaccination is a valid 2015 influenza season vaccination (prior to conception) without a vaccine during pregnancy for mothers who delivered in January to May 2016, prior to active roll out of 2016 immunisation in late April. Mothers who did not receive any vaccination during pregnancy but received both 2015 and 2016 influenza vaccination were coded as the 'pre-conception and postpartum vaccination' group.

Residential location, obtained from the perinatal registry, was coded into the 4 regions of Darwin, Katherine, East Arnhem and Alice Springs. Births delivered in Barkly were coded as Alice Springs due to small sample size. Indigenous status was coded as Indigenous or non-Indigenous. Maternal age was grouped as under 25 years, 25–34 years, and 35 years and above.

Preterm births were defined as live births before 37 weeks of GA and sub-classified as extreme preterm (less than 28 weeks), very preterm (28 to 31 weeks) and moderate to late preterm (32 to 36 weeks) based on WHO classification.

Urban locality was defined as births in Alice Springs and Darwin with all other births classified as remote locality. The linkage of data obtained from the NTPR and NTIR allowed for calculation of maternal age at the time of delivery and gestational age of pregnancy during administration of the influenza vaccine.

Mean maternal age and gestational age at delivery in the vaccinated cohort were compared using two-sided *t*-tests assuming equal variances between Indigenous and non-Indigenous mothers. Coverage between Indigenous and non-Indigenous mothers was compared using a chi-squared test.

Socio-demographic factors affecting uptake of maternal influenza vaccination were explored using a binary logistic regression model. Individual binary logistic regression models were used for each variable and the data were controlled for Indigenous status to reduce the confounding effect. Adjusted odds ratios (AOR) and 95 % confidence intervals (CI) were calculated. A *p*-value of <0.05 was considered statistically significant.

Significance of the logistic regression model was tested using the chi-squared test.

## Results

In 2016, there were 3,392 viable births (GA $\geq$ 24), including 40 twin births, in NT public hospitals.

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ii Since April 2019, ATAGI has recommended for women who received an influenza vaccine late in the 2018 influenza season to revaccinate if the 2019 influenza vaccine becomes available before the end of pregnancy

Baseline socio-demographic characteristics of the mothers who delivered in 2016 are summarised in Table 1.

### Indigenous Status

1,547 (45.7%) women received valid influenza vaccine as per the current guidelines. In 2015, 39.3% of pregnant women received influenza vaccination. Vaccination coverage was significantly higher in Indigenous mothers (68.5%) than in non-Indigenous mothers (31.7%) with  $p < 0.001$ . There was a significant increase in coverage in the non-Indigenous mothers from 23.2% in 2015 to 31.7% in 2016 ( $p < 0.001$ ).<sup>16</sup>

There was an increase in vaccine coverage in both Indigenous and non-Indigenous mothers with the inclusion of pre-conception vaccination as a valid vaccine dose for babies born between January to April 2016. The coverage increased from 56.51% to 68.46% in Indigenous women in comparison to 30.03% to 31.73% in non-Indigenous women.

### Maternal Age

The highest vaccination coverage was noted in mothers below 25 years at 56.1%, followed by 42.7% for mothers aged between 25–34 years and 37.5% for mothers 35 years and above.

The mean age of vaccinated Indigenous mothers was 25.87 years and of vaccinated non-Indigenous mothers was 30.54 years ( $p < 0.001$  using a two-sided test of equal variance).

### Preterm Delivery

In 2016 there were 322 preterm births in NT, representing 9.4% of all births. The difference in the rates of preterm births in Indigenous mothers (14.5%) and non-Indigenous mothers (6.44%) was significant with  $p < 0.001$  using a chi-squared test. The influenza vaccination coverage was significantly higher in Indigenous mothers (65.05%) than in non-Indigenous mothers (27.20%) with preterm delivery,  $p < 0.001$ .

There were 19 postpartum vaccinations of mothers who delivered preterm infants, with 73.68% uptake in Indigenous women.

### Plurality

There were 40 women who birthed twins in 2016 in the NT, constituting 1.2% of all births. Influenza coverage in this cohort was 37.5% ( $n = 15$ ), comprising coverage of 52.63% in Indigenous mothers and 26.32% in non-Indigenous mothers.

