

INCREASED RISK OF WHEEZING ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) IN A MULTI-COUNTRY CROSS-SECTIONAL SURVEY OF PARENT'S PERCEPTION

EAACI 2024

31st May – 3rd June, Valencia, Spain

Adnan Custovic, Jorge Mestre-Ferrandiz, Leyla Kragten-Tabatabaie, Julie Laurent, Laury Sellem, Mary Koslap-Petraco, Chiara Cadeddu.

Disclosures

Authors Affiliations

Prof Adnan Custovic¹, Dr Jorge Mestre-Ferrandiz², Dr Leyla Kragten-Tabatabaie³, Ms Julie Laurent⁴, Dr Laury Sellem⁴, Dr Mary Koslap-Petraco⁵, Dr Chiara Cadeddu⁶

1. Professor of Paediatric Allergy, National Heart and Lung Institute, Imperial College London, London, UK
2. Health Economist, Profesor Asociado, Universidad Carlos III, Madrid, Spain
3. ReSVINET foundation, Board of Directors, Zeist, The Netherlands
4. Carenity, Online Patient Community, Paris, France
5. Clinical Assistant Professor, Stony Brook University School of Nursing, NY, USA
6. Erasmus School of Health Policy & Management, Erasmus University Rotterdam

COI disclosure

AC declares the payments received for the support provided throughout the project and reports personal fees from Novartis, personal fees from Sanofi, personal fees from Stallergenes Greer, personal fees from AstraZeneca, personal fees from Worg Pharmaceuticals, from GSK, outside the submitted work. JMF declares the payments received for the support provided throughout the project and reports consulting honoraria from Sanofi in other related work to RSV. LKT, MKP, LS, and JL declare no conflict of interests. CC declares having received expert consultant fees from Sanofi, expert consultant fees from GSK, and expert consultant fees from MSD.

Funding statement

This project is supported by Sanofi, and financially supported by Sanofi and AstraZeneca.

Background and objectives

- By two years of age, >90% of children will have had at least one RSV infection.
- Among infants, RSV is a leading cause of hospitalization for acute lower respiratory tract diseases such as bronchiolitis and pneumonia.
- RSV bronchiolitis may be associated with an increased risk of subsequent wheezing.
- With the upcoming arrival of new immunization solutions, it is important to document the full burden of RSV including its short/medium term complications.

References: Shi et al (Lancet, 2017), Xing & Proesman (Eur J Pediatr, 2019), Binns et al (J Paediatr Child Health 2022)

- 1 Document potential link between RSV infection and subsequent wheezing based on parents' insights**
- 2 Document impact of RSV infection and subsequent wheezing on healthcare and family cost**
- 3 Understand parents' perception of unmet needs and expectations for preventative solutions**

Methods

Study design

- Cross-sectional self-reported online survey (February 10th to April 28th 2023):
 - (1) Parents of children who had a past diagnosed case of RSV;
 - (2) Parents of children who had not been infected with RSV.

Data sources

- Recruitment through Carenity platform:
 - Over 500,000 members in 5 European countries and the United States.
 - Targeted Carenity members aged 25 to 40 years registered in the US, UK, Spain and Italy.
 - Invited to participate in the survey via emails and private messages (~7% of the total sample).
- Recruitment through online campaigns and local partners:
 - Targeted online advertisements about the survey were displayed on Google and Facebook (~3%)
 - Local partners specialised in patient studies (90% of the total sample).

Methods

Inclusion criteria:

- Parents of children under age 6 years; living in the US, UK, Spain, or Italy
- Age 18 years or older
- **RSV group:**
 - Parents of children diagnosed with bronchiolitis by a Health Care Professional (HCP) or tested positive for RSV during their first and second year of life in the past 5 years.
- **Reference group:**
 - Have never been diagnosed or hospitalised with bronchiolitis or RSV infection.

