Associations Between Maternal Immunisation and Reduced Rates of Preterm Birth and Stillbirth: A Population Based Retrospective Cohort Study

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Stillbirth and preterm birth (PTB) remain two of the most important, unresolved challenges in modern pregnancy care. Approximately 10% of all births are preterm with nearly one million children dying each year due to PTB. It remains the most common cause of death among children under five years of age. The numbers for stillbirth are no less shocking with 2.6 million babies still born each year. With minimal impact on the rate of these adverse birth outcomes over the past decade there is an urgent need to identify more effective interventions to tackle these problems. In this retrospective cohort study, we used whole-of-population data, to determine if maternal immunization during pregnancy against influenza and/or pertussis, is associated with a lower risk of PTB, delivering a small-for-gestational age (SGA) infant, developing preeclampsia or stillbirth. Women with a singleton pregnancy at 28 or more weeks' gestation delivering in Victoria, Australia from July 2015 to December 2018 were included in the analysis. Log-binomial regression was used to measure the relationship between vaccination during pregnancy against influenza and against pertussis, with preterm birth, SGA, preeclampsia and stillbirth. Variables included in the adjusted model were maternal age, body mass index, first or subsequent birth, maternal Indigenous status, socio-economic quintile, smoking, public or private maternity care and metropolitan or rural location of the hospital. Women who received influenza vaccine were 75% less likely to have a stillbirth (aRR 0.25; 95% CI 0.20, 0.31), and 31% less likely to birth <37 weeks (aRR 0.69; 95% CI 0.66, 0.72). Women who received pertussis vaccine were 77% less likely to have a stillbirth (aOR 0.23; 95% CI 0.18, 0.28) and 32% less likely to birth <37 weeks gestation (aRR 0.68; 95% CI 0.66, 0.71). Vaccination also reduced the odds of small for gestational age by 13% and reduced the odds of pre-eclampsia when restricted to primiparous women. This association was seen over four different influenza seasons and independent of the time of year suggesting that any protective effect on obstetric outcomes afforded by maternal vaccination may not
be due to a pathogen-specific response but rather due to pathogen-agnostic immune-modulatory effects.

**Keywords:** immunisation, pregnancy, influenza, pertussis, preterm birth

## INTRODUCTION

Maternal immunisation is an established strategy to reduce the morbidity and mortality of pregnant women, and their newborn infants through transplacental transfer of pathogen specific IgG antibodies (1). In 1988, the World Health Organization (WHO) estimated that 787,000 newborns worldwide died of tetanus (2), calling for maternal and neonatal tetanus elimination (MNTE). Routine immunisation of pregnant women with tetanus toxoid containing vaccine was a key component of MNTE, together with better birth and umbilical cord care hygiene. By 2015, the WHO estimated that there had been a 96% reduction in neonatal mortality from tetanus (3). This was the first immunisation programme specific to pregnant women to be recommended globally (2). It marked the beginning of maternal immunisation being adopted as an approach to saving maternal and infant lives, particularly in low-resource settings.

Whilst in some countries, such as the United States, maternal influenza vaccination has been recommended since the 1950s, it was not until the H1N1 pandemic in 2009 that coverage rates increased (4). Reflecting that pregnant women are at higher risk of serious morbidity and mortality from influenza than the general population, in 2012 the WHO identified pregnant women as a priority population for seasonal influenza vaccination (5). Similarly, maternal vaccination with a diphtheria-tetanus-acellular pertussis vaccine (dTpa) has become standard care in many countries, including the UK, USA and Australia (6–8), reducing infant deaths from pertussis by 95% (9).

Some authors have suggested that maternal influenza vaccination may be protective against adverse pregnancy outcomes such as preterm birth (PTB), small for gestational age (SGA) and stillbirth (10–13), but others have not confirmed this finding (14, 15). There are several likely explanations for these different findings, including varying study designs and settings, different influenza seasons and vaccine matching, and variable capability in accurately measuring gestational age. However, if maternal influenza vaccination was protective against PTB and stillbirth then it would be an effective public health measure against two adverse pregnancy outcomes that have been stubbornly resistant to improvement (16, 17). Whether maternal diphtheria-tetanus-pertussis vaccination in combination with influenza vaccination has any protective effect on these pregnancy outcomes has not been reported.