### Timing of Influenza Vaccination

The majority of pregnant women vaccinated for influenza received their vaccine during April to June 2016. The peak uptake from April 2016 to June 2016 was consistent irrespective of the gestational age or Indigenous status (Figure 1). A much lower uptake of maternal influenza vaccination was noted during the peak 2016 Australian influenza season (July to August 2016) as shown in Figure 2. Despite higher uptake of maternal influenza vaccine between April to June 2016, percentages of infants born to vaccinated mothers, each month, were consistent through the year 2016 (Figure 3).

### Postpartum Vaccination

A total of 194 mothers received postpartum influenza vaccination only. Of these postpartum vaccinations, 116 (59.7%) were administered to Indigenous mothers. This further increases the coverage in Indigenous mothers protecting postpartum women and infants with 77.5% ( $n = 993$ ) vs 35.4% ( $n = 748$ ) in non-Indigenous women.

### Factors affecting maternal influenza vaccination uptake

Initial logistic regression analysis revealed that remote location was associated with lower maternal influenza coverage (OR=1.46), but after adjusting for Indigenous status, remote location was not a significant predictor (AOR=0.93, 95% CI 0.74, 1.18,  $p = 0.591$ ). Higher maternal age was associated with lower maternal influenza cover-

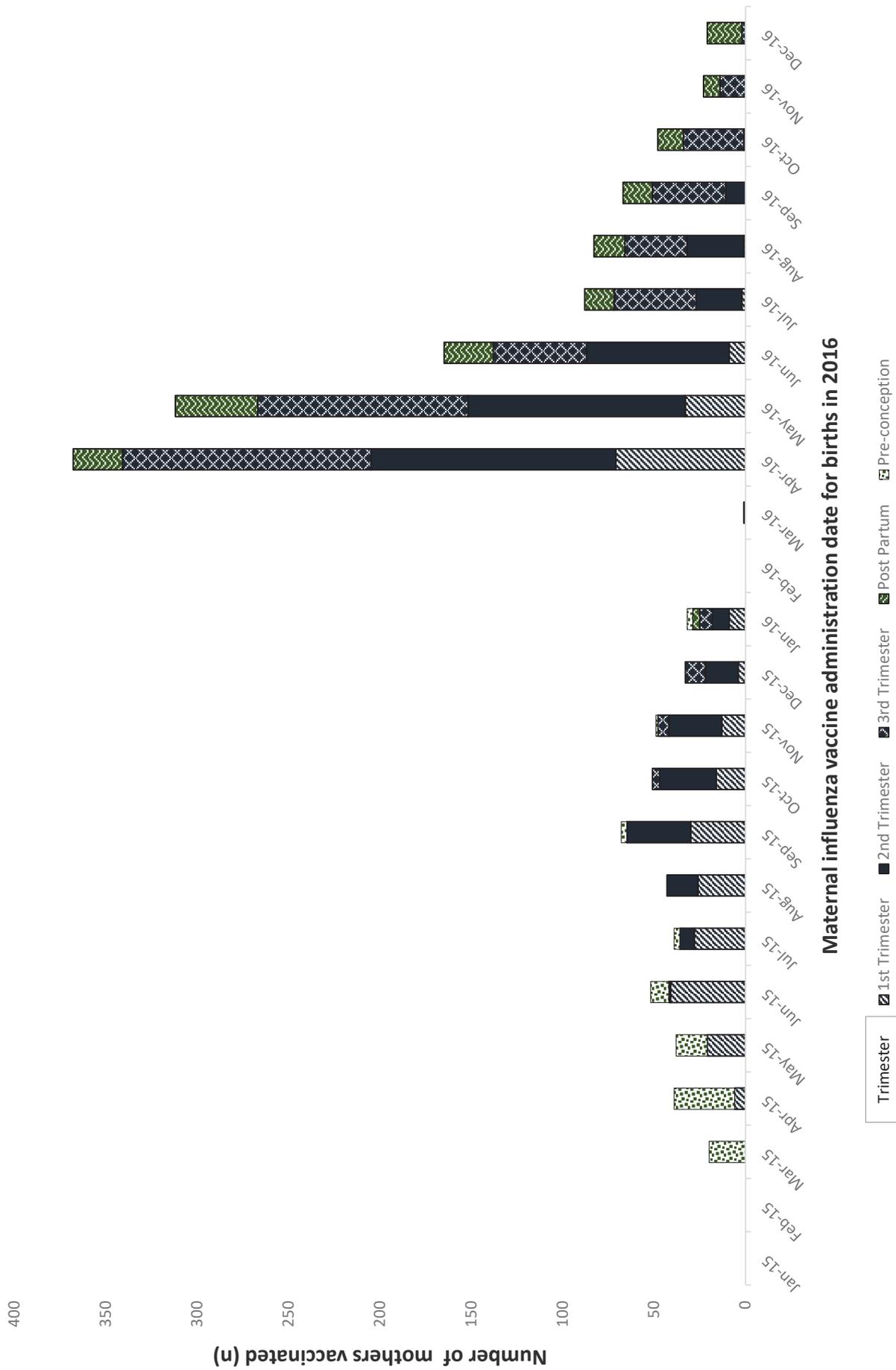
Table 1. Baseline characteristics of births in Northern Territory in 2016 based on maternal influenza vaccination status.