Questionnaire: 45 questions, including 4 open-ended text fields

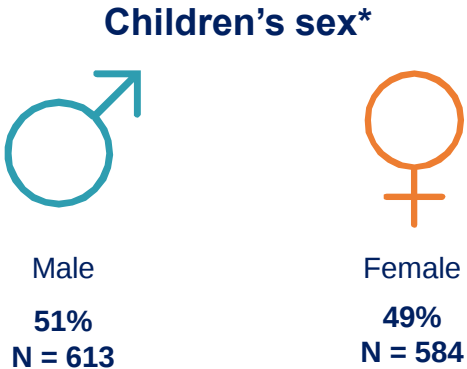
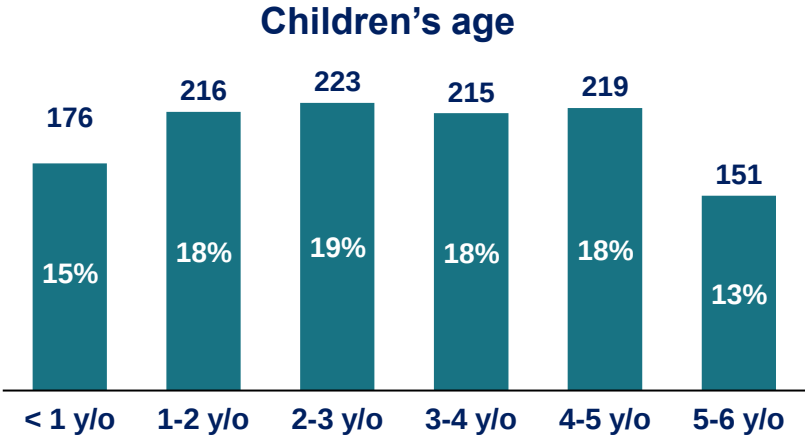
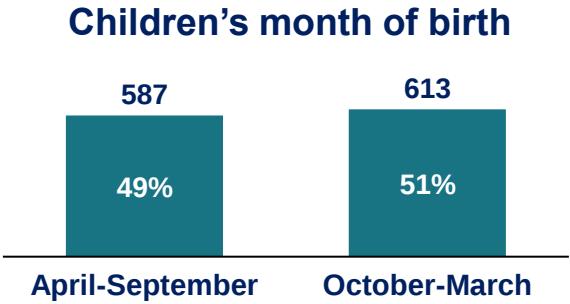
Ethical Approval: IRB approval from WIRB-Copernicus.

Statistical analyses

- χ^2 or Fisher's exact tests for categorical outcomes; Student or Wilcoxon's rank sum tests for continuous.
- Multivariable logistic regression models to assess the association between the presence of wheezing in children and risk factors

Results: Study population; n=1200

				
Number	300	300	300	300
RSV group	150	150	150	150
Reference group	150	150	150	150

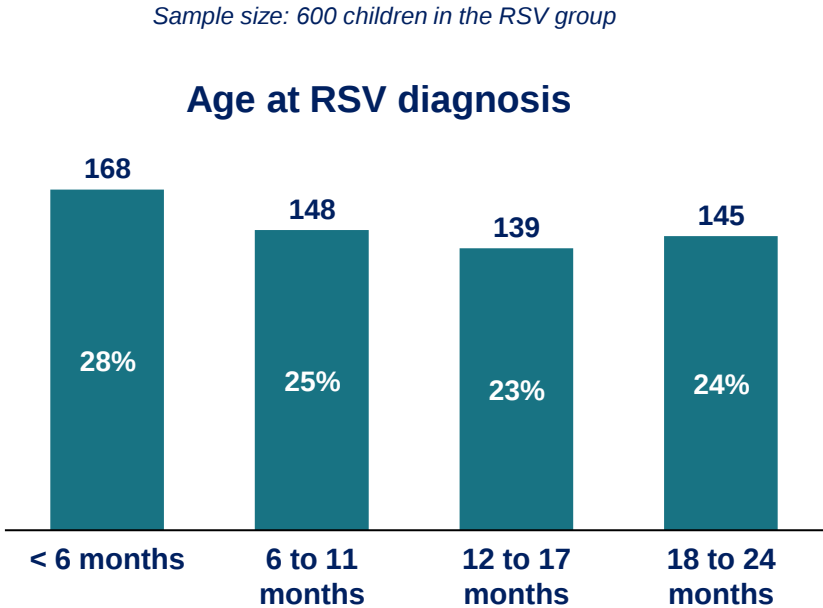
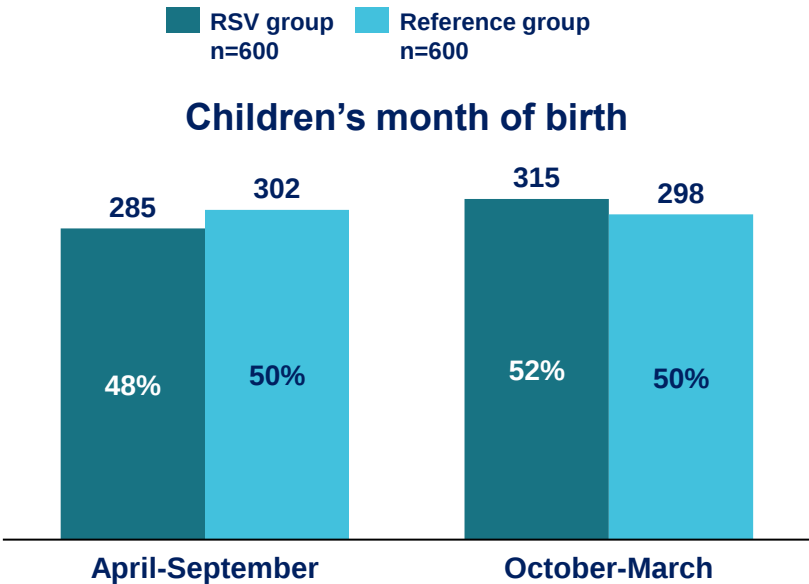


