Burden of respiratory syncytial virus-associated acute respiratory infections during pregnancy

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PROMISE
Preparing for RSV Immunisation and Surveillance in Europe

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Background

RSV vaccines for pregnant individuals (PI) have recently been licensed in USA and Europe. While the primary goal of antenatal RSV vaccination is focused on providing protection to young infants, antenatal vaccination could also have protective benefits for PI and the pregnancy similar with other maternal immunizations [1, 2]. Scarce data are available about the burden of RSV infection among PI or the association between antenatal RSV and adverse perinatal outcomes [3]. We conducted a systematic review and meta-analysis of studies that reported laboratory tested RSV among PI to estimate the proportion of ARI episodes that are positive for RSV, incidence rates of antenatal RSV infection, and number of RSV-associated hospitalizations and deaths. We also characterized RSV-associated perinatal outcomes.

Methods

We searched articles in 5 databases: Medline (Ovid), Embase (Ovid), Global Health (Ovid), Web of Science, and Global Index Medicus. We contacted observational study authors to obtain additional unpublished data pertinent to our review. We included data from studies related to PI with ARI who had been tested for RSV by culture, antigen, serology, and molecular testing. We used random-effects meta-analysis to estimate the proportion of PI with ARI who were positive for RSV; the RSV incidence rate; the RSV-associated hospitalization rate; and the association between RSV infection and perinatal outcomes: preterm birth (birth before 37 weeks' gestational age), low birth weight (<2500 g), stillbirth, and miscarriage [4].
PROSPERO registration: CRD42022372847

Results

Included studies identification (see Figure 1)
Database search: 6 studies; citation search: 2 studies; and unpublished Data: provided by authors of 3 observational studies.

Included studies characteristics

- Data collection period: 2010 to 2022
- Study locations: High-income countries (6 studies): (Australia, Canada, Israel, Panama, and United States), Upper-middle-income countries (2 studies): (South Africa and Thailand), and Lower-middle-income countries (4 studies): (El Salvador, Kenya, Mongolia, and Nepal)
- Study duration: Year-round (4 studies): duration: 2-6 years and Seasonally (7 studies): duration: 1-8 seasons
- Gestational age details (5 studies): all 3 trimesters: 1 study, second and third trimesters: 3 studies, and first and second trimesters: 1 study

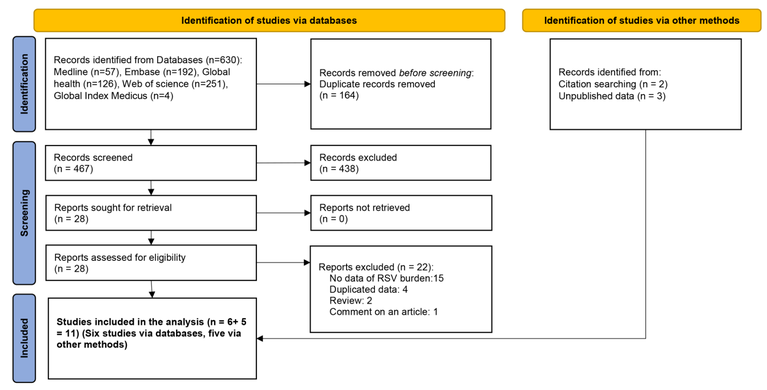

Figure 1: Study selection

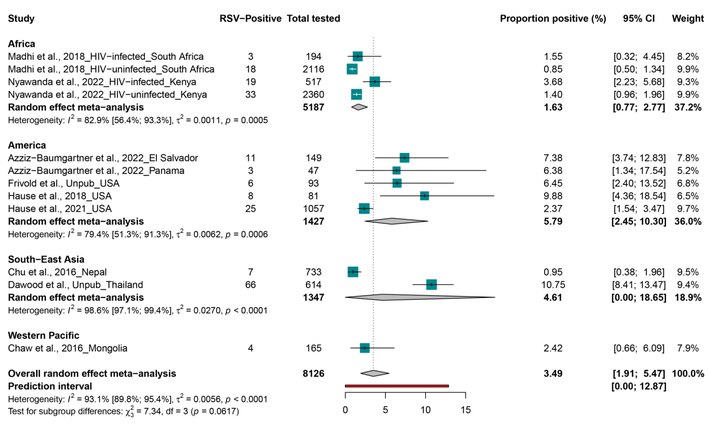

Figure 2: Proportion positive for RSV in pregnant individuals with acute respiratory infections

Proportion of pregnant individuals with RSV-positive acute respiratory infections

- Total tested: 8126; total RSV cases: 203; RSV positivity range [0.9%-10.7%]
- Pooled RSV positivity **(see Figure 2)**: 3.4% (95% CI: 1.9; 5.4)
- RSV positivity by study timing (p<0.001): during RSV seasons: 4.4% (95% CI: 0.8; 10.1) and year-round studies: 2.5% (95% CI: 1.3; 4.0)
- RSV positivity by case ascertainment settings: outpatients: 9.8% (95% CI: 4.3; 18.5), community participants: 5.5% (95% CI: 0.6; 14.0), outpatients & inpatients: 3.6% (95% CI: 0.3; 8.8), and community, outpatient, & inpatient participants: 1.7% (95% CI: 0.8; 2.7)

