Infectious Diseases and Therapy

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REGAL: RSV Evidence — a Geographical Archive of the Literature

Objectives and Methodology

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Abbreviations

- BPD: Bronchopulmonary dysplasia
- CHD: Congenital heart disease
- CLD: Chronic lung disease
- ICU: Intensive care unit
- LOS: Length of stay
- MV: Mechanical ventilation
- RCT: Randomized controlled trial
- RSV: Respiratory syncytial virus
- RSVH: Respiratory syncytial virus hospitalization
- RTI: Research Triangle Institute
- SOE: Strength of Evidence
- wGA: weeks' gestational age

REGAL: RSV Evidence — a Geographical Archive of the Literature

- Understanding the incidence and complications of RSV disease is essential:
  - Planning strategies to control RSV infection
  - Optimize the use of RSV prophylaxis and future RSV vaccines

- Primary objective:
  - To carry out a series of systematic literature reviews
  - To assess, quantify, summarize and grade the evidence base

- Outcome:
  - Defined the current state of the art in our understanding of RSV
  - Identified gaps in our knowledge and future areas of research

REGAL: Expert Panel

Neonatologists, Pediatricians, Pediatric Infectious Disease Specialists, Pediatric Cardiologists, and Pediatric Pulmonologists:

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REGAL: Study Questions

Seven specific research questions were addressed:

1. What is the overall epidemiology and disease burden of severe RSV infection in Western countries, and what are the associated risk factors for RSVH?[1]
2. What is the predisposition and associated morbidity, long-term sequelae and mortality of preterm infants (<37 wGA) without CLD/BPD or CHD, overall, and split by gestational age segments, to severe RSV infection, and what are the risk factors associated with RSVH?[2]
3. What is the predisposition and associated morbidity, long-term sequelae and mortality of infants with underlying CLD/BPD to severe RSV infection in Western countries?[3]
4. What is the predisposition and associated morbidity, long-term sequelae and mortality of infants with underlying CHD to severe RSV infection in Western countries?[4]
5. What is the nature, incidence and impact of long-term respiratory morbidity associated with RSVH in infancy in Western countries, specifically early and late wheeze?[5]
6. What other groups of infants with underlying medical conditions or chronic diseases are at high risk of RSVH and associated morbidity?[6]
7. What are the optimal approaches and strategies for the prevention and treatment of severe RSV infection and what are the future perspectives in this regard?[7]

1. Bont L et al. Infect Dis Ther. 2016.
2. Figueras-Aloy J et al. Infect Dis Ther. 2016.
3. Paes B et al. Infect Dis Ther. 2017.
4. Checchia PA et al. Infect Dis Ther. 2017.
5. Fauroux B et al. Infect Dis Ther. 2017.
6. Manzoni P et al. Infect Dis Ther. 2017.
7. Simões EAF et al. Infect Dis Ther. 2018.

REGAL: Overall Methodology

- **Systematic review:** MEDLINE (PubMed), Embase, The Cochrane Library, and Clinicaltrials.gov
- **Time and Place of study:**
  - Western countries: The United States, Canada, and Europe (including Turkey and the Russian Federation)
  - Published between Jan 1, 1995 and Dec 31, 2015
- **Age:** ≤18 years
- **Additional search:** hand-searching of online journals and reference lists of identified citations and relevant meeting abstracts
- **Type of study:** RCTs, non-RCTs, crossover trials, single-arm studies, cohort studies, case–control studies, case series, registries, and medical databases

REGAL: Definition of severe RSV infection and Outcomes

- Severe RSV infection defined as: 'RSV infection requiring hospitalization'

Short-term outcomes	Long-term & other outcomes
• Incidence rates of severe RSV infection requiring medical treatment during the first or subsequent years of life • RSVH rates • LOS in hospital • RSVH-related outcomes ○ ICU admission, LOS in ICU, requirement for, and duration of, MV, non-invasive ventilation, oxygen • Case-fatality rate • Risk factors for RSVH • Effectiveness of palivizumab in reducing RSVH	• Subsequent respiratory disease, including recurrent wheezing and asthma up to adulthood (≤18 years) following RSVH in infancy • Effectiveness of palivizumab in reducing recurrent wheeze/asthma • Rates and associated morbidity, long-term sequelae and mortality in different subgroups of children with or without CLD/BPD • Future developments in RSV research

Bont L, et al. Infect Dis Ther. 2017.

REGAL: Data Synthesis

- Included publications were graded according to the Oxford Centre for Evidence-Based Medicine Levels of Evidence

Level	Definition
1	• Local and current random sample surveys or censuses
2	• Systematic review of surveys that allow matching to local circumstances
3	• Local non-random sample
4	• Case series

- For RCTs, a quality assessment for each citation was carried out using the five-point (1 = low quality; 5 = high quality) Jadad Scale

- For each study, a risk of bias assessment was undertaken:
  - Observational studies: RTI Item Bank (score of 1 = very high risk of bias; score of 12 = very low risk of bias)
  - RCTs: Cochrane Collaboration's tool for assessing risk of bias

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