	Vaccinated		Unvaccinated	
	n	%	n	%
Total participants	1,547	45.6	1,845	54.4
<b>Indigenous Status</b>				
Indigenous (n=1,281)	877	68.5	404	31.5
Non Indigenous (n=2,111)	670	31.7	1,441	68.3
GA <sup>a</sup> mean (SD)	38.47 (2.15)	-	38.64 (2.11)	-
<b>Maternal Age</b>				
Median (IQR)	27.77 (8.61)	-	29.57 (7.62)	-
Below 25 years (n=935)	525	56.1	410	43.9
25-34 years (n=1,948)	831	42.7	1,117	57.3
35 years and above (n=509)	191	37.5	318	62.5
<b>Region</b>				
Alice Springs (n=820)	433	52.7	387	47.3
East Arnhem (n=131)	96	73.3	35	26.7
Katherine (n=240)	104	43.3	136	56.7
Darwin (n=2,201)	914	41.5	1,287	58.5
<b>Timing of influenza vaccination</b>				
1 <sup>st</sup> trimester (GA ≤ 12 <sup>(6)</sup> )	312	20.2	-	-
2 <sup>nd</sup> trimester (13 <sup>(6)</sup> ≤ GA ≤ 27 <sup>(6)</sup> )	548	35.4	-	-
3 <sup>rd</sup> trimester (GA ≥ 28 <sup>(6)</sup> )	498	32.2	-	-
Pre-conception	90	5.8	-	-
Pre-conception and Post-Partum	99	6.4	-	-

	Vaccinated		Unvaccinated	
	n	%	n	%
Twin Births (n=40)	15		25	
<b>Indigenous Status</b>				
Indigenous (n=19)	10	52.6	9	47.4
Non Indigenous (n=21)	5	23.8	16	76.2
<b>Maternal age</b>				
Below 25 years (n=11)	5	45.5	6	54.5
25-34 years (n=23)	10	43.5	13	56.5
35 years and above (n=6)	0	0	6	100
<b>Region</b>				
Alice Springs (n=9)	5	55.6	4	44.4
Darwin (n=31)	10	32.3	21	67.7
<b>Preterm Births (&lt;37 weeks)</b>				
Extreme: GA < 28 <sup>+0</sup> (n=23)	11	47.8	12	52.2
Very: GA 28 <sup>+0</sup> - 31 <sup>+6</sup> (n=53)	24	54.7	29	45.3
Moderate: GA 32 <sup>+0</sup> - 36 <sup>+6</sup> (n=246)	123	50.0	123	50.0
<b>Indigenous Status</b>				
Indigenous (n=186)	121	65.1	65	34.9
Non Indigenous (n=136)	37	27.2	99	72.8

