

Defining the Epidemiology and Burden of Severe Respiratory Syncytial Virus Infection Among Infants and Children in Western Countries

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Abbreviations

- ARI: Acute respiratory infection
- hBoV: Human bocavirus
- hMPV: human metapneumovirus
- ICU: Intensive care unit
- LOS: Length of stay
- MV: Mechanical ventilation
- REGAL: RSV Evidence — a Geographical Archive of the Literature
- RV: Rhinovirus
- RSV: Respiratory syncytial virus
- RSVH: Respiratory syncytial virus hospitalization
- SOE: Strength of Evidence
- wGA: weeks' gestational age

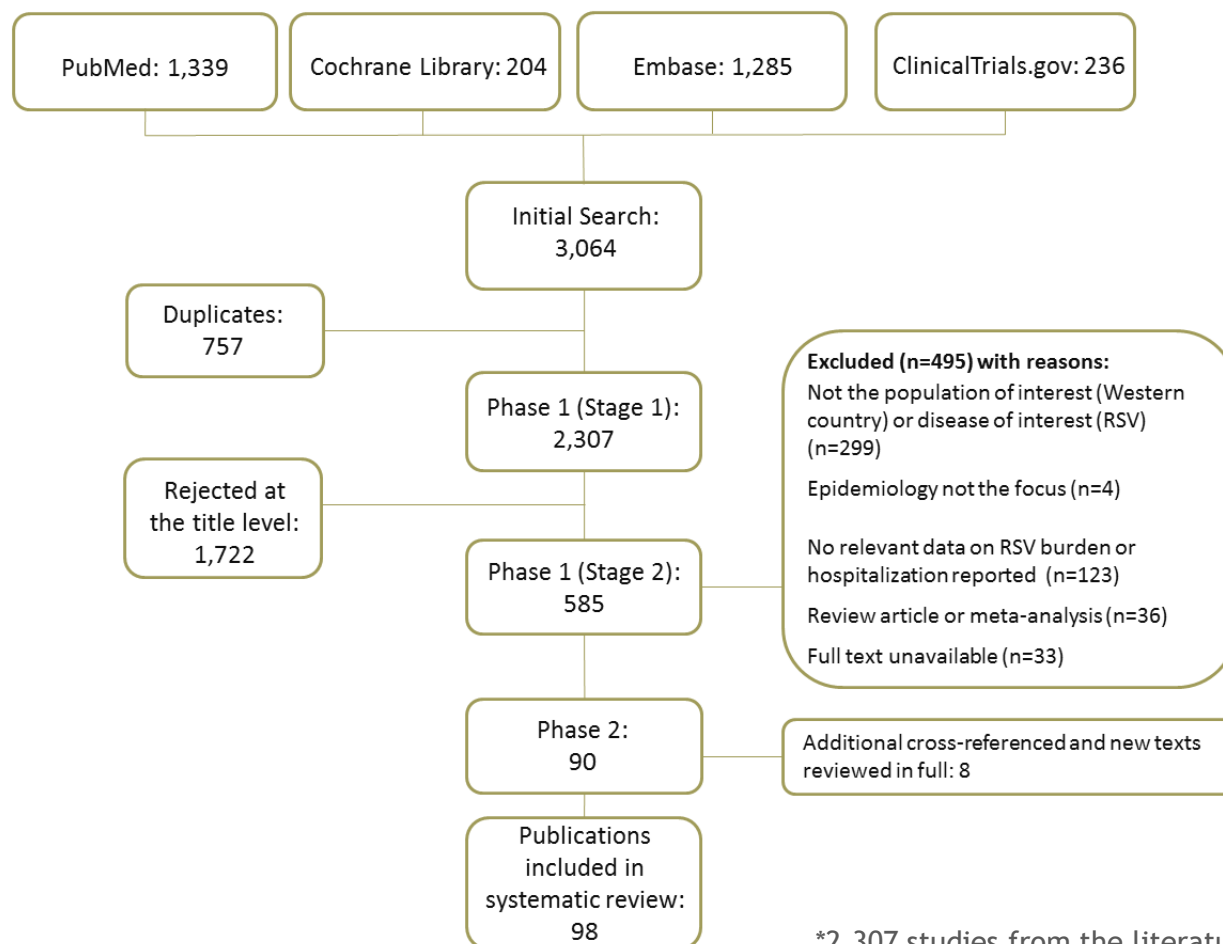
REGAL 1: Overall Epidemiology and Burden of RSV

