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Pregnant women's knowledge and attitude to maternal vaccination including group B streptococcus and respiratory syncytial virus vaccines

Michelle L Giles [a,b,d,*], Jim Buttery [c,d], Mary-Ann Davey [a], Euan Wallace [a]

[a] The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University, Monash Medical Centre, 246 Clayton Road, Clayton, Victoria 3168, Australia
[b] Women's and Children's Health, Monash Health, 246 Clayton Road, Clayton, Victoria 3168, Australia
[c] School of Public Health and Preventive Medicine and Department of Pediatrics, Monash University, 246 Clayton Road, Clayton, Victoria 3168, Australia
[d] Monash Immunisation, Monash Health, 246 Clayton Road, Clayton, Victoria 3168, Australia

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ABSTRACT

Background: Maternal immunisation is an important strategy to reduce neonatal mortality and morbidity. New maternal vaccines such as Respiratory Syncytial Virus (RSV) and Group B streptococcus (GBS) are in development and/or clinical trials. However, little is known about pregnant women's knowledge about these diseases.

Methods: Women attending antenatal clinics in Melbourne, Australia were invited to complete a questionnaire collecting demographic information, past vaccination history, understanding of risk of GBS and RSV disease in pregnancy and likelihood to accept these theoretical vaccines in the future.

Findings: 495 women (48% born outside of Australia, from 48 different countries) completed the questionnaire. A large number of women had never heard of GBS (63%) or RSV (83%). Women over 35 years, born in Australia and women who had more than one child were more likely to have heard of GBS or RSV ($p < 0.001$). Women who had received influenza or pertussis vaccine in pregnancy were more likely to accept a RSV or GBS vaccine ($p < 0.001$).

Conclusions: This study has shown that knowledge of GBS and RSV is poor. However, when provided with information about the two diseases, acceptance of a hypothetical vaccine for both diseases was high. This study highlights the enormous amount of work that needs to be done in educating pregnant women about the seriousness of these two diseases if a future vaccine is ever to be accepted and high coverage achieved among the target population.

1. Background

Maternal immunisation is a well-recognised strategy for protecting mothers and their young infants against vaccine preventable diseases such as tetanus, influenza and pertussis. It provides protection to the newborn through transplacental transfer of maternally derived pathogen specific IgG [1,2]. In 2014, a review of the evidence by the pregnancy sub-group of the Global Advisory Committee for Vaccine Safety of the World Health Organization (WHO) determined that maternal immunisation was safe for both the mother and the infant [3].

In 1988, the WHO estimated that 787,000 newborns died of neonatal tetanus worldwide. In response, the Maternal and Neonatal Tetanus Elimination (MNTE) initiative was launched. It has resulted in most countries eliminating neonatal tetanus. Only 13 countries are still to reach MNTE status (<1 per 1000 live births) [4]. The success of this program has relied on integration of immunisation within antenatal settings, improved access to the vaccine, and acceptance by pregnant women through education, healthcare provider recommendation, and informed understanding of the safety and benefit of the vaccine.

Building on this proof of concept, pregnant women are a WHO priority group for influenza vaccination. Maternal influenza vaccination is recommended at any stage of pregnancy [5]. To date however, the majority of influenza vaccine uptake has been in resource rich settings such as the Americas, Europe and the Western Pacific. Few low and middle-income countries have successfully integrated maternal influenza vaccination programs into their antenatal care [6]. Another maternal immunisation program that has been implemented in middle and high-income countries including the Americas, Europe and Oceania [7–15] is Pertussis. Unlike tetanus and influenza, this has been recommended almost exclusively for

* Corresponding author at: The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University, Monash Medical Centre, 246 Clayton Road, Clayton, Victoria 3168, Australia.
E-mail address: michelle.giles@monash.edu (M.L Giles).

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infant benefit rather than maternal benefit. Evaluation of maternal pertussis programs have reported greater than 90% efficacy in reducing laboratory-confirmed pertussis, hospitalizations and deaths in infants up to 3 months of age [16–22].

