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Antigen specific vaccine hesitancy in pregnancy

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ABSTRACT

Background: Vaccinations in pregnancy are recommended for the potential benefits of preventing severe pertussis disease in newborns and for preventing the impact of influenza on the pregnant woman, her foetus in utero and, the newborn in the first six months of life. Published data in Australia suggested that coverage rates were sub-optimal so the reasons for this were reviewed.
Methods: A cross-sectional survey of 1014 postnatal women, aged 18 years and older, who had given birth in the previous six months was undertaken on the Gold Coast in Queensland, Australia. Participants completed a brief questionnaire on provided smart tablets at public vaccination clinics or with a researcher by phone or via an on-line link.
Results: Just over 85% of survey respondents received a pertussis booster with many of those not receiving vaccine having had it in a recent pregnancy. Only 36.7% of respondents had an influenza vaccine in pregnancy with key barriers being belief in influenza vaccine, seasonality of parturition and a lack of recommendation from the attending obstetric carers.
Discussion: While maternal pertussis vaccine programs are a success, work needs to be done to improve the public perception of the risk benefit equation surrounding influenza vaccine in general, and particularly its use in pregnancy. Research is required into approaches to altering practitioner attitudes as well as how to alter public perceptions.

1. Background

Vaccinations in pregnancy are recommended for the potential benefits of preventing severe pertussis disease in newborns and for preventing the impact of influenza on the pregnant woman, her foetus in utero and, the newborn in the first six months of life [1,2].

Pertussis is a highly infectious respiratory disease associated with severe disease in very young children. It remains a challenging disease to control. Control of pertussis is problematic because immunity, whether from immunisation or infection, wanes over time, resulting in renewed susceptibility to infection, ongoing transmission and periodic epidemics in the community [3,4]. Immunity provided by individual early childhood vaccines is limited, and around three doses are required before young children are protected. Attempts to protect children through vaccinating families, the "cocoon strategy", have not been successful [5].

Influenza disease in pregnant women and in children under six months who are too young to be vaccinated, is also more severe with increased risk of hospitalisation in both groups [6,7]. The World Health Organisation Special Advisory Group of Experts looking at the effectiveness of vaccine response and the burden of disease decreed that pregnant women were the highest priority group to be immunised against influenza ahead even of those with chronic diseases and age-based indications [8].

The Australian Technical Advisory Group on Immunisation recommends pregnant women have both vaccines every pregnancy. As part of Queensland Health's Immunisation Program, both vaccines are provided free to all pregnant women.

International studies have not shown any safety signals in relation to use of either of these inactivated vaccines in pregnancy with respect to increased risk of adverse pregnancy outcomes (such as stillbirth, foetal distress or low birth weight) [9–11].

Pregnancy vaccine coverage studies in Australia and anecdotal local information on the Gold Coast suggested that despite the availability of national recommendations and free vaccine, coverage rates were less than optimal, and some women were unaware of the need for vaccine [12,13].

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Acceptance of vaccine in general is high in Australia with coverage rates for the broad paediatric program, including pertussis vaccines, being high at around 94% [14]. However, suboptimal coverage is seen for all groups recommended to access influenza vaccine due to their increased risk of severe outcomes.

Other studies on pregnancy vaccine uptake have identified concerns about the vaccine impact on the foetus, a lack of awareness of disease severity, a lack of provider support and difficulty accessing vaccine as important barriers to vaccine receipt [15].

Increasing vaccine hesitancy generally, leading to outbreaks of "old diseases" such as measles in many parts of the world [16], is not as prevalent in Australia and did not appear to be impacting on pregnancy vaccine uptake. In particular, the recent report linking spontaneous abortion in recipients of monovalent H1N1pdm09 pandemic vaccines attracted minimal coverage in Australia and was not thought likely to be a factor in influenza vaccine refusals [17].

As the antenatal influenza vaccine coverage was estimated to be about 23–27% [18,19] and the antenatal pertussis vaccine boosting program was a recent policy change, an intervention program was commenced involving education sessions for doctors, the production of videos for antenatal women and the use of fluorescent stickers on hand held pregnancy records (Fig. 1) to ensure that obstetric care givers were reminded of the importance of vaccine.

After this, a study was implemented to assess antenatal knowledge of disease importance, knowledge of availability and benefit of vaccine, and the factors that influenced women to accepting pertussis and influenza vaccination in pregnancy. The study results will be used to assist altered education strategies for expectant mothers and clinicians in future to improve vaccination uptakes.