* n = 3 answered "prefer not to say"

Average age: 2.9 years; similar distribution across 1-year age categories from 0 to 6 years; similar proportions born in the Spring-Summer or in the Autumn-Winter seasons.

Characteristics of the study population

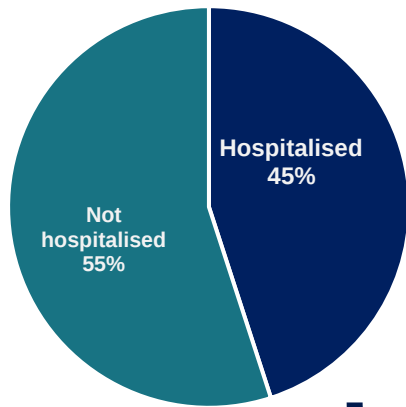
- Participants in RSV group younger (median age 2.7 vs. 3.1 years, $p=0.03$), significantly more likely to have maternal history of asthma and allergies, more likely to be born pre-term (25% vs 18%, $p<0.001$) and have personal history of chronic disorders.
- Month of birth did not differ between the RSV and Reference groups.
- The distribution of children’s age at diagnosis was consistent across 6-month increment categories and was similar in all countries.



RSV episodes and hospital admissions

Sample size: 600 children in the RSV group

Hospitalisation as a result of bronchiolitis or RSV infection

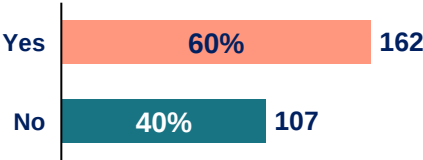


Severe RSV group
(hospitalised children)
N = 269

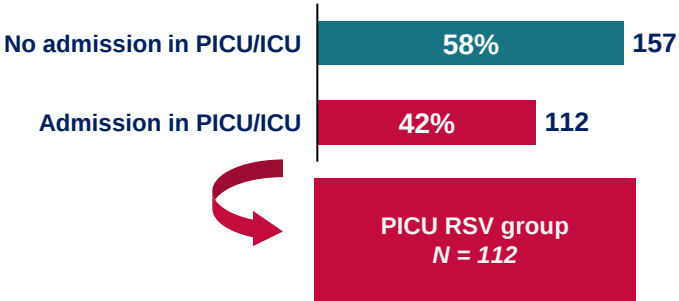
Average length of hospital stay (in days)

Estimator	Value
Mean	8.3
95% CI	[7.0 ; 9.7]
Standard Deviation (SD)	11.3
1 st quartile (25%)	3.0
Median	5.0
3 rd quartile (75%)	11.3

Placement under respiratory support



Admission in paediatric intensive care unit (PICU)