Unlike previous studies we set out to determine if maternal immunisation, influenza and/or diphtheria-tetanus-pertussis, is associated with a lower risk of PTB, SGA, preeclampsia or stillbirth using whole-of-population data including with mandatory documentation of vaccination status and reliable capture of gestational age.

## METHODS

We conducted a population based retrospective cohort study using data on all singleton births in Victoria at 28 or more weeks’ gestation from July 2015 to December 2018. Attending clinicians, usually midwives, provide data on maternal socio-demographic characteristics, pre-existing medical conditions, reproductive history, complications of pregnancy, procedures, details of the labour and birth, maternal morbidity, and neonatal details and mortality on all births to the Consultative Council on Obstetric and Paediatric Mortality and Morbidity (CCOPMM). This data is captured during pregnancy and forms the Victorian Perinatal Data Collection (VPDC). Maternal vaccination against pertussis and influenza (yes/no/not known) were added to the VPDC as mandatory items for all births from 1 July 2015. In Australia the nationally funded vaccine against pertussis is the diphtheria-tetanus-pertussis vaccine and will be referred to as ‘pertussis’ vaccine for the remainder of this manuscript. Influenza vaccine is also recommended and funded by the government for all women in every pregnancy.

We excluded births before 28 weeks because, until very recently, it has been common in Victoria for women to be offered pertussis containing vaccination only from 28 weeks onwards. We also excluded multiple pregnancy because of the association between multiple pregnancy and higher rates of preterm birth and stillbirth.

The exposures of interest were vaccination against influenza, and/or pertussis during the current pregnancy. The control group chosen was women who received no vaccination at all (as the focus was on the non-specific effects of vaccination). A sensitivity analysis was performed comparing influenza vaccine compared with no influenza vaccine (regardless of pertussis status meaning women in either group may have received pertussis vaccine) and a similar analysis for pertussis vaccine versus no pertussis vaccine (regardless of influenza status meaning women in either group may have received an influenza vaccine). The outcomes of interest were PTB <37 weeks, <34 weeks and <32 weeks, stillbirth, SGA (defined as a birthweight <10th centile for gestation and sex) and pre-eclampsia.

We included potential confounding factors for preterm birth and stillbirth in the analysis: maternal age, body mass index (BMI), parity, smoking, maternal region of birth, socioeconomic status, onset of labour, method of birth, public versus private admission for the birth, maternal Indigenous status and previous stillbirth.

### Analyses

We compared proportions of women with these characteristics who were vaccinated against pertussis and against influenza
using the chi square test. A p-value <0.05 was considered statistically significant. We generated new variables to represent birth during the local influenza season (April to September) and non-influenza season (October to March); spontaneous onset of labour vs medically initiated birth (induction of labour or pre-labour caesarean section). Maternal country of birth was classified according to the Standard Australian classification of countries (SACC) 2016. For births in 2015 and 2016 the SACC 2011 was used. Maternal residential address was used to classify socio-economic status according to the Index of Relative Social Disadvantage for statistical Area 1 (a census district of approximately 400 people). This was determined by the Australian Bureau of Statistics census in 2011 for births in 2015 and 2016, and for births in 2017 and 2018 the 2016 Australian Bureau of Statistics census was used.

We used log-binomial regression to measure the relationship between vaccination during pregnancy against influenza and against pertussis, with PTB (<37 weeks, <34 weeks and <32 weeks), or subsequent birth, maternal Indigenous status, socio-economic quintile, smoking during pregnancy (yes/no/not known), public or private maternity care and metropolitan or rural location of the hospital. Analyses of stillbirth also adjusted for any prior stillbirth. Analyses of preeclampsia were restricted to primiparous women. To interrogate the consistency of the results, sub-group analyses were planned for the most socially disadvantaged and the most advantaged quintiles of women, women who smoked in pregnancy, women born outside Australia, obese women, young women, women attending rural hospitals, those receiving private maternity care, those giving birth during influenza season and outside influenza season, and those who had a spontaneous onset of labour.

## RESULTS

A total of 269,493 women, with a singleton pregnancy >28 weeks in Victoria gave birth between July 2015 and the December 31, 2018 and are included in our analysis. Table 1 summarises the demographic details of the women. 138,698 (51.5%) women received influenza vaccination and 192,487 (71.4%) received pertussis vaccination during their pregnancy.