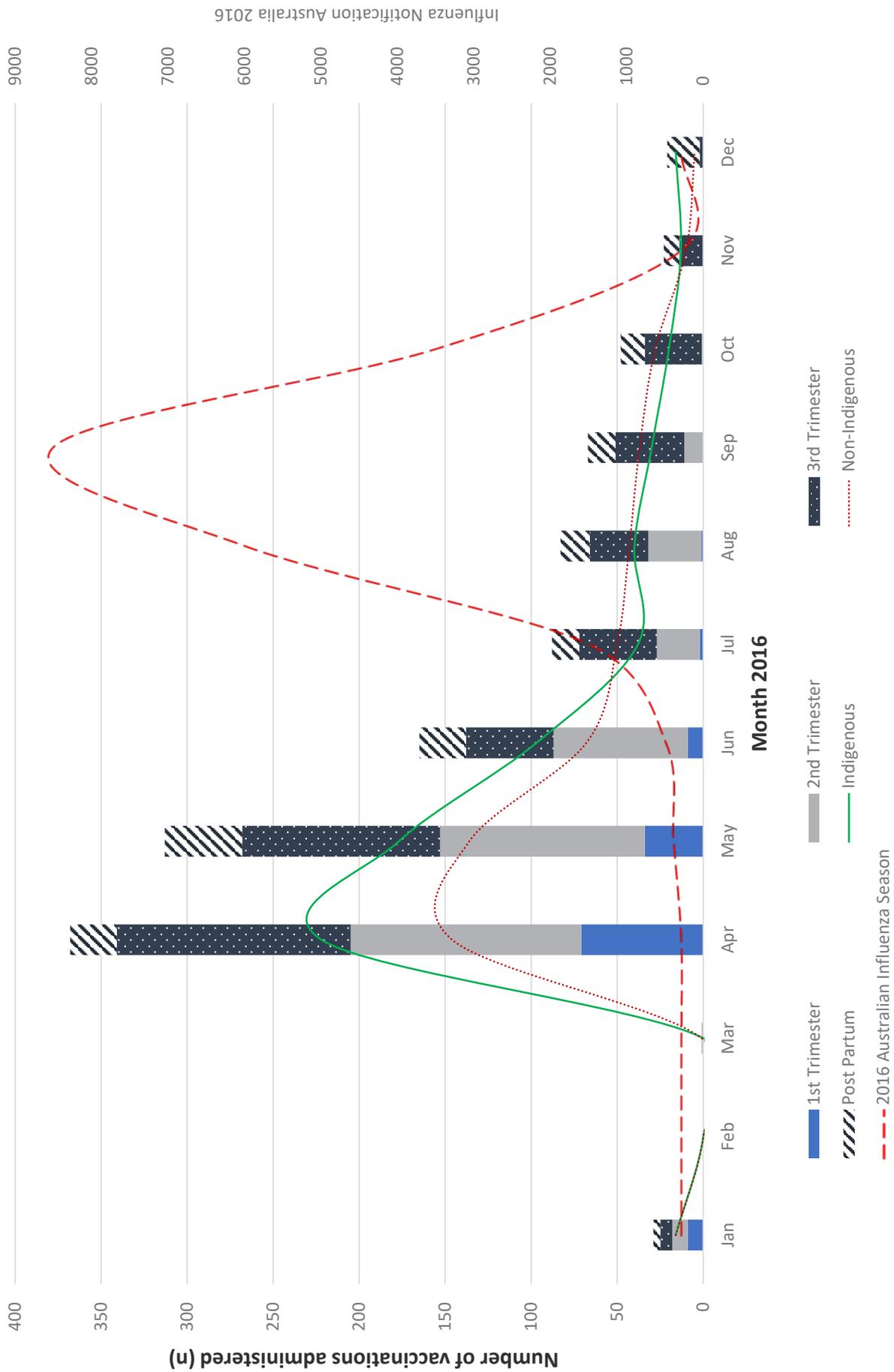
a GA: Gestational age

Figure 1. Maternal influenza vaccination uptake based on gestational age for mothers delivered in 2016 in Northern Territory<sup>a</sup>