- Target population was previously healthy term children or studies with mixed populations of term and preterm (<37 wGA) children and those with comorbidities
- Short-term outcomes of interest included:
 - Hospitalization rates due to severe RSV
 - Hospital LOS
 - ICU admission and LOS
 - Oxygen requirement
 - Need for and duration of MV and/or non-invasive ventilation
 - Case-fatality rates
 - Risk factors for severe RSVH

‘What is the disease burden of RSV infection in Western countries, and what are the associated risk factors for severe disease?’

Systematic Review

- 2,315 studies* were identified of which 98 were included



*2,307 studies from the literature search (excluding duplicates) plus 8 additional cross-references

RSV is a major cause of infant hospitalization (high SOE)

RSV has been associated with

12-63%
of all ARIs

19-81%
of all viral ARIs

Hospitalization rates for RSV ARIs
increased with decreasing age

≤1 year
3.2-42.7
/1000/year

1-4 years
0.6-7.8
/1000/year

Of children hospitalized with
RSV-related ARI/bronchiolitis

>70%

had no underlying medical
conditions

75-90% of RSVHs were in infants ≤12 months

Annual incidence of RSVH varies over time (moderate SOE)

- In temperate, northern hemisphere countries, the RSV season typically starts in **October** or **November**, peaks between **December** and **February** and ends in **March** or **April**
- The annual incidence of RSVH varied over time; some longitudinal studies reported an **increase**, some a **decrease**, and others **relative stability**
- Season-on-season RSVH rates varied by up to a factor of **2** to **3** in the same geographic region

Highlighted the need for rigorous and uniform longitudinal surveillance

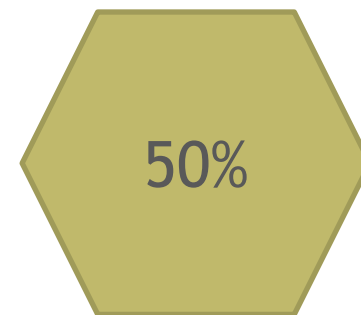
RSV is associated with a high rate of co-infection (high SOE)

- RSV has shown a high rate of co-infection with respiratory viruses with similar seasonal patterns

e.g. influenza, RV, hMPV, HBoV as well as bacterial pathogens

- Some studies reported that multiple infections were associated with more severe disease than with single RSV infections. Others found the opposite relationship or no differences