With this experience in mind, new vaccine candidates against Respiratory syncytial virus (RSV) and Group B streptococcus (GBS) are in development and/or clinical trials. These two pathogens are important causes of neonatal morbidity and mortality, while GBS is also an important maternal pathogen [23,24]. Safe and effective vaccines would have significant potential to greatly improve maternal and child health globally.

RSV is an important cause of viral lower respiratory tract disease in infants worldwide. It is responsible for one third of deaths from acute lower respiratory infections in young infants [25], 1.4 million hospital admissions and nearly 30,000 infant deaths less than six months of age worldwide [25]. Recently, an RSV vaccine candidate completed a phase III clinical trial (www.clinicaltrials.gov NCT02624947) in women in the third trimester of pregnancy. Data in relation to effectiveness and safety are yet to be published, however initial reports from the manufacturer suggest efficacy against RSV lower respiratory tract infection (LRTI) requiring hospitalization and support the safety of the vaccine when given between 28 and 36 weeks of gestation.

Similarly, GBS is an important cause of neonatal sepsis and meningitis. An estimated 205,000 newborn infants develop early onset disease (defined as occurring between birth and six days of age) and 11,400 infants late onset disease (between 7 and 90 days of age). It is also estimated that GBS accounts for 57,000 fetal infections/stillbirths and 33,000 cases of invasive GBS disease occur in pregnant or post partum women [24]. The most common strategy currently to reduce neonatal sepsis is screening for GBS colonisation in pregnant women and administration of intrapartum antibiotics to those who are colonized, with alternate strategies providing prophylaxis to women with clinical risk factors [26]. This strategy is challenging in settings where women infrequently attend for antenatal care and where access to diagnostic testing and intravenous antibiotics during labour is limited, thereby making a GBS vaccine appealing. GBS candidate vaccines have been assessed in phase I and phase II clinical trials assessing safety and immune responses [27–32,33]. More recently, attention has been given to pentavalent vaccines covering the five GBS serotypes responsible for more than 90% of invasive neonatal disease (Ia, Ib, II, III and V) [34].

However, the successful implementation of any maternal vaccine programme depends on women's willingness to accept vaccination. A number of factors contribute to acceptance including knowledge of the disease to be prevented, the implications for the mother and/or her baby, reassurance that the vaccine is safe, knowledge about the vaccine efficacy and healthcare provider recommendation [35].

There is little published literature exploring women's knowledge and attitude to either GBS or RSV disease or vaccines. As with any new vaccine, this is important to inform how best to support women to feel safe with and accept new vaccines. One study of pregnant women and antenatal care providers in the UK found only 29% of women knew what GBS was and only 43% reported that they would be likely to accept a vaccine against GBS [36]. A larger survey of UK women of reproductive age, only 2% of whom were pregnant, reported that 29% had never heard of GBS [37]. One further study in the United States among pregnant and recently delivered women (83% of respondents white, non-Hispanic) reported that 78% agreed a GBS vaccine would be a good way to protect newborns. However, 39% of women believed that it was generally dangerous for pregnant women to get vaccines [38].

The primary objective of this study is to survey pregnant women, from diverse cultural backgrounds living in Australia to explore what they know about GBS and RSV and their attitudes to future GBS and RSV vaccination. The secondary objective of this study was to explore whether attitude and uptake of other maternal vaccines such as influenza and pertussis impact on this knowledge and attitude to new maternal vaccines.

1.1. Methods

Women attending public antenatal clinics at two hospitals in Melbourne, Australia were approached and invited to either self-complete the questionnaire or consent to interview and have completion assisted by the researcher between November 2017 and June 2018. All women were eligible for the study, although the questionnaire was not translated into other languages. Women who spoke a language other than English could still complete it if they had an interpreter present. This interpreter may have been a family member, friend or hospital interpreter booked for the antenatal appointment. The responses were either directly entered onto a web based survey platform Survey Monkey® by the researcher, or by the researcher subsequent to completion of the questionnaire by the woman. Data were then exported to Microsoft Excel for analysis.