Table 2 summarises the proportion of women vaccinated against either influenza or pertussis according to maternal characteristics. The uptake of influenza vaccination was lower in younger women, those with a low BMI, smokers, the most disadvantaged and those who identified as Indigenous. Higher

### TABLE 1 | Maternal characteristics (includes those with missing vaccination status; excludes <28w and multiples).

| Vaccinated during pregnancy against influenza | n | % |
|----------------------------------------------|---|---|
| Yes                                          | 138698 | 51.5 |
| Not reported/inadequately described          | 18640  | 6.8 |

| Vaccinated during pregnancy against pertussis | n | % |
|----------------------------------------------|---|---|
| Yes                                          | 192487 | 71.4 |
| Not reported/inadequately described          | 20033  | 7.5 |

| Vaccinated during pregnancy against influenza and pertussis | n | % |
|-----------------------------------------------------------|---|---|
| Yes                                                       | 124140 | 46.10 |
| No/not known                                              | 145353 | 53.90 |

| First birth | n | % |
|-------------|---|---|
| Yes         | 117395 | 43.6 |
| Not stated  | 3   | 0.0 |

| Maternal age group | n | % |
|--------------------|---|---|
| Younger than 20    | 3684 | 1.4 |
| 20-24 years        | 24983 | 9.3 |
| 25-29 years        | 68764 | 25.5 |
| 30-34 years        | 102527 | 38.0 |
| 35-39 years        | 56683 | 21.0 |
| 40-44 years        | 11975 | 4.4 |
| 45+ years          | 897  | 0.3 |
| Not reported/inadequately described                    | 30   | 0.0 |

| BMI group | n | % |
|-----------|---|---|
| <18.5     | 8106 | 3.0 |
| 18.5-25   | 133720 | 49.6 |
| 25-30     | 70807 | 26.3 |
| 30-35     | 31349 | 11.6 |
| 35-40     | 13225 | 4.9 |
| 40+       | 8027  | 3.0 |
| Not reported/inadequately described                    | 4259 | 1.6 |

| Maternal Indigenous status | n | % |
|---------------------------|---|---|
| Aboriginal                | 3839 | 1.4 |
| Non-Aboriginal             | 264821 | 98.3 |
| Not reported/inadequately described | 833 | 0.3 |

| Socio-economic status    | n | % |
|--------------------------|---|---|
| Most disadvantaged       | 53308 | 19.8 |
| 2                        | 53215 | 19.8 |
| 3                        | 53387 | 19.8 |
| 4                        | 53098 | 19.7 |
| Least disadvantaged      | 52900 | 19.6 |
| Not reported/inadequately described | 3585 | 1.3 |

| Maternal region of birth | n | % |
|--------------------------|---|---|
| Australia                | 165153 | 61.6 |
| Americas                 | 3771  | 1.4 |
| North Africa and the Middle East | 9725 | 3.6 |
| North-East Asia          | 14154 | 5.3 |
| North-West Europe        | 7625  | 2.8 |
| Oceania and Antarctica   | 7657  | 2.9 |
| South-East Asia          | 17766 | 6.6 |
| Southern and Central Asia| 31392 | 11.7 |
| Southern and Eastern Europe | 4976 | 1.9 |
| Sub-Saharan Africa      | 6021  | 2.2 |
| Not reported/inadequately described | 1253 | 0.5 |

| Location of hospital    | n | % |
|-------------------------|---|---|
| Metro                   | 208403 | 77.3 |
| Rural                   | 61090  | 22.7 |

| Smoking during pregnancy | n | % |
|--------------------------|---|---|
| None                     | 235343 | 87.3 |
| Smoked at all             | 23142  | 8.6 |
| Not reported/inadequately described | 11008 | 4.1 |

| Onset of labour         | n | % |
|-------------------------|---|---|
| Spontaneous and not augmented | 85668 | 31.8 |
| Induced                 | 88435 | 32.8 |

(Continued)
uptake of influenza and pertussis vaccination was reported in women during their first pregnancy.

After adjusting for possible confounding factors including parity, maternal age, BMI, socioeconomic status, smoking, private/public admission for birth, maternal Indigenous status, maternal region of birth, metropolitan/rural location of hospital and any prior stillbirth (for stillbirth analysis only) receipt of either influenza or pertussis vaccination was associated with a significantly lower rate of PTB, FGR, stillbirth and preeclampsia for primiparous women (Table 3). There was little difference in the effect when the analysis was restricted to spontaneous PTB suggesting the main effect of vaccination on PTB appears to be on spontaneous PTB rate (Table 3). Overall, compared to women who received no vaccine, women who received both influenza and pertussis vaccine had 79% lower odds of stillbirth and 61% lower odds of PTB <32 weeks (Table 3).