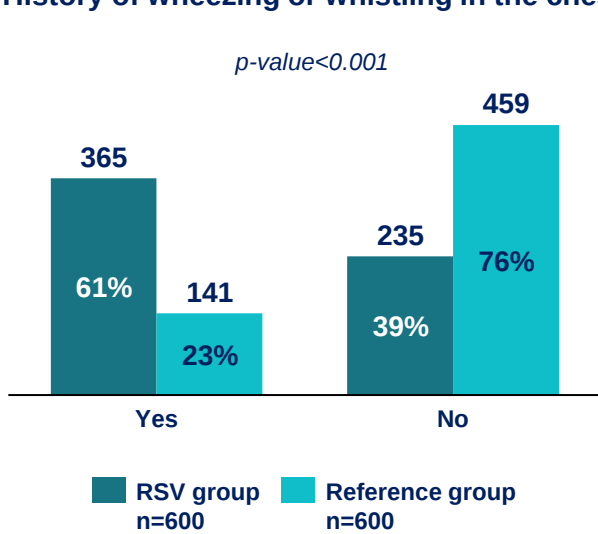


- 45% of children in the RSV group were hospitalised; median hospital stay 5 days.
- Among those, 42% admitted to a PICU, and 60% placed under respiratory support.

Association between RSV infection and wheezing

Sample size: 1200 children

History of wheezing or whistling in the chest

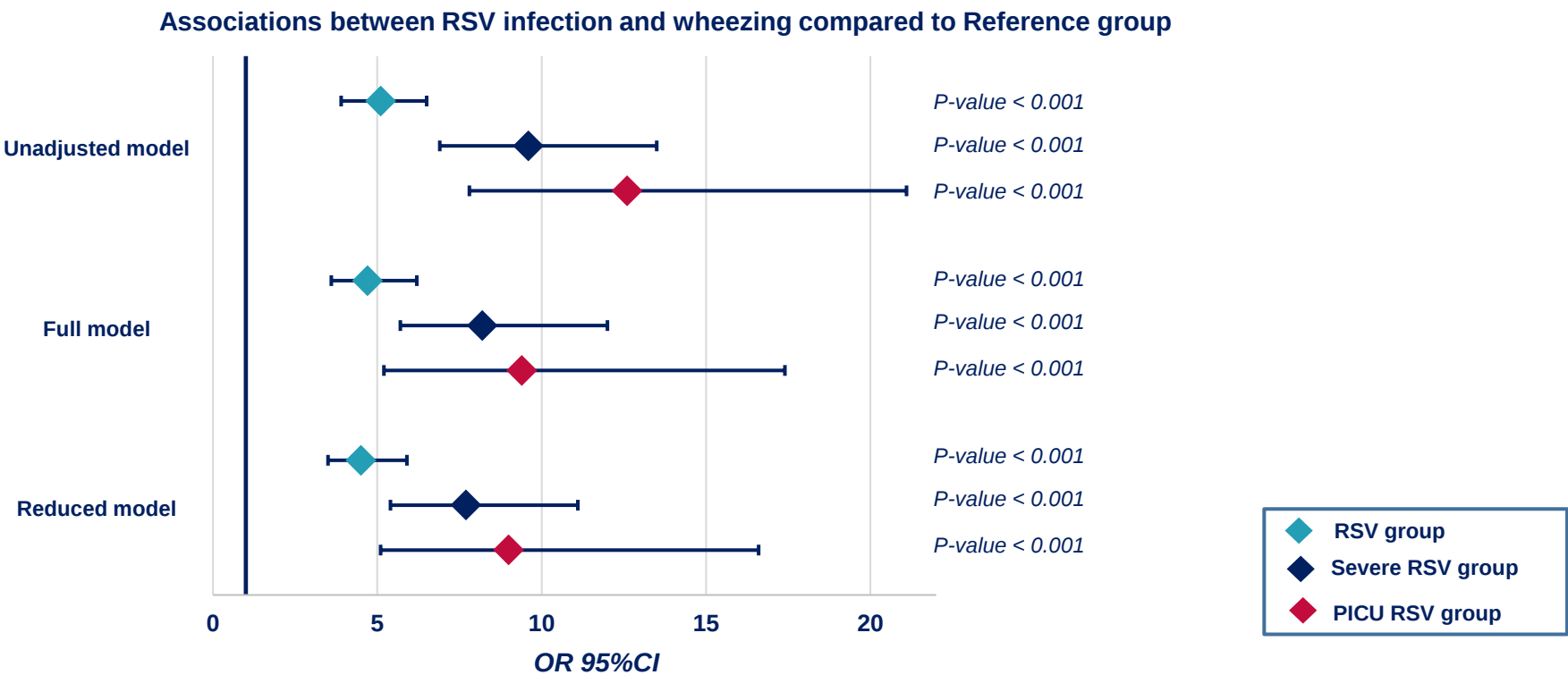


	RSV (n=150)	Reference (n=150)	RSV (n=150)	Reference (n=150)	RSV (n=150)	Reference (n=150)	RSV (n=150)	Reference (n=150)
History of wheezing	63%	27%	80%	33%	57%	21%	43%	14%
p-value	<0.001		<0.001		<0.001		<0.001	

- The **proportion of children with wheezing markedly higher in the RSV group (61% vs. 23%)**
 - Reported prevalence of wheezing in the RSV group varied from 43% in Italy to 80% in the UK.
- **The frequency of wheezing increased with RSV severity**