1.1. Study objective

The objective of this study was to identify the vaccination status of mothers birthing in the previous six months and to determine the factors that influenced women to receive vaccines in pregnancy including provider behaviour and information, health belief models, access to vaccine and perception of risk benefit.

2. Materials and methods

A cross-sectional survey of postnatal women, aged 18 years and older, was undertaken at public vaccination clinics on the Gold Coast in Queensland, Australia with participants completing a brief ten minute questionnaire on provided smart tablets. Mothers could also complete the survey over the phone with a research assistant or on-line via a link forwarded to other respondents. The survey was conducted from April to October 2017.

Data collected was de-identified via the allocation of a unique, non-nominal identifier (letters and numbers). Some identifying data such as date of birth (month and year), hospital identifier (number) and date of delivery were collected. The questionnaire also gathered basic demographics, pregnancy number, gestation at birth, self-reported health status, pertussis and influenza immunisation history in pregnancy and the advice participants received during pregnancy and from whom. Recruitment continued for six months.

Women under the age of 18 years and those unable to comprehend a survey in English were excluded.

2.1. Ethics

Ethics approval was granted by the Gold Coast Hospital and Health Service ethics committee (Approval number GC/QGC/265). For patients delivering at a private hospital ethics approval was granted by Greenslopes Ethics committee (Approval Number 16/68).

2.2. Analysis

Power calculations based on previously reported immunisation coverage of 23% [18,19] with a study power of 80%, and probability of 0.05 for alpha, suggested a sample size of 277 would be required. With 6000 deliveries locally each year (3000 over a six month period), a projected 50% response rate and a 30% attrition rate over 1000 participants were expected.

Fig. 1. Flourescent reminder stickers used on pregnancy charts.

SPSS Inc statistical package (version 24) [20] was used to analyse the data. Descriptive analysis was used to describe the number and percentage of women who had vaccine. The differences between the vaccinated and unvaccinated groups in age, education, income, location of living, and presence of co-morbid conditions was analysed by Chi-Square test.

Variables including age, education, income, and disease history showing differences between the vaccinated and non-vaccinated groups at alpha level $p < 0.10$ were considered as potential confounding factors, and were subsequently entered into the stepwise logistic regression models assessing factors influencing vaccine uptake including antenatal knowledge of disease importance, knowledge of availability and benefit of vaccine, and the factors that influenced women to accepting pertussis and influenza vaccination in pregnancy. In the unadjusted regression model, confounding factors including age, education, income and disease history were not included, but they were controlled for in the adjusted regression model. Probability at alpha 0.05 level was stated as statistical significance.

3. Results

3.1. Recruitment

Different components of the study attracted different response rates. The Gold Coast public clinics were attended by 119 eligible mothers and of these 107 completed the questionnaire (90%). A further 1412 mothers were contactable via phone. Of these, 183 completed a survey at the time over the phone, and an additional 724 completed the survey on-line subsequently. Overall 1014 women of a possible 1521 completed the survey, a response rate of 66%.

A total of 48 women completed the pertussis section of the survey but not the influenza section reducing the completion rate for the influenza component of the survey to 63% (see Fig. 2).

3.2. Pertussis

Of the 1014 women who completed the pertussis questionnaire, 864 had been vaccinated, a vaccine coverage rate of 85.2%.

There were no significant differences between vaccinated and unvaccinated women in age distribution, education, income, seasonality of vaccine receipt or previous parity (Table 1). Women who were aware that pertussis vaccine was recommended for pregnant women were statistically more likely to be vaccinated (99.1% coverage), and women with tertiary level education were statistically more likely to be vaccinated on Chi-square analysis.

In the multivariate regression analysis, only awareness of the recommendation for pertussis vaccine was important, with this group 27 times more likely to be vaccinated when age education and income were controlled for in the analysis (Table 2).

3.3. Influenza

Of the 968 women who completed the influenza questionnaire, only 355 had been vaccinated a vaccine coverage rate of 36.7%.

On bivariate analysis there were significant age differences with women between 25 and 34 years more likely to be vaccinated (41.1%) than those younger or older (Table 3). Similar impacts were seen in women with a household income over $80,000 being somewhat more likely to be immunised (41%). Education level was not a major factor in vaccine decisions and neither was whether this was the first or subsequent pregnancy. The three most important factors on univariate analysis were whether the mother had received an influenza vaccine in the previous year, the season of vaccine delivery and whether there was a recommendation by an obstetric care provider (Table 3).