Responses to questions asking about likelihood of accepting a hypothetical GBS or RSV vaccine were dichotomised into 'very likely' versus any other response (likely; unlikely; very unlikely; I would not get the vaccine). Proportions were compared using Chi-square and Fisher's Exact tests. P-values <0.05 were considered statistically significant. Statistical analyses were conducted using Stata15 (Stata Corp, College Station, Texas).

The questionnaire was modified from previously validated surveys [39,40], with input from a consumer representative from the Human Research and Ethics Committee to ensure language was understandable to women. The questionnaire was reviewed by a convenience sample of clinicians to check wording of questions, clarity of questions and time for completion.

For the question "How serious do you think the following conditions are during pregnancy or immediately after pregnancy?" a number of non-infectious conditions such as bleeding in pregnancy, high blood pressure and gestational diabetes were provided as comparators. These were chosen based on the assumption that they were common and well known to pregnant women. The scale used was "very serious, may be life threatening; serious, but not life threatening; not very serious; I don't know.

Prior to questions on acceptance of a future vaccine, a paragraph explaining GBS and RSV were included. The wording of this information was as follows:

> *"GBS is a bacteria that can live in a woman's vagina and be passed onto her baby during birth. A small number of these babies may then develop serious infection and/or meningitis (an infection in the brain). Currently in Australia we use medicine called antibiotics during labour to try and prevent this. A vaccine for GBS to protect babies is being developed and has been trialled in adults and pregnant women. So far it has not been shown to cause any harm"*

> *"RSV is a virus that can cause mild cold-like symptoms in adults but can cause more serious illness in young babies. It is the most common cause of a lung infection (also known as bronchiolitis or pneumonia) in children under one year of age. A vaccine for RSV to protect babies is being developed and has been trialled in adults and pregnant women"*

These paragraphs were either read by the participant if the woman elected to complete the survey independently or was read to her if she elected to have the researcher assist with completion of the survey.

Ethics approval for the study was obtained from the Monash Health Human Research and Ethics Committee (NMA HREC Ref LNR/17/MonH/479).

2. Results

2.1. Demographics

495 women completed the questionnaire; Table 1 details the demographic characteristics of these women. Their mean age was 30.4 years (Standard Deviation 5.4 years). The 237 women born overseas came from 48 different countries, the most common being India (69 women), Afghanistan (25 women), and China (22 women).

2.2. Antenatal care

A midwife was reported as the main healthcare provider seen during the pregnancy (306, 62%), followed by an obstetrician (133, 27%). Women also reported their provider (either the midwife or obstetrician) as the most trusted source of information for vaccines during pregnancy, (316, 64%), followed by their GP (150, 30%).

2.3. Vaccine awareness

Only a small number of women had not/or did not intend to receive pertussis vaccination during the current pregnancy (30, 6%) (Table 2). A larger proportion (137, 28%) of women did not intend to receive influenza vaccine during the current pregnancy.

Table 1
Characteristics of women completing the questionnaire.

Characteristic	N (%)
Country of birth	
• Australia	258 (52)
• Not Australia	237 (48)
• Indigenous	12 (5)
• Non Indigenous	483 (95)
Primary language	
• English	283 (57)
• Language other than English	212 (43)
Highest level of education	
• University	224 (45)
• High school	143 (29)
• Other eg TAFE	74 (15)
• Primary school	54 (11)
Employment	
• Full time/Part time	215 (43)
• Home duties	78 (16)
• Maternity leave	51 (10)
• Unemployed	139 (28)
Number of children	
• 0	205 (41)
• 1	202 (41)
• 2	60 (12)
• >2	28 (6)

Table 2
Acceptance of pertussis or influenza vaccination in pregnancy.

Vaccine	Yes received vaccine or intend to n(%)	Yes aware of vaccine but do not intend to receive n(%)	Not heard of vaccine n(%)
Pertussis	420 (85)	30 (6)	45 (9)
Influenza	330 (67)	137 (28)	28 (5)

Table 3
Knowledge of (potential) vaccine preventable diseases.