 - 61% overall in the RSV group, 75% in the severe-hospitalized and 79% in the PICU RSV group

Association between RSV infection and wheezing

Sample size: 1200 children including 600 in the Reference group, 600 in the RSV group, 269 in the Severe RSV group, and 112 in the PICU RSV group.



Adjusted multivariable logistic regression: Compared to the Reference group, the odds of wheezing:

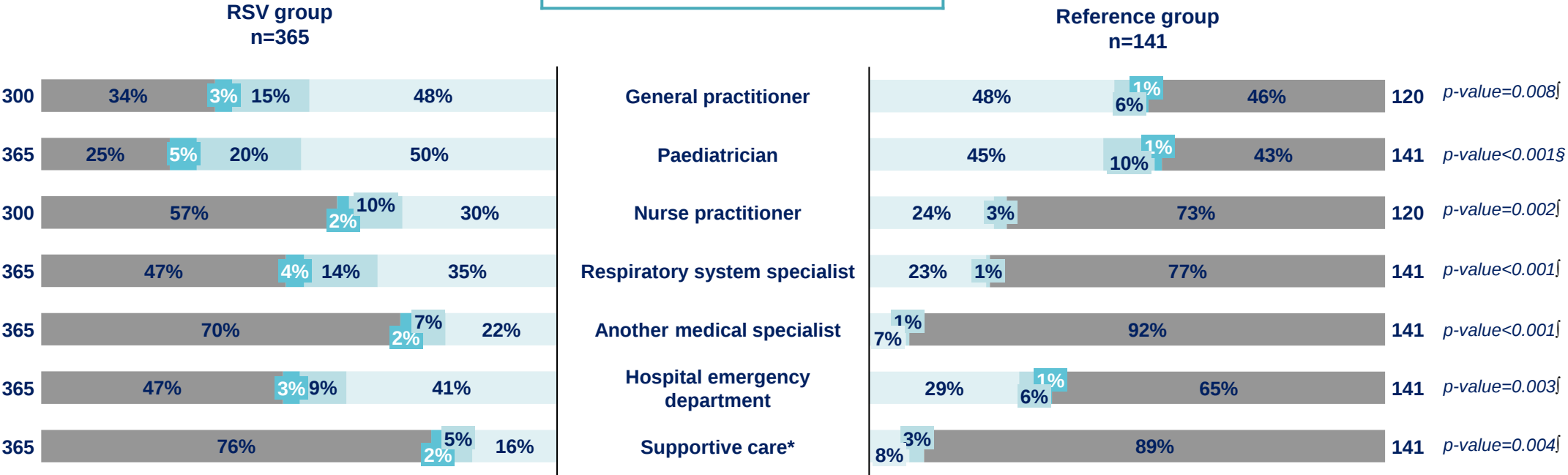
- 4.5 times higher in the RSV group, 7.7 times higher in the severe RSV group, and 9.0 times higher in the PICU RSV group.

Use of healthcare resources and costs

RSV vs. Reference group, children with a history of wheezing

Sample size: 506 children who have experienced wheezing

Statistical comparison between groups
Chi-squared test § Fisher's exact test ¶



* Supportive care includes: acupuncturist, chiropractor, homeopath, physiotherapist, or psychologist.