In the multivariate regression analysis, the pattern was similar (Table 4). In this model, developed by stepwise addition and subtraction of variables, age and income were not statistically associated with receipt/non-receipt of influenza vaccine. The critical determinants of vaccine receipt were receipt of influenza vaccine in the previous year (Odds ratio 5.47), the seasonality of delivery with women delivering in winter being 5.21 times more likely to be immunised and most importantly, a recommendation by a doctor made it 14 times more likely that the mother would receive vaccine.

4. Discussion

While the high antenatal pertussis coverage seen in our study could reflect participation bias it has also been reflected in other reports from Australian jurisdictions and is a clear national success story over the last three years after the failure of the state-based cocoon strategies [21,22]. These successes come as a response to various state-based funding initiatives after a failure to achieve funding for a national program.

The success also follows a series of continuing public and social media campaigns highlighting the issue, most notably the "Light for Riley" campaign supported by various pro-vaccine organisations, which is very active on social media and at various expos across Australia [23]. Locally, a short facebook video, made by a vaccine skeptic whose neonate spent four weeks in hospital with pertussis, after she declined antenatal boosting, went viral achieving over one million hits and being reported around the world [24].

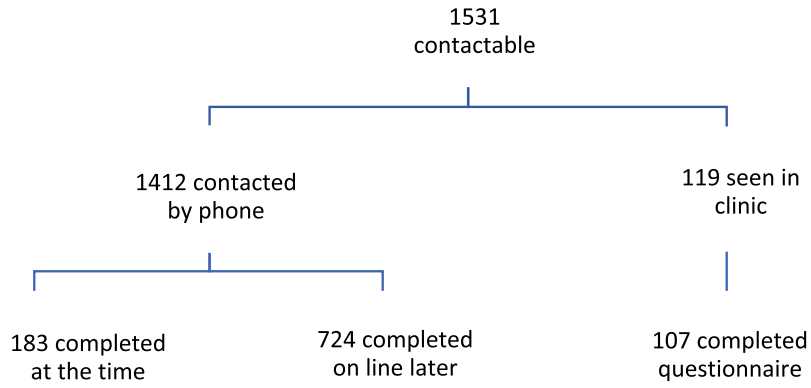

Fig. 2. Sampling framework and responses.

Table 1
Pertussis: Comparison of vaccinated and unvaccinated groups.

Variables	No pertussis vaccine n (%) (N = 150)	Pertussis vaccine n (%) (N = 864)	χ^2	P
Age				
18–24	7 (5.2)	35 (4.4)	1.59	0.45
25–34	89 (66.4)	490 (61.8)		
34 and more	38 (28.4)	268 (33.8)		
Total	134	793		
Missing	16	71		
Education				
High school	33 (24.8)	128 (16.4)	5.94	0.05
Some tertiary	14 (10.5)	76 (9.7)		
Tertiary and postgraduate	86 (64.7)	576 (73.8)		
Total	133	780		
Missing	17	84		
Income				
20,000–40,000	3 (2.5)	50 (7.3)	3.78	0.15
40,001–80,000	27 (22.7)	155 (22.5)		
80,001 and more	89 (74.8)	483 (70.2)		
Total	119	688		
Missing	31	176		
Vaccine season				
Jan-Mar	61(40.7)	346 (40.0)	2.88	0.41
Apr-June	35 (23.3)	163 (18.9)		
July-Sep	32 (21.3)	187 (21.6)		
Oct-Dec	22 (14.7)	168 (19.4)		
Total	150	864		
First pregnancy				
Yes	65 (43.3)	406 (47.0)	0.69	0.41
No	85 (56.7)	458 (53.0)		
Total	150	864		
Did you have a GP during your pregnancy?				
Yes	86 (57.3)	398 (46.1)	6.51	0.01
No	64 (42.7)	466 (53.9)		
Total	150	864		
Did any doctor recommend pertussis vaccine?				
Yes	139 (92.7)	775 (90.5)	0.70	0.40
No	11 (7.3)	81 (9.5)		
Total	150	856		
Missing	0	8		
Were you aware pertussis vaccine was recommended?				
Yes	119 (79.3)	856 (99.1)	134.68	<0.001
No	31 (20.7)	8 (0.9)		
Total	150	864		
Where were you told to access vaccine?				
GP	46 (30.7)	327 (37.8)	2.83	0.09
Others	104 (69.3)	537 (62.2)		
Total	150	864		

Table 2
Pertussis Vaccine: Regression analysis of factors impacting vaccine uptake.