Vaccine preventable disease	I have never heard of it n(%)	I have heard of it but don't know much about it n(%)	I have heard of it and understand what it is n(%)
Influenza	8 (2)	59 (12)	428 (86)
Pertussis	33 (7)	131 (26)	331 (67)
GBS	312 (63)	139 (28)	44 (9)
RSV	412 (83)	50 (10)	32 (7)

Women were asked if they had a preference in relation to receiving influenza and pertussis vaccine together or separated in time during pregnancy. Just over half of women preferred to have them separated in time (257, 52%) versus receiving them together (171, 35%).

A large proportion of respondents had never heard of either GBS (63%) or RSV (83%) (Table 3).

2.4. Women's attitudes/beliefs of seriousness of pregnancy complications

More women scored the pregnancy complications bleeding, high and low blood pressure, and gestational diabetes as 'serious and life-threatening' than either pertussis or influenza infection in the mother, or any GBS/RSV related disease in either the baby or the mother (Fig. 1). Pertussis infection in the baby was rated as 'serious and life-threatening' by almost three quarters of women (364, 74%). In contrast, less than one quarter of women (115, 23%) reported influenza infection in pregnant women to be 'serious and life-threatening'. However, 299 (60%) graded influenza infection in their baby to be 'serious and life-threatening'.

2.5. GBS vaccine

After receiving information about GBS disease, women were asked how likely they would be to receive the vaccine if available. The majority (396, 74%) were very likely, 105 (21%) likely, 10 (2%) unlikely, 8 (2%) very unlikely and 7 (1%) stated they would not get it.

When asked to compare vaccination with intrapartum antibiotics, the majority of women (440, 89%) stated they would prefer to receive a GBS vaccine. Thirteen (3%) women stated that they would not accept either antibiotics or a vaccine.

2.6. RSV vaccine

After receiving information about RSV disease, women were asked how likely they would be to receive the vaccine if available. The majority were very likely (378, 77%), followed by likely (91, 18%), unlikely (15, 3%) and very unlikely (9, 2%).

2.6.1. What information is important to women when considering new maternal vaccines?

The most important information about a vaccine desired by women is its safety for themselves and their baby (Table 4), followed by proven benefit to their baby. Only two respondents felt that benefit to them was the most important information.

2.6.2. Factors associated with knowledge of GBS or RSV

Women older than 35 years, born in Australia, speaking English only or having more than one child were more likely to have heard of either RSV or GBS ($p < 0.001$). University education was also associated with being more likely to have heard of both RSV and GBS compared with primary or secondary education only. There were also significant differences in awareness by employment