To explore possible pathways to reduced PTB and stillbirth, we examined whether maternal vaccination was associated with impaired fetal growth and preeclampsia. Maternal vaccination was associated with modest reductions in the rates of both SGA and preeclampsia (Table 3). Women who received influenza vaccine were 13% less likely to have a baby <10th centile for birthweight and 11% less likely to have preeclampsia. The reduction in preeclampsia was only significant when the analysis was restricted to primiparous women (Table 3).

The associations between reduced stillbirth and PTB, and maternal influenza vaccination were just as strong when analysed according to birth during or outside of influenza season (Table 4) and across different years (Table 5), irrespective of the severity of the influenza season.

Sub-group analyses were largely consistent with the overall results though some of the relationships were stronger including in younger women, women who smoked in pregnancy and those attending rural hospitals, and weaker in women receiving private maternity care. Similarly, sensitivity analyses comparing receipt of influenza vaccine versus no vaccine (regardless of pertussis status) and receipt of pertussis vaccine versus no pertussis vaccine (regardless of influenza status) were largely consistent, although the magnitude of protection was slightly greater for pertussis vaccine (Supplementary Table).

**DISCUSSION**

This is the largest study published to date exploring the association between maternal immunisation with influenza and pertussis vaccines and the pregnancy outcomes of PTB, preeclampsia, giving birth to a SGA infant and stillbirth. We found that influenza vaccination and pertussis vaccination during pregnancy were both associated with lower rates of PTB, including very PTB (<32 weeks gestation) and stillbirth. Given the persistently high rates of PTB and stillbirth globally, the potential implications for low, middle- and high-income settings are significant.

We wished to explore possible effects of vaccination on preeclampsia and impaired fetal growth because they are both on the causal pathways to preterm birth and stillbirth (18, 19). While vaccination was associated with reductions in both preeclampsia and SGA, the aRRs for each were more modest than those for PTB and stillbirth. Together with the late pregnancy timing of vaccination, this suggests to us that any mechanisms of action may not be via improved placentation. Closer examination of classifications of stillbirth and/or timing of vaccination in pregnancy may provide further clues to possible mechanisms although this data was not available at the time of our study.

The association between maternal vaccination and improved obstetric outcomes was afforded by either vaccination, was relatively consistent across years irrespective of differences in influenza activity, and was present outside of influenza season. This suggests that any underlying mechanism(s) of protection may not be pathogen-specific.

**Interpretation**

We suggest that maternal vaccination may be associated with improved pregnancy outcomes via pathogen-agnostic immune-modulatory effects. Pregnancy itself is a state of heightened inflammation (20) but PTB, particularly spontaneous PTB, and preeclampsia are conditions characterized by excessive and progressive systemic maternal inflammation (18–21). We suggest that maternal vaccination may modify the maternal immune trajectory, reducing harmful systemic inflammation such that pregnancy outcomes are improved. The suggestion that vaccines impact the host beyond the pathogen-specific immune response is not new (22). For example, neonatal BCG induces a rapid onset granulopoiesis that protects newborns from non-TB sepsis (23). It is this observation that prompted researchers to consider BCG vaccine to protect against and/or modify the clinical response to SARS-CoV-2 infection. Indeed, vaccination-induced pathogen-agnostic collateral immune effects are just beginning to be recognized more widely as promising approaches to improve neonatal health (24).
Strengths
Strengths of our findings are that our data are from a whole population over multiple years, and that the accuracy of the data has been previously confirmed (25). Further, while most previously published data on obstetric outcomes is heavily weighted to the H1N1 pandemic, when a monovalent vaccine was used, our study covers a period during which trivalent and quadrivalent vaccines were in use. In comparison, the meta-analysis by Jeong and colleagues (14), which did not report a significant association, included several observational studies, the largest one included 130,996 vaccinated women. Whilst acknowledging the discordance in results to a recently published pooled analysis of three randomized controlled trials (10,002 women) our study included data on a much larger population dataset (269,493 women) in a resource rich setting with accurate determination of gestational age at delivery.