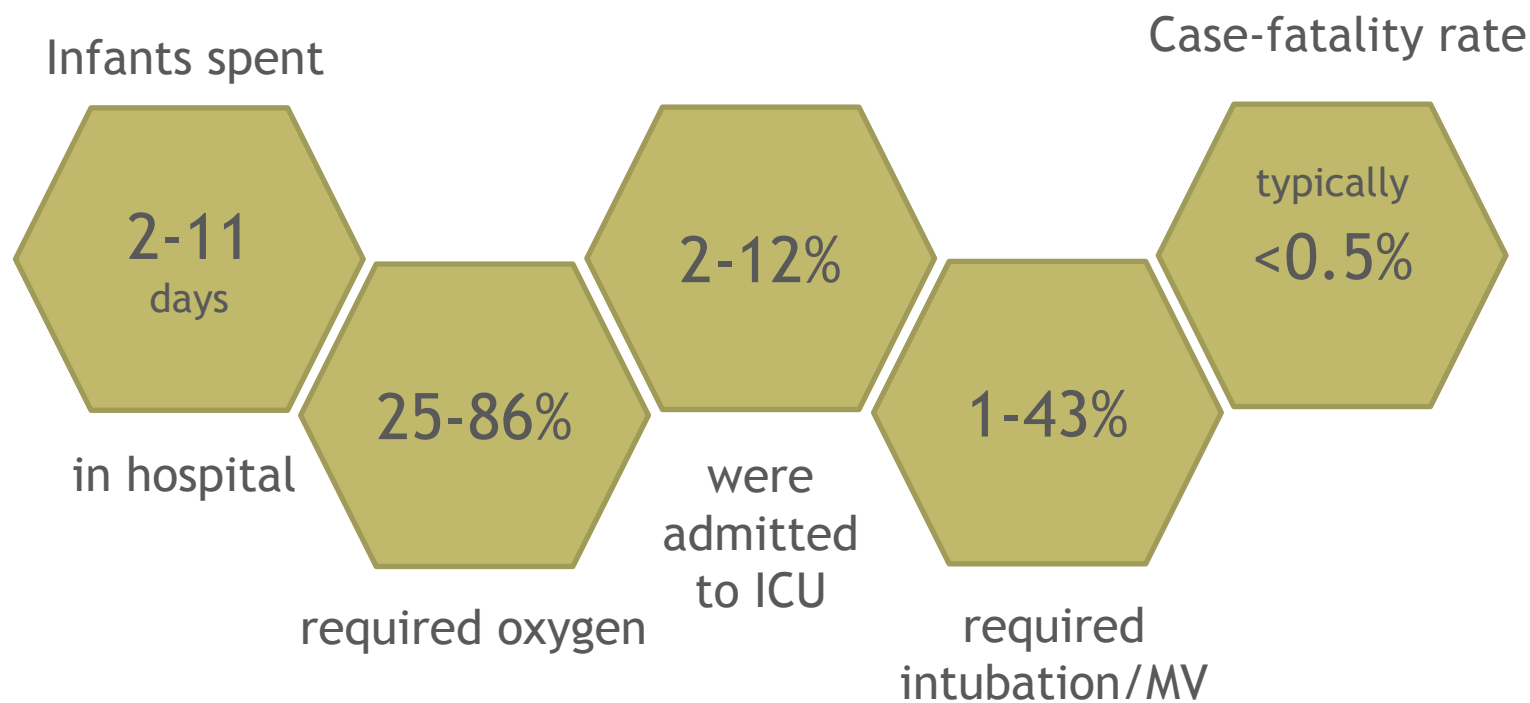
Co-infections have been reported to occur in up to