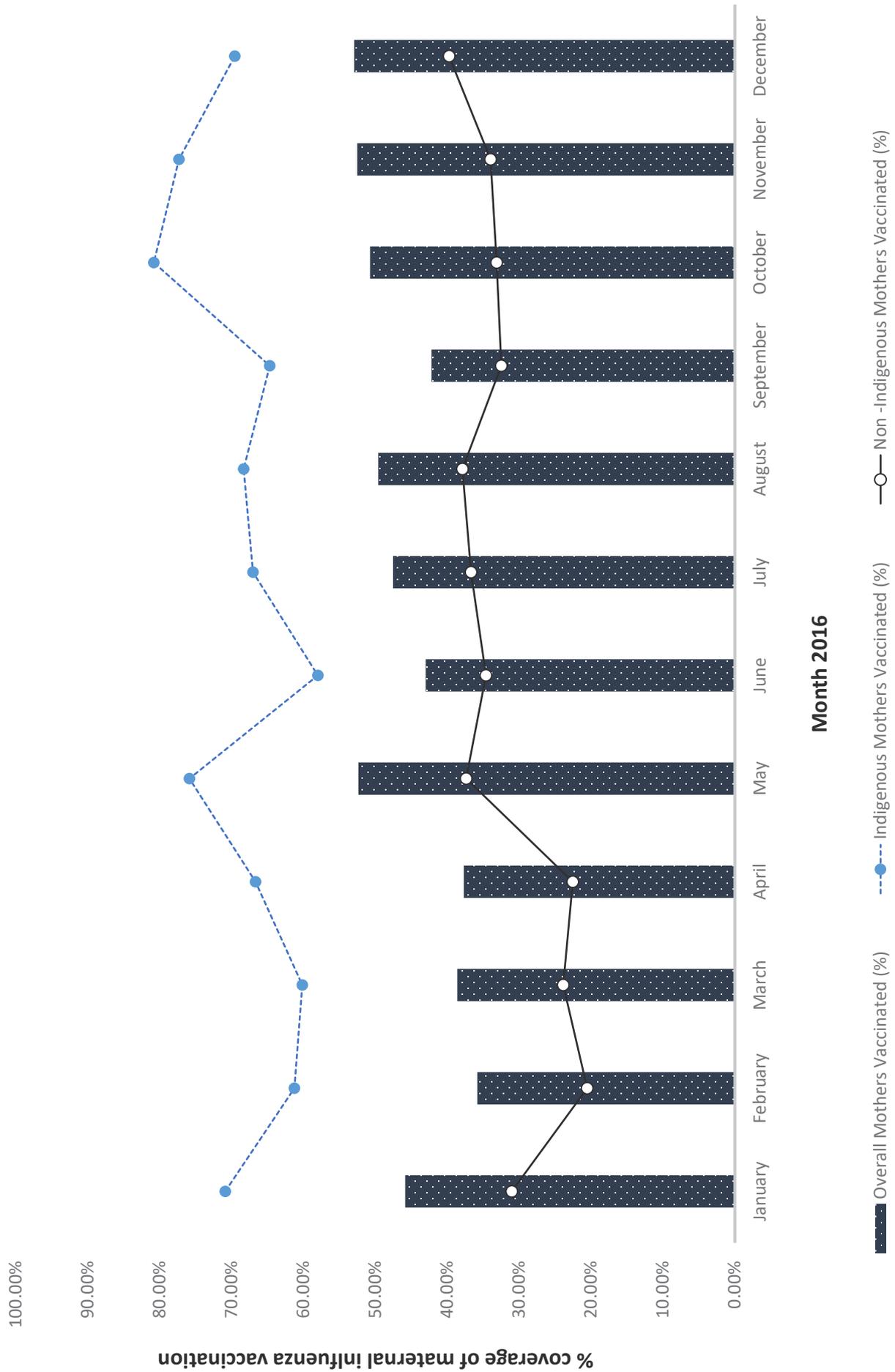
<sup>a</sup> Mothers who received both 2015 and 2016 influenza vaccine were not plotted to reduce data duplication.

Figure 2: Trend in influenza vaccination uptake in pregnancy based on Indigenous status and gestational age during 2016 Influenza season<sup>a</sup>



<sup>a</sup> Data for 2016 Influenza season was plotted from the 2016 Influenza Surveillance report from CDNA.<sup>17</sup>

Figure 3. Trend of babies born in 2016, based on month of birth, in Northern Territory to mothers vaccinated against influenza



age, similarly adjusting for Indigenous status was not a significant predictor for vaccination uptake (AOR=1.09, 95% CI 0.88, 1.34,  $p=0.402$ ). Potential socio-demographic factors that may influence influenza vaccination are presented in Table 2.

The major predictors of increased maternal influenza coverage were Indigenous status and month of vaccination (during April to June) (see Figure 1).