Limitations
Given the observational nature of our study, we cannot exclude confounding although an attempt to control for this was made by

| TABLE 2 | Proportion of women vaccinated according to maternal characteristics. |
|-------------------------------------------------|
| Influenza vaccine given | Pertussis vaccine given |
| Yes n % | No n % | p-value* | Yes n % | No n % | p-value* |
| **First birth** | | | | | | |
| Yes | 65327 59.7 | 44146 40.3 | <0.001 | 89073 81.9 | 19712 18.1 | <0.001 |
| No | 73371 51.9 | 68009 48.1 | | 103414 73.6 | 37160 26.4 | |
| **Maternal age group** | | | | | | |
| Younger than 20 years | 1567 45.3 | 1892 54.7 | <0.001 | 2564 7.4 | 901 26 | <0.001 |
| 20-24 years | 11290 48.5 | 11983 51.5 | | 17760 75.9 | 5656 24.2 | |
| 25-29 years | 34608 53.8 | 29757 46.2 | | 50680 78.7 | 13732 21.3 | |
| 30-34 years | 54736 57.4 | 40658 42.6 | | 74027 78.2 | 20609 21.8 | |
| 35-39 years | 29897 56.9 | 22265 43.1 | | 38878 75.1 | 12898 24.9 | |
| 40-44 years | 6135 55.7 | 4875 44.3 | | 7985 73.7 | 2586 26.3 | |
| 45+ years | 462 56.6 | 354 43.4 | | 589 73.7 | 210 26.3 | |
| **BMI group** | | | | | | |
| <18.5 | 3833 51.6 | 3602 48.5 | <0.001 | 5366 73 | 1981 27 | <0.001 |
| 18.5-<25 | 69870 56.2 | 54430 43.8 | | 95142 77.3 | 27941 22.7 | |
| 25-<30 | 36840 55.5 | 29274 44.5 | | 51688 78.2 | 14427 21.8 | |
| 30-<35 | 15963 53.8 | 13525 46.2 | | 23085 78.3 | 6410 21.7 | |
| 35-<40 | 6589 53.1 | 5830 46.9 | | 9610 77.1 | 2894 22.9 | |
| 40+ | 4016 53.7 | 3461 46.3 | | 5694 76 | 1800 24 | |
| **Maternal Indigenous status** | | | | | | |
| Indigenous | 1656 45.0 | 2025 55.0 | <0.001 | 2571 69.9 | 1107 30.1 | <0.001 |
| Not Indigenous | 136799 55.5 | 109774 44.5 | | 189495 77.3 | 55585 22.7 | |
| **Socio-economic status** | | | | | | |
| Most disadvantaged | 25938 51.6 | 23824 48.4 | <0.001 | 37019 74.9 | 12411 25.1 | <0.001 |
| 2 | 26845 53.9 | 22923 46.1 | | 39005 78.4 | 10748 21.6 | |
| 3 | 27710 55.4 | 22321 44.6 | | 38849 78.1 | 10909 21.9 | |
| 4 | 28391 57.5 | 20988 42.5 | | 38308 78.2 | 10675 21.8 | |
| Least disadvantaged | 28693 58.4 | 20456 41.6 | | 36974 76.8 | 11201 23.3 | |
| **Maternal region of birth** | | | | | | |
| Australia | 85903 55.2 | 69848 44.9 | <0.001 | 121769 78.9 | 32573 21.1 | <0.001 |
| Americas | 1981 56.5 | 1525 43.5 | | 2662 76.6 | 809 23.4 | |
| North Africa and the Middle East | 4042 45.8 | 4783 54.2 | | 5569 63.2 | 3244 36.8 | |
| North-East Asia | 6978 54.4 | 5845 45.6 | | 9310 72.7 | 3504 27.4 | |
| North-West Europe | 4268 60.0 | 2892 40.4 | | 5688 80.4 | 1385 19.6 | |
| Oceania and Antarctica | 3501 49.8 | 3527 50.2 | | 5008 71.3 | 2013 28.7 | |
| South-East Asia | 9391 58.8 | 6580 41.2 | | 12103 75.9 | 3842 24.1 | |
| Southern and Central Asia | 17405 60.5 | 11346 39.5 | | 22858 79.1 | 6025 20.9 | |
| Southern and Eastern Europe | 2120 46.8 | 2411 53.2 | | 3282 72.6 | 1240 27.4 | |
| Sub-Saharan Africa | 2625 48.2 | 2827 51.9 | | 3570 65.8 | 1860 34.3 | |
| **Smoking during pregnancy** | | | | <0.001 | | <0.001 |
| None | 123418 56.4 | 95252 43.6 | | 169219 77.9 | 47977 22.1 | |
| Smoked at all | 9497 43.6 | 12278 56.4 | | 15718 72.2 | 6049 27.8 | |
| **Admission status** | | | | <0.001 | | <0.001 |
| Public | 102875 54.5 | 86037 45.5 | | 151963 80.0 | 38121 20.1 | |
| Private | 35808 57.9 | 26042 42.2 | | 40508 68.4 | 18729 31.6 | |
| **Location of hospital** | | | | <0.001 | | <0.001 |
| Metropolitan area | 107277 56.2 | 83570 43.8 | <0.001 | 142457 75.2 | 46947 24.8 | |
| Rural area | 31421 52.4 | 28588 47.6 | | 50030 83.4 | 9926 16.6 | |