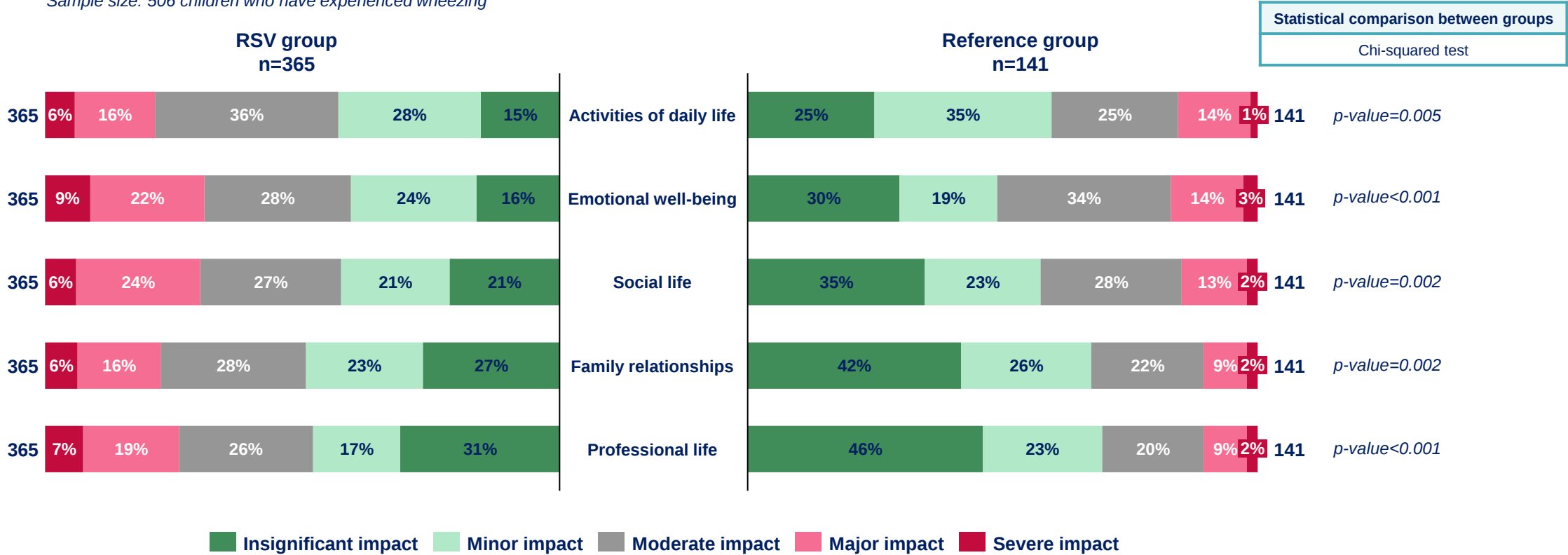
1 to 3 4 to 12 > 12 None

Among children who wheezed, wheezing-related visits to HCPs were more frequent in in the RSV group than in the Reference group.

Impact of wheezing on daily life

RSV vs. Reference group, children with a history of wheezing

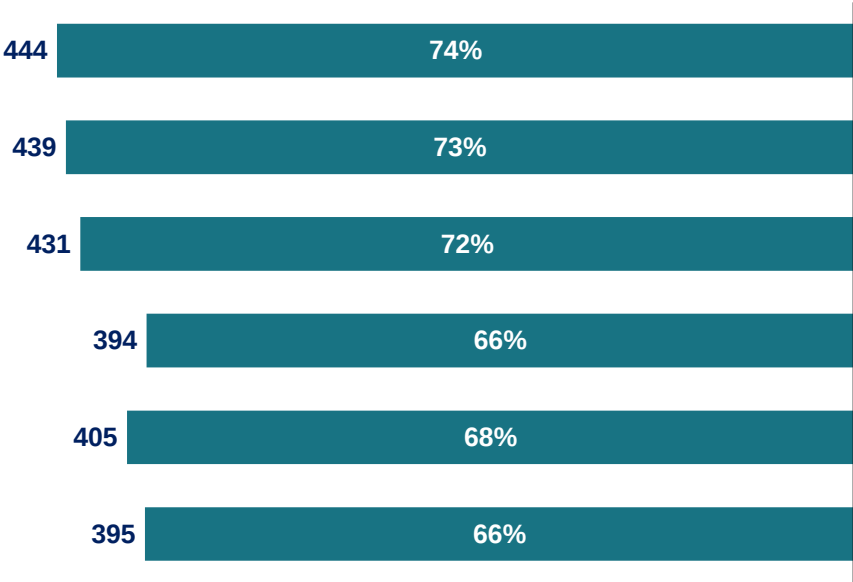
Sample size: 506 children who have experienced wheezing