Incidence rate of RSV in pregnant individuals

- RSV incidence rate range: [0.2; 24.0] per 1000 person-months
- Pooled RSV Incidence rate **(see Figure 3)**: 2.1 [CI 95%: 1.3; 3.0] per 1000 person-months
- Incidence rate by study timing (p<0.01): seasonal studies: 1.7 [CI 95%: 1.0; 2.3] per 1000 person-months and year-round studies: 4.9 [0.3; 9.5] per 1000 person-months

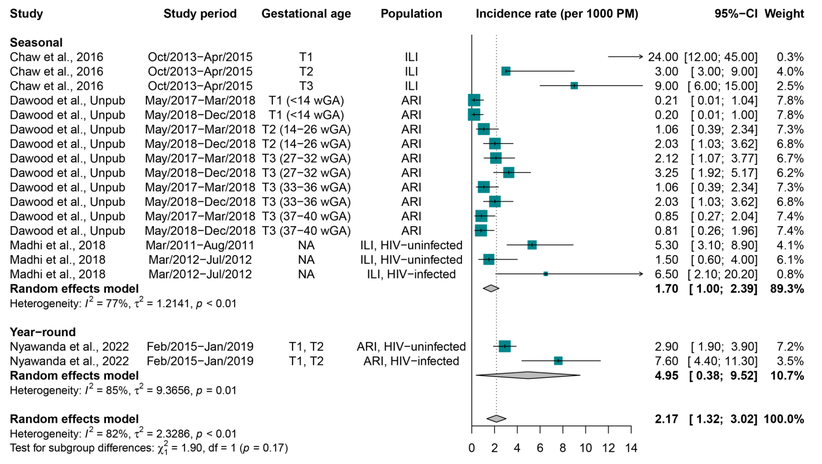

Figure 3: Incidence rate of RSV in pregnant individuals

ARI: Acute respiratory infections; HIV: human immunodeficiency virus; ILI: Influenza-like illness; NA: Not available; PM: person-months; RSV: Respiratory syncytial virus; T1: First trimester; T2: Second trimester; T3: Third trimester; wGA: weeks' gestational age

RSV-associated hospitalizations and deaths in pregnant individuals

- RSV hospitalization rate in PI: El Salvador study (3.0 per 1000 person-years) (Azziz-Baumgartner et al., 2022) and Unpublished study from Thailand (2.4 [CI 95%: 0.4; 17.3] per 1000 person-years) (Dawood et al.)
- No deaths (203 RSV+ among 4708 PI; n= 5 studies).

Perinatal outcomes in pregnant individuals with RSV-associated acute respiratory infections (see Figure 4)

- Outcomes not impacted by antenatal RSV infection: stillbirths, small for gestational age, miscarriage, low birth weight
- Difference in odds of preterm birth: Significant difference between RSV-positive vs. RSV-negative PI; Odds Ratio (OR): 3.6 [95% CI: 1.3; 10.3]; (3 studies)

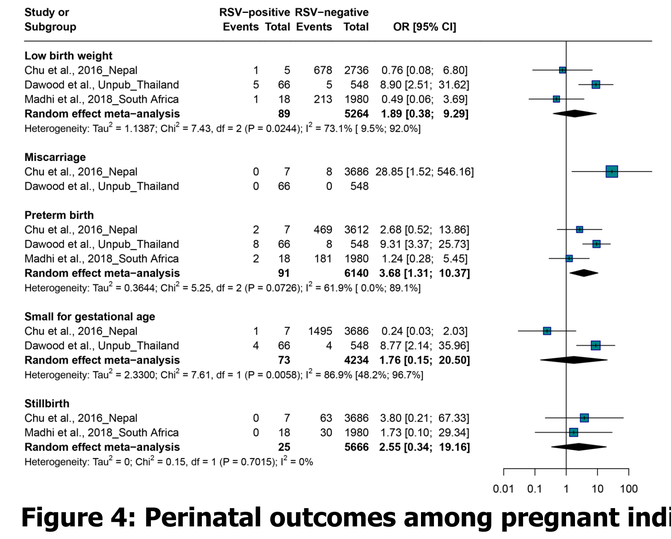

Figure 4: Perinatal outcomes among pregnant individuals with and without RSV

Conclusions and implications

- RSV incidence rates in PI comparable to those observed in adults aged 18-49 years with comorbidities;
- Compared with older adults or young children, incidence of RSV-associated severe disease, particularly hospitalizations in PI, appears to be lower;
- Few data available on the burden (hospitalizations and deaths) of RSV in PI;
- Few studies have been conducted on potential correlations between RSV infection during pregnancy and perinatal outcomes.
- As the quest for passive immunization with a safe and effective maternal RSV vaccine continues, these results underscore the need for ongoing research to ensure a comprehensive understanding of the RSV infection effects during pregnancy.

References

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The project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under Grant Agreement No. 101034339.

This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.