	Unadjusted model		Adjusted model	
	Odds ratio	P	Odds ratio	P
Did your general practitioner provide pertussis vaccine?				
No	1		1	
Yes	0.64 (0.45–0.90)	0.01	0.75 (0.46–1.21)	0.24
Were you aware pertussis vaccine is recommended in pregnancy?				
No	1		1	
Yes	27.87 (12.52–62.07)	<0.001	27.41 (11.23–66.94)	<0.001
Where did they suggest you get the pertussis vaccine?				
Others	1		1	
GP	1.38 (0.95–2.00)	0.09	1.43 (0.86 – 2.37)	0.17
Education				
Tertiary	1		1	
High school	0.58 (0.37–0.90)	0.02	0.60 (0.34–1.04)	0.07
Some tertiary	0.81 (0.44–1.50)	0.50	0.78 (0.79–0.38)	0.53
It is recommended by hospital	1.06 (0.84–1.35)	0.63	0.98 (0.91–1.06)	0.62
Pertussis vaccine cannot give me pertussis	1.01(0.79–1.30)	0.93	1.03 (0.97–1.10)	0.27

In the adjusted model, classification is 88.4%, P value for Hosmer and Lemeshow Test is 0.75, Nagelkerke R Square is 17.4%.
Adjusted model: all variables in Table 2 were entered to the model.

Table 3
Comparison between vaccinated and unvaccinated influenza groups.

Variables	Vaccinated n (%) (n = 355)	Not Vaccinated n (%) (n = 613)	χ^2	P
Age				
18–24	12 (3.5)	30 (5.1)	9.80	0.007
25–34	239 (68.9)	342 (58.7)		
34 and more	96 (27.7)	211 (36.2)		
Total	347 (37.3)	583 (62.7)		
Missing	8	30		
Education				
High school	56 (16.5)	105 (18.2)	6.65	0.04
Some tertiary	23 (6.8)	67 (11.6)		
Tertiary and postgraduate	260 (76.7)	405 (70.2)		
Total	339 (37.0)	577 (63.0)		
Missing	16	36		
Income				
20,000–40,000	16 (5.2)	37 (7.4)	8.50	0.01
40,001–80,000	56 (18.1)	127 (25.4)		
80,001 and more	238 (76.8)	336 (67.2)		
Total	310 (38.3)	500 (61.7)		
Missing	45	113		
Season vaccinated				
Jan-Mar	87 (24.5)	302 (49.3)	83.85	<0.001
Apr-June	62 (19.5)	126 (20.6)		
July-Sep	120 (33.8)	87 (14.2)		
Oct-Dec	86 (24.2)	98 (16.0)		
Total	355 (36.7)	613 (63.3)		
First pregnancy				
Yes	171 (48.2)	276 (45.0)	0.89	0.34
No	184 (5.18)	337 (55.0)		
Total	355 (36.7)	613 (63.3)		
Received flu vaccine last year?				
Yes	196 (55.2)	111 (18.1)	142.91	<0.001
No	159 (44.8)	502 (81.9)		
Total	355 (36.7)	613 (63.3)		
Influenza vaccine recommended by a doctor?				
Yes	319 (90.1)	232 (38.0)	248.77	<0.001
No	35 (9.9)	379 (62.0)		
Total	354 (36.7)	611 (63.3)		
Missing	1	2		

Table 4
Influenza Vaccine: Regression analysis of factors impacting influenza vaccine uptake.