*Chi square for vaccinated vs not vaccinated.
including many potential confounding factors from the perinatal data system. In addition, we were only able to control for socioeconomic status by an area-level summary statistic for a woman’s census district, rather than individual-level data on family income. A further limitation of our data is the lack of information on the timing of vaccination during pregnancy. The VPDC does not collect date of vaccination therefore analysis according to timing of exposure (vaccination) could not be done. Immortal time bias refers to a period of follow-up during which, by study design the outcome cannot occur. In pregnancy studies, this means that the protective effect of the intervention may be overestimated as the shortened pregnancy duration association with adverse fetal outcomes limits the opportunity to be exposed. When considering studies exploring the risk or benefit of vaccination, it necessarily biases the results in favour of the treatment by conferring a spurious advantage to the treatment group. In previously published studies however, even when accounting for this, some associations remain (26).

**Implications**

Irrespective of mechanisms, every year 2.6 million babies are stillborn around the world (16). Referred to as the ‘silent epidemic’, there has been a worldwide call to action to address this. In 2014, the Every Newborn Action Plan proposed a global target of reducing the stillbirth rate to ten per 1000 births or less in every country by the year 2035 (27). Similarly, an estimated 15 million babies are born preterm annually around the world, with 80% of these being born in sub-Saharan Africa and Asia (28). Prematurity is the world’s single biggest cause of newborn death, and the second leading cause of all child deaths, after pneumonia. In many countries the rate of PTB is actually increasing (28), highlighting the urgent need to find new strategies that address both of these global health issues. If our findings represent a causal relationship, then there may be opportunities to finally make a significant impact in reducing these adverse obstetric outcomes that have been stubbornly resistant to interventions (29).

Critically, many of the countries with the highest rates of stillbirth and PTB are yet to add influenza or pertussis vaccine to their maternal immunisation programme. In 2014, only 115 of 194 countries (59%) had a national influenza policy and, of these, fewer than half included pregnant women (30). The addition of maternal vaccines beyond tetanus toxoid containing vaccine in low- and middle-income countries has been slow (31). Likely reasons for this include the cost and/or challenges with prioritization over other healthcare expenses. Further research is required across all income settings, to better understand the immune trajectory of pregnancy and how maternal immunisation may impact this immune trajectory and other health outcomes. Any non-specific vaccine effects may ultimately provide further health economic justification for considering the addition of maternal vaccines in national immunisation programmes.

**CONCLUSION**

While the initial causes of PTB and stillbirth are clearly complex and diverse, many are a spectrum of one underlying immune mediated...
problem. Our observation that maternal immunisation may be associated with reduction in the incidence of stillbirth, PTB and SGA offers hope that we can purposefully harness and manipulate maternal immunology to improve pregnancy outcomes. Our results have also identified important areas for future research, such as the need to understand the immunological effects of vaccination during pregnancy, by type of vaccination, number and timing of vaccination, and to explore this in relation to the pathophysiology of PTB and stillbirth. Such insights may shed light on new opportunities to prevent PTB and stillbirth.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because the release of potentially identifiable information to any persons not listed in s.41 of the Public Health and Wellbeing Act is only permitted for the purpose of research. Requests to access the datasets should be directed to Consultative Council on Obstetric and Paediatric Mortality and Morbidity, Victorian Perinatal Data Collection.

ETHICS STATEMENT

This study was approved by the Monash University Human Research and Ethics Committee. Written informed consent for participation was not required for this study in accordance with national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

MG and EW developed the concept, contributed to interpretation of the data and writing of the manuscript. M-AD performed the statistical analysis, contributed to interpretation of the data and writing of the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fimmu.2021.704254/full#supplementary-material
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