

## REGAL: RSV Evidence — a Geographical Archive of the Literature

### Objectives and Methodology

Louis Bont • Paul A. Checchia • Brigitte Fauroux • Josep Figueras-Aloy •  
Paolo Manzoni • Bosco Paes • Eric A. F. Simões • Xavier Carbonell-Estrany

Infect Dis Ther.

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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

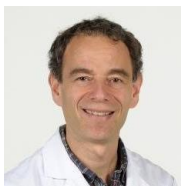
Neonatologists, Pediatricians, Pediatric Infectious Disease Specialists, Pediatric Cardiologists, and Pediatric Pulmonologists:



**Xavier Carbonell-Estrany**  
*Hospital Clinic, Institut  
d'Investigacions Biomediques August  
Pi Suñer (IDIBAPS), Barcelona, Spain*



**Josep Figueras-Aloy**  
*Hospital Clínic, Catedràtic de  
Pediatría, Universitat de Barcelona,  
Barcelona, Spain*



**Louis Bont**  
*University Medical Center Utrecht,  
Utrecht, The Netherlands*



**Paolo Manzoni**  
*Neonatology and NICU, Sant'Anna  
Hospital, Turin, Italy*



**Paul A. Checchia**  
*Baylor College of Medicine, Texas  
Children's Hospital Houston, Texas,  
USA*



**Bosco Paes**  
*Department of Pediatrics (Neonatal  
Division), McMaster University,  
Hamilton, ON, Canada*



**Brigitte Fauroux**  
*Necker University Hospital and Paris  
5 University, Paris, France*



**Eric A. F. Simões**  
*Colorado School of Public Health,  
University of Colorado School of  
Medicine, Aurora, CO, USA*

## 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?<sup>1</sup>
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?<sup>2</sup>
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?<sup>3</sup>
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?<sup>4</sup>
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?<sup>5</sup>
6. What other groups of infants with underlying medical conditions or chronic diseases are at high risk of RSVH and associated morbidity?<sup>6</sup>
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?<sup>7</sup>

## 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:**  $\leq 18$  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
<ul style="list-style-type: none"><li>• Incidence rates of severe RSV infection requiring medical treatment during the first or subsequent years of life</li><li>• RSVH rates</li><li>• LOS in hospital</li><li>• RSVH-related outcomes<ul style="list-style-type: none"><li>○ ICU admission, LOS in ICU, requirement for, and duration of, MV, non-invasive ventilation, oxygen</li></ul></li><li>• Case-fatality rate</li><li>• Risk factors for RSVH</li><li>• Effectiveness of palivizumab in reducing RSVH</li></ul>	<ul style="list-style-type: none"><li>• Subsequent respiratory disease, including recurrent wheezing and asthma up to adulthood (<math>\leq 18</math> years) following RSVH in infancy</li><li>• Effectiveness of palivizumab in reducing recurrent wheeze/asthma</li><li>• Rates and associated morbidity, long-term sequelae and mortality in different subgroups of children with or without CLD/BPD</li><li>• Future developments in RSV research</li></ul>

## REGAL: Data Synthesis

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

Level	Definition
1	<ul style="list-style-type: none"><li>• Local and current random sample surveys or censuses</li></ul>
2	<ul style="list-style-type: none"><li>• Systematic review of surveys that allow matching to local circumstances</li></ul>
3	<ul style="list-style-type: none"><li>• Local non-random sample</li></ul>
4	<ul style="list-style-type: none"><li>• Case series</li></ul>

- 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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