	Unadjusted model		Adjusted model	
	Odds ratio	P	Odds ratio	P
Did you receive a flu vaccine in the year before you were pregnant?				
No	1	<0.001	1	<0.001
Yes	5.58 (4.16–7.48)		5.47 (3.67–8.17)	
Did any doctor recommend influenza vaccine in pregnancy?				
No	1	<0.001	1	<0.001
Yes	14.89 (10.13–21.89)		13.94 (8.79–22.11)	
Season				
Jan-Mar	1		1	
Apr-Jun	1.71 (1.16–2.51)	0.007	1.69 (0.99–2.88)	0.05
Jul-Sep	4.29 (3.33–6.70)	<0.001	5.21 (3.15–8.64)	<0.001
Oct-Dec	3.05 (2.09–4.43)	<0.001	2.68 (1.69–4.48)	<0.001
Education				
Tertiary	1		1	
High school	0.83(0.58–1.19)	0.31	1.13 (0.67–1.91)	0.65
Some tertiary Income	0.54 (0.33–0.88)	0.01	0.36 (0.18–0.71)	0.003
80,001 or more	1		1	
20,000–40,000	0.61 (0.33–1.12)	0.11	1.03 (0.44–2.39)	0.94
40,001–80,000	0.62 (0.44–0.89)	0.009	0.68 (0.43–1.06)	0.09
Age				
18–24 Years	1		1	
25–34 Year	1.75 (0.88–3.48)	0.11	0.91 (0.31–2.68)	0.86
35 and more	1.14 (0.56–2.32)	0.72	0.70 (0.23–2.14)	0.53

In the adjusted model, classification is 78.9%, Hosmer and Lemeshow Test is 0.13, Nagelkerke R Square is 50.1%.

A small number of women did not have vaccine recommended and thus did not access it. Anecdotal commentary at the time of the survey suggested many of these cases related to confusion about the need for repeat boosting after a recent previous pregnancy when boosting occurred then.

The provision of vaccine in hospital antenatal clinics has been critical to improving the coverage rates overall. Previous studies highlighted the improvement in rates when vaccine was available at the time of a recommendation to have it [25]. This coupled with fluorescent stickers in pregnancy records, requiring a signature after completion of the vaccine discussion, ensures few women are unaware of the recommendation.

Some debate continues about the best time to give the vaccine. Australian policy remains to give it after 28 weeks despite data suggesting that it may be advantageous to give it earlier than this [26]. Third trimester recommendations risk vaccine being given quite late and breakthrough cases in neonates have occurred in Queensland when vaccine administration was too close to the delivery date.

The influenza vaccine coverage was disappointing and again reflects report in other parts of Australia about coverage rates in pregnant women [18,19].

The major factor impacting coverage was any doctor recommending vaccine in pregnancy, increasing the chance of receipt by over an order of magnitude. Recommendations by midwives or others were not important suggesting that despite the importance of midwives in obstetric care it remains the physicians who influence interventions and discussions on safety factors. The poor level of recommendations by physicians comes despite education campaigns targeting them. Some even actively dissuaded influenza vaccine.

The fluorescent sticker campaign incorporated both pertussis and influenza vaccine but only pertussis boosting was provided at the time in antenatal clinic. Moving forward both vaccines will be available in antenatal clinic. A campaign in a Melbourne hospital achieved over 80% coverage with both vaccines by concentrating activity at the hospital level.

This may not be enough to increase coverage rates in other places unless there is a complementary strong recommendation by carers. Sadly, the influenza vaccine coverage rate in staff in the 'Womens and Childrens' network of the local Gold Coast public hospital was 30%, suggesting a strong lack of belief in the benefits of influenza vaccination among this core influencing group.

The impact of previous vaccine receipt increasing the rates suggests that there is an element of belief in influenza vaccine itself that was important. Reviews of public perceptions of influenza vaccine have continuously identified prevailing views of influenza not being an important issue, influenza vaccine not being safe (including giving people influenza infection), and influenza vaccine being ineffective.

The described importance of seasonality on receipt of vaccine was well recognised in Australia with a usual period of three months between when a previous year vaccine was deemed 'out of date' and new season vaccine arrived. This has been partially addressed in 2018 with a change in shelf life of two available influenza vaccines now extending to the end of February, although we will still need healthcare providers through the spring and summer months to think influenza vaccine when seeing pregnant clients.

5. Conclusions

One out of every two pregnant women surveyed accessed a pertussis vaccine booster but not an influenza vaccine. While incremental improvements are still possible in antenatal pertussis programs, influenza vaccine programs in pregnancy need major changes.

Critical to any success moving forward is research to provide a better understanding of what approaches work best to turn around the prevailing public and medical carer view that, apart from possibly in older persons, the risk benefit equation for influenza vaccines favours non-vaccination.

Conflict of interest

The authors declared that there is no conflict of interest.

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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.2019.04.021.

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