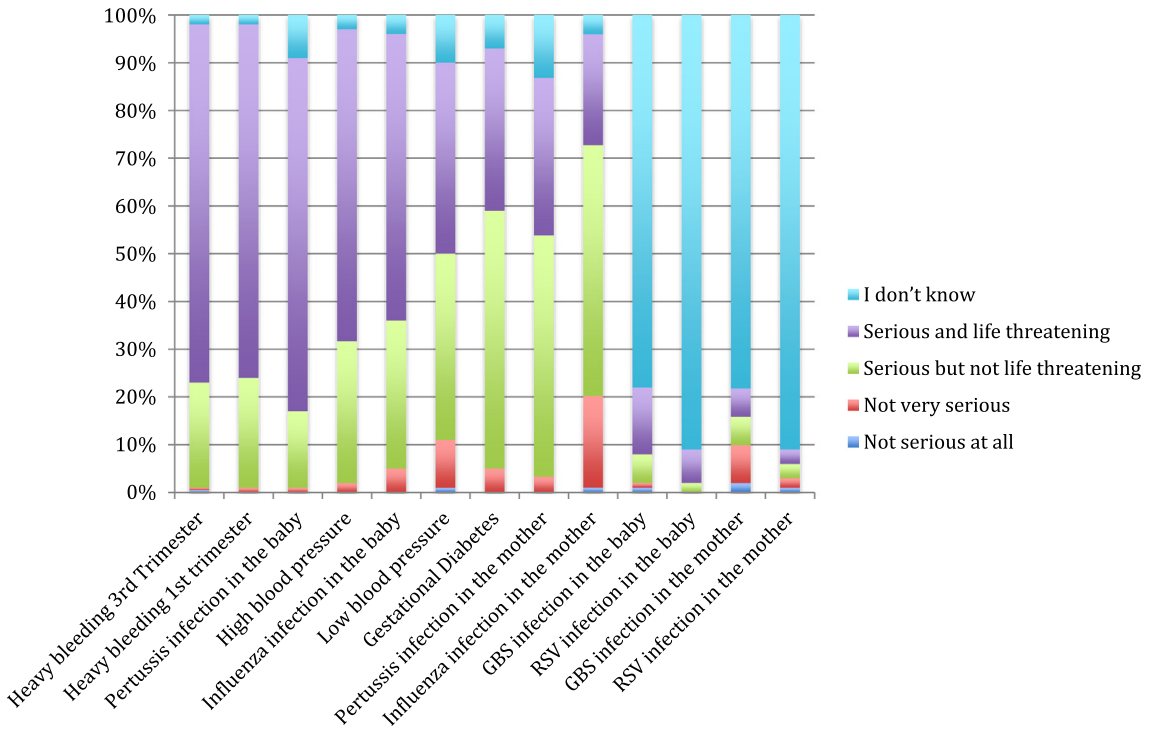

Fig. 1. Perceived seriousness of obstetric complications and infections in pregnancy or postnatally in the infant.

Table 4
Information most important to women before accepting a vaccine during pregnancy.

What is the most important information you would require before you would be willing to receive the vaccine in pregnancy?	GBS n (%)	RSV n (%)
Proven safety for me and my baby	396 (80)	399 (81)
Proven benefit for me	0	2 (0.4)
Proven benefit for my baby	63 (13)	55 (11)
Used by very large numbers of women first	23 (5)	25 (5)
Not applicable; I would not accept a new maternal vaccine	11 (2)	12 (2)

status with those who are employed, on maternity leave or have home duties as their occupation more likely to be aware of RSV and GBS compared to students or unemployed women (Table 5). Of the students, 22% were in the youngest age group and 32% of the unemployed were in the youngest age group compared to 6% of the employed (data not shown). A different pattern emerged however for employment status, with 56% of employed, 90% of home duties, 44% of students and 48% unemployed having at least one child (data not shown).

2.6.3. Factors associated with likelihood to accept a future GBS or RSV vaccine

The only factors associated with likelihood to accept either a RSV or a GBS vaccine were having already received influenza vaccine ($p < 0.001$) or pertussis vaccine ($p < 0.001$) Table 6.

3. Discussion

In this study of a largely educated but culturally diverse group of pregnant women we have shown that knowledge of GBS and RSV is poor. However, when provided with information about the two diseases and potential vaccines, acceptance, albeit hypothetical, of vaccination for both diseases was high. To our knowledge, these are the first insights into pregnant women's knowledge and attitudes to RSV vaccination in pregnancy and, we believe, provide useful insights into women's understanding of the severity of the vaccine preventable diseases for currently recommended and future vaccines. The gaps in knowledge and prioritisation of safety data above all else including efficacy, in relation to acceptance of any new vaccine are critical in development and implementation of future maternal immunisations.

Prior to this study there have been two published reports surveying pregnant women's attitude to a hypothetical GBS vaccine [37,38]. The two reports on GBS were conducted in the United Kingdom and the United States. In the study from the United States, the demographic characteristics of the population were 83% white, non-Hispanic. From an implementation perspective, it is essential to understand different populations' knowledge and attitudes to maternal vaccines to inform the barriers that may exist in different settings or populations [39,40]. We did however find that receipt of either influenza or pertussis vaccine in pregnancy was the only factor significantly associated with likelihood to accept a future GBS or RSV vaccine. This may reflect that women who are prepared to accept existing maternal vaccinations are less likely to be vaccine hesitant toward future vaccines.