## Discussion

In Australia, the influenza season typically occurs from May to October, except in the tropical region, where circulating influenza is recorded year-round.<sup>18</sup> In the tropical region, a bimodal influenza season is seen, with peaks during December to January and July to August.<sup>18</sup> Each year, there is a range of seasonal inactivated influenza vaccines available for antenatal administration, as part of the NIP. The overall maternal influenza vaccination coverage in our cohort was 45.61%. However, there was a significant disparity in the distribution of the coverage among the Indigenous mothers (68.5%) and non-Indigenous mothers (31.7%). The odds ratio for Indigenous versus non-Indigenous mothers receiving influenza vaccine was 4.67 (95% CI 4.02, 5.42,  $p<0.001$ ). This is in contrast to previously published literature that noted that Indigenous mothers had lower coverage of influenza vaccination.<sup>19</sup> Higher rate of vaccina-

tion uptake in Indigenous mothers is likely to be linked to the annual free influenza vaccine offered to all Indigenous Australians from age 15 years old, regardless of their pregnancy status. The higher uptake in Indigenous mothers persisted in preterm births (65.05%) and multiple births (52.63%).

Amongst mothers with valid immunisation status, 20.2% ( $n=312$ ) received the influenza vaccine in the first trimester, 35.4% ( $n=548$ ) during the second trimester and 32.2% ( $n=498$ ) in the third trimester.

In our study, factors associated with an increased uptake of maternal influenza vaccination (unadjusted for Indigenous status) were maternal age below 35 years, birthing at remote locations and birthing at Central Australian hospitals. The preponderance of vaccinations between April and June 2016 (58.9% of the 2016 total,  $p<0.001$ ) strongly suggests the timing of presentation to a doctor was also a factor, with the probability of vaccination uptake influenced by concurrence with the national influenza campaign and/or greater vaccine availability at this time. Plurality and infant gestational age at delivery were not independent predictors of maternal influenza uptake.

Despite the differences in coverage based on Indigenous status and trimester of vaccination, our study identified timing of influenza vaccine administration was similar for all subgroups

**Table 2. Binary logistical regression of categorical predictors of maternal influenza vaccination**

Predictors of maternal influenza uptake <sup>a</sup>	OR	95% CI	AOR	95%CI	<i>p</i> -value <sup>b</sup>
Indigenous vs non -Indigenous mothers	4.67	4.02, 5.42	4.67	4.02, 5.42	<0.001
Singleton vs plurality	1.40	0.73, 2.67	1.74	0.87, 3.48	0.108
Term vs preterm deliveries	0.85	0.68, 1.07	1.22	0.95, 1.57	0.112
Maternal age below 35 vs 35 years old and above	1.47	1.21, 1.79	1.09	0.88, 1.34	0.402
Remote location vs urban location	1.46	1.17, 1.81	0.93	0.74, 1.18	0.591
Vaccination between April to June 2016	2.67	1.95, 3.66	2.78	2.02, 3.82	<0.001
Central vs Top End birthing hospital	1.46	1.25, 1.71	1.05	0.89, 1.25	0.510

a OR = odds ratio; CI = confidence interval. Adjusted odds ratio (AOR) was only adjusted for Indigenous status.

b *p*-value calculated on AOR using Wald chi-squared test.

(pre-conception; during pregnancy; postpartum; and pre-conception and postpartum). This is consistent for all gestational ages, irrespective of Indigenous status.

After adjusting for Indigenous status, the odds ratio for 2016-vaccinated pregnant women receiving influenza vaccine between April and June 2016, against receiving it during the year's other quarters, was 2.78 (95% CI 2.02, 3.82;  $p < 0.001$ ). This correlates with the annual influenza immunisation campaign by NT and the Australian Government. While the hypothesis of Indigenous Australians (including the subset of antenatal population) receiving the vaccine during the annual flu vaccination campaign seems a valid explanation for this trend, the data also highlight a similar peak in the uptake of influenza vaccine in non-Indigenous women from April to June 2016 (Figure 2).

In 2016, the Australian flu season was between July to October with a peak between late August and mid-September. The distinct pattern of the uptake regardless of Indigenous status highlights a low uptake during peak influenza season and an opportunity to continue to promote influenza vaccine. During April and May, there are intense promotional campaigns by governmental and non-governmental sectors promoting the influenza vaccine on various platforms including social media and electronic media such as radio and television. Health clinics and pharmacies offer walk-in vaccination clinics from April to May when the vaccines are rolled out and this has likely led to promotion of vaccine at this time. However, the vaccination drive is not sustained throughout the influenza season with dwindling advertisements later in the year. We postulate that this likely influenced the uptake of influenza vaccination in the maternal population in our cohort.

An analysis of the 2017 influenza season from NT highlighted that pregnancy remained a significant risk factor for influenza with an odds ratio of 3.5 (CI 2.46, 4.90,  $p < 0.001$ ).<sup>20</sup> There needs to be a targeted approach to address concerns of

non-Indigenous mothers and increase vaccination uptake in these women due to the morbidity associated with influenza.