of RSV-hospitalized children

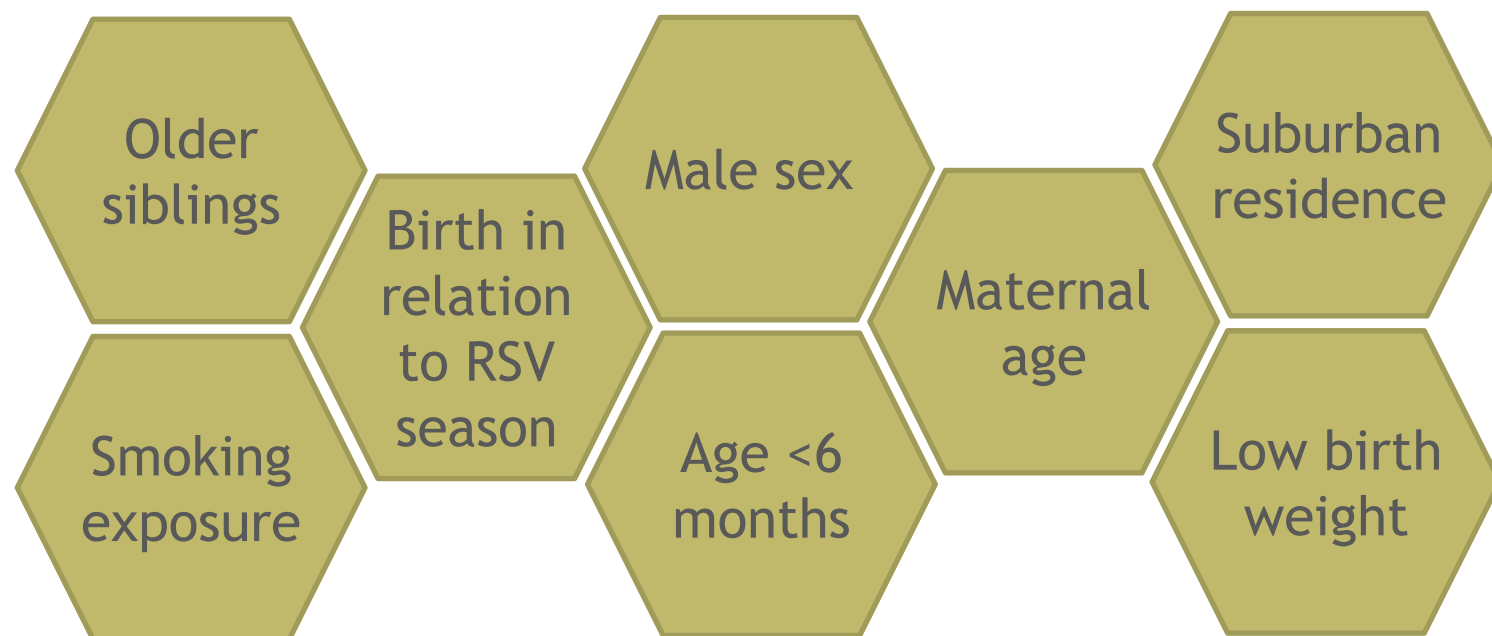
Co-infections represented a major confounder in burden of disease analyses of RSV infection

RSV is associated with significant morbidity (moderate SOE)



RSV ARI has been associated with more severe disease than non-RSV ARI

Several independent risk factors for RSVH have been identified (high SOE)



Risk factors are important to identify strategies to prevent infections and to inform guidelines for RSV prophylaxis

Key statements/Findings	Level of Evidence
In western countries, RSV has been associated with 12-63% of all ARIs and 19-81% of viral ARIs causing hospitalization in children	1
Annual hospitalization rates for RSV-associated ARIs ranged from 3.2/1000 children to 42.7/1000 in the first year of life, and decreased with decreasing age to 0.6/1000-1.78/1000 in children 1-4 years	1
Longitudinal studies have reported varying annual incidences of RSVH over time: some have reported an increase, some a decrease, and others relative stability	2

RSVH is associated with significant morbidity and represents a large burden of disease in Western countries

Key statements/Findings	Level of Evidence
RSV co-infections were frequent (bacterial and viral co-infections have been reported in up to 50% of patients hospitalized with severe RSV ARI). However, the relationship with severity of disease was not clear	1
Infants spend an average of 2-11 days in hospital for RSV ARIs, approximately 2-12% are admitted to the ICU, and the mortality rate is <0.5% and limited to children with severe comorbidity	1/2
A number of risk factors have been independently associated with an increased risk for severe RSV disease in children, including: male sex; age <6 months; birth during the first half of the RSV season; crowding; siblings and day-care exposure	1

RSVH is associated with significant morbidity and represents a large burden of disease in Western countries

Further development

- Key areas for research:
 - Epidemiological studies to determine the true burden of severe RSV disease, particularly in the outpatient setting
 - Impact of co-infections on severity of disease
 - Case-fatality rates and associated risk factors such as RSV seasons
 - Geographical differences in RSV epidemiology
- Well-coordinated surveillance programs with high RSV testing rates for inpatients and outpatients would be the ideal
- Development of more effective preventative strategies - in high-risk and healthy children - is essential to reduce the overall burden of RSVH

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