Notably, even among a relatively educated population with moderate uptake of influenza and pertussis there remained very poor knowledge of GBS and RSV. The knowledge gaps in relation to GBS remained even when 59% of women had had a child before. At the institution where this study was undertaken, antibiotics are routinely administered to women whose infants are considered at risk for early onset GBS disease. Even considering that a proportion of the multiparous women may have birthed at a different institution for their first pregnancy, it was still surprising that so many had still not heard of GBS given they may have been screened for GBS or considered for treatment in a previous pregnancy. These findings are crucial to policy makers, funders and educators for consideration if and when a new GBS or RSV maternal vaccine becomes available. Women's perception of the risk of disease to themselves and their baby, including an appreciation of the severity of disease and potential complications including death, can

Table 5
What factors are associated with knowledge of GBS and RSV.

Factor	I have heard of RSV			I have heard of GBS		
	n	%	p-value	n	%	p-value
Age						
18–24 yrs	5	7.14		11	15.7	
25–34 yrs	52	16.1		126	38.9	
35 + yrs	26	25.7	0.005	46	45.4	<0.001
Country of Birth						
Australia	60	23.4		120	46.5	
Outside Australia	23	9.8	<0.001	63	26.7	<0.001
Language other than English (yes/no)						
English only	60	21.3		126	44.7	
Speaks another language	23	11	0.002	57	27	<0.001
Education						
Primary	2	3.7		6	11.1	
Secondary	18	12.8		39	27.7	
University	46	20.5		102	45.5	
Other	17	22.7	0.006	36	47.4	<0.001
Employment						
Emp/mat leave	61	22.8		123	45.7	
Home duties	15	19.2		36	46.2	
Student	2	22.2		2	22.2	
Unemployed	5	3.6	<0.001	22	15.8	<0.001
Children						
none	23	11.2		55	26.8	
1+	60	20.8	0.005	128	44.1	<0.001
Receipt of influenza vaccine						
yes	66	20		138	41.8	
no/not heard of it	17	10.4	0.007	45	27.3	0.002
Receipt of pertussis vaccine						
yes	76	18.1		170	40.5	
no/not heard of it	7	9.3	0.06	13	17.3	<0.001

Table 6
Factors associated with likelihood to accept a future GBS or RSV vaccine.

Factor	I would be VERY likely to get RSV vaccine			I would be VERY likely to get GBS vaccine		
	n	%	p-value	n	%	p-value
18–24 yrs	47	68.1		46	66.7	
25–34 yrs	250	77.4		242	74.9	
35 + yrs	81	80.2	0.164	75	74.3	0.364
Born in Australia	188	73.2		180	70.4	
Born outside australia	189	80.4	0.057	182	77.5	0.063
Speaks english only	214	76.4		198	70.7	
Speaks another language	163	77.3	0.831	164	77.7	0.081
Highest education level completed						
Primary	38	71.7		35	66.0	
Secondary	109	77.3		103	73.1	
University	180	80.7		174	78.0	
Other	51	67.1	0.082	51	67.1	0.14
Employment						
Emp/mat leave	202	75.4		197	73.5	
Home duties	58	74.4		54	69.2	
Student	6	66.7		5	55.6	
Unemployed	112	81.2	0.467	107	77.5	0.337
No Children	154	75.5		145	71.1	
One or more children	224	77.5	0.602	218	75.4	0.28
Receipt of influenza vaccine						
Yes	268	81.7		257	78.4	
No/not heard of it	110	66.7	<0.001	106	64.2	0.001
Receipt of pertussis vaccine						
Yes	335	80.1		327	78.2	
No/not hear of it	45	57.3	<0.001	36	48	<0.001

have a significant impact on the successful implementation of this prevention strategy. The findings from our study highlight the enormous amount of education that is required in relation to these two diseases.