It is prudent to promote early influenza vaccination uptake, but it is crucial to continue to encourage influenza vaccination throughout the influenza season, especially for the maternal population.

In addition to protecting the mother, recent studies have shown great benefit from antenatal and postpartum influenza vaccination.<sup>1-3,10,21</sup> A recent randomised control trial showed maternal immunisation protects newborn infants from hospitalisation associated with lower respiratory tract infections during the first 6 months with a vaccine efficacy of 43.1%.<sup>1</sup> There is transplacental transfer of influenza antibodies and breast milk transfer of immunoglobulin A and G protecting newborns up to 6 months of life.<sup>11,22</sup> As the influenza vaccine only becomes available for use from 6 months of age onwards, infants rely on passive transfer maternal immunity for protection against influenza. Therefore, the most effective way to protect newborns from the adverse effects of influenza infection is through maternal vaccination.

However, as the exact timing of pregnancy cannot be accurately predicted, vaccination should be offered all year round with sustained vaccination health promotion campaigns specifically targeting the maternal population. The high uptake of the vaccine from April to June in both Indigenous and non-Indigenous women suggests acceptance towards the vaccine when linked to nationwide influenza health promotion campaigns.

Studies have shown that provider recommendation is a strong predictor of uptake for maternal immunisation.<sup>23-26</sup> As there is an extremely high uptake during the initial roll out of the vaccine, we postulate that there is a waning of vaccine recommendation by health care providers during the second half of each year. The lack of uptake shows the need for greater awareness by healthcare providers on the availability of influ-

enza vaccine and on the benefits of influenza vaccine for the maternal population, protecting the mother and baby throughout the year.

A nationwide year-round maternal immunisation campaign is essential to increase awareness. Education of healthcare workers on the availability of the influenza vaccine and the benefits to antenatal mothers beyond the pregnancy should be reinforced to ensure confidence in recommending influenza vaccine. Consistent recommendations from antenatal care providers are critical to improving influenza vaccine coverage in pregnant women. With the established safety of influenza vaccines, a year-round vaccination campaign is key to increase confidence in women and therefore improve uptake.<sup>1,27,28</sup>

### Strengths and limitations

A limitation in our study was the lack of data available from the private hospital in NT. In 2016 there were an estimated 550 births in the private hospital. There is a possibility that the inclusion of data of pregnant women who delivered in the private hospital may increase the coverage rate among non-Indigenous pregnant women. While this is feasible, the low coverage in non-Indigenous women delivering in the public hospitals in the NT needs to be addressed regardless. There may be missing data, not reflected in the NTIR, for non-Indigenous mothers that receive influenza vaccination as part of workplace vaccination campaigns.

All other antenatal influenza vaccination data from interstate and overseas have been based on surveys and a sampled cohort. Our study includes all pregnant women that delivered in the public hospitals in NT in 2016 with validated vaccination status, providing an accurate overview of the current behavioural pattern of maternal influenza uptake in the NT.

### Conclusion

A nationwide robust year-round maternal influenza vaccination campaign is required to promote the benefits of influenza vaccina-

tion to both mothers and babies. The timing of influenza vaccine in relation to the gestational age of the pregnancy correlates with the availability of the vaccine and influenza promotional campaign. There should be a greater emphasis on targeting non-Indigenous pregnant women in the NT. Healthcare providers should be aware of the availability of flu vaccine and should promote the vaccine all year round. Antenatal care providers, including midwives, have a key role in providing evidence-based recommendations to pregnant women with a need to encourage uptake throughout the year. A year-round promotional campaign may address the gaps in maternal influenza vaccination, reduce missed opportunities and increase uptake in non-Indigenous mothers.

### Acknowledgements

We acknowledge the Northern Territory Perinatal Register and Northern Territory Immunisation Register for their data contribution.

### Declarations

The datasets generated and analysed during the current study are not publicly available due identifiable patient data.

### Author contributions

PJ: Study concept and design, analysis or interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis.

PG: Analysis or interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis.

RW: Study concept and design, acquisition of data, analysis or interpretation of data, critical revision of the manuscript for important intellectual content.

PJ and PG are co-first authors.

Obtained funding: nil.

The authors declare that they have no competing interests.

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