In our study, it was striking that 89% of women reported that they would prefer to receive a GBS vaccine to prevent GBS disease in their infants than antibiotics. This may reflect women's preference to avoid medication during pregnancy and labour, although this was not specifically explored further in this study. Maternal vaccination as a strategy to reduce antibiotic use is appealing as it may help combat antimicrobial resistance, a serious threat to global public health that requires action across all government sectors and society [41]. The vast majority of the burden of disease (early and late onset disease, and possibly stillbirth) occurs in low and low-middle income countries [24]. However, even the standard of care practised in some high-income countries

(screening for colonization and intra-partum antibiotic prophylaxis) has only been partially effective in controlling the early onset disease burden [42]. GBS vaccine development seems technically feasible and several candidates are in, or about to enter, clinical development, however unless considerable progress is made in understanding the challenges to future GBS vaccine introduction, in particular women's knowledge of the disease, then many of these development efforts may be in vain.

Our results highlight that even fewer women had heard of RSV compared to GBS. A staggering 83% of pregnant women had never heard of RSV. Not surprisingly, given 83% of women had never heard of RSV, 91% did not know if RSV infection in their newborn was serious. As suggested in previous studies [37,43] emphasising protection for the baby rather than the mother may lead to increased uptake. In settings where both influenza and pertussis vaccines are both recommended, there is often higher uptake of pertussis vaccination compared to influenza including in the findings of this study. One possible explanation for this is the messaging and communication to women around the benefit to the baby versus the benefit to the mother. Our findings suggest that the message of protection for the baby afforded by maternal pertussis vaccination is understood by pregnant women as 74% of women ranked pertussis infection in the baby to be life threatening, and a further 16% ranked pertussis infection in the baby as serious but not life threatening.

From an implementation viewpoint, the gaps in knowledge (for both currently recommended maternal vaccines as well as future vaccines) highlighted by this study will require significant training and education of healthcare workers and pregnant women to facilitate successful implementation. Furthermore, additional vaccines during pregnancy will require careful consideration of optimal gestation for administration and how these will be administered alongside existing maternal vaccine schedules so as not to compromise compliance. The importance of this and the amount of work required needs to be appreciated across all levels of public health, including funders, policy makers, and those involved in implementation across all levels of healthcare provision.

Our findings also confirm that the most important information women demand prior to acceptance of a new vaccine in pregnancy is safety data. This was found to be more important than efficacy data. The importance of safety monitoring and the provision of this information for consumers have been reflected in the development of guidelines to harmonize data collection for monitoring safety across all phases of clinical trials of vaccines in pregnant women [44,45].

Even though this study was conducted in a resource rich setting, important learnings can be considered from a global public health perspective. Globally, there are an estimated 90,000 deaths annually in children under three months of age and 33,000 cases of invasive GBS disease in pregnant or post-partum women [24]. In addition, RSV is the most important cause of viral lower respiratory tract disease in infants globally, associated with 13–22% of deaths from acute lower respiratory infection (ALRI) [46–48]. A recent systematic review estimated that globally, there were 1.4 million hospital admissions annually for ALRI due to RSV, and 27,300 in-hospital deaths in infants under six months of age [48]. An effective and safe maternal vaccine against GBS or RSV has potential to impact significantly on childhood mortality in the age group most vulnerable (less than 6 months of life) and in whom few other interventions are available or practicable.

It is important to remember however, that achieving the maximal potential of any maternal vaccine in the future will require simultaneous strengthening of antenatal care services (particularly in low and middle income countries), adequate attendance for antenatal visits to facilitate receipt of information and opportunities for access to vaccines, robust monitoring and surveillance systems, sustainable funding and human resources. In addition, it is vital to remember that at the centre of all these vaccine initiatives is the pregnant woman who needs to understand the rationale behind current and any future maternal vaccines and the safety data and evidence for efficacy. Our study demonstrates that it is in this space that gaps exist both for GBS and RSV and need to be the focus moving forward.

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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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