- 57% of parents reported their child’s wheezing to have moderate to severe impact on their emotional well-being.
- 3% reported a moderate to severe impact on their daily life activities and/or their social life.
- All aspects of parents’ lives were more impacted by wheezing in the RSV group than in the Reference group.

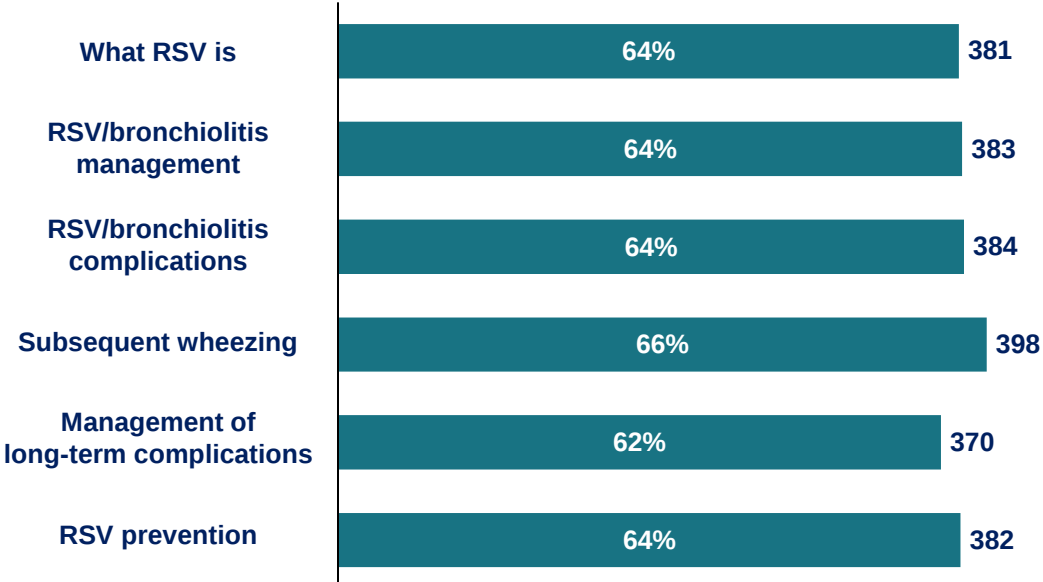
Awareness about RSV and perceived unmet needs

At the time of infection, parents in the RSV group felt they lacked knowledge about...



Sample size: 600 parents in the RSV group

Today, parents in the Reference group feel they lack knowledge about...



Sample size: 600 parents in the Reference group

Compared to parents in the Reference group, more parents in the RSV group reported lacking knowledge about what RSV is, how to manage RSV and RSV complications.

Limitations

- **Selection bias:** Online access, IT and literacy bias, overrepresentation of those looking for healthcare information, and members of Carenity communities
 - Selection bias in favour of more severe RSV cases: 45% of children were reported to have been hospitalized for their RSV infection - possibly explained by the self-enrolment design of the survey.
- **Recall bias:** 67% of parents responded to the survey at least 1 year after their child's RSV episode.
- Relied on parentally-reported symptoms and self-reported perceptions
- Wheezing appeared before diagnosis in 28% of cases.
 - This could be explained by early symptoms before diagnosis, by wheezing due to causes other than RSV (e.g. smoking, pollution), or by a pre-disposition to wheezing that could have been exacerbated by RSV infection.

Conclusions



RSV infection before age 2 years is associated with wheezing in pre-school age

- The odds of wheezing ~5 times higher in the RSV group.
- This association increased in strength with increasing RSV severity



Wheezing increases use of healthcare resources and is a financial burden for the family

- Involves repeated healthcare visits, increased long-term healthcare utilization, and contributes to a significant psychological, clinical, and economic burden
- Burden higher amongst wheezers in RSV compared to non-RSV group



Child's wheezing represents an emotional and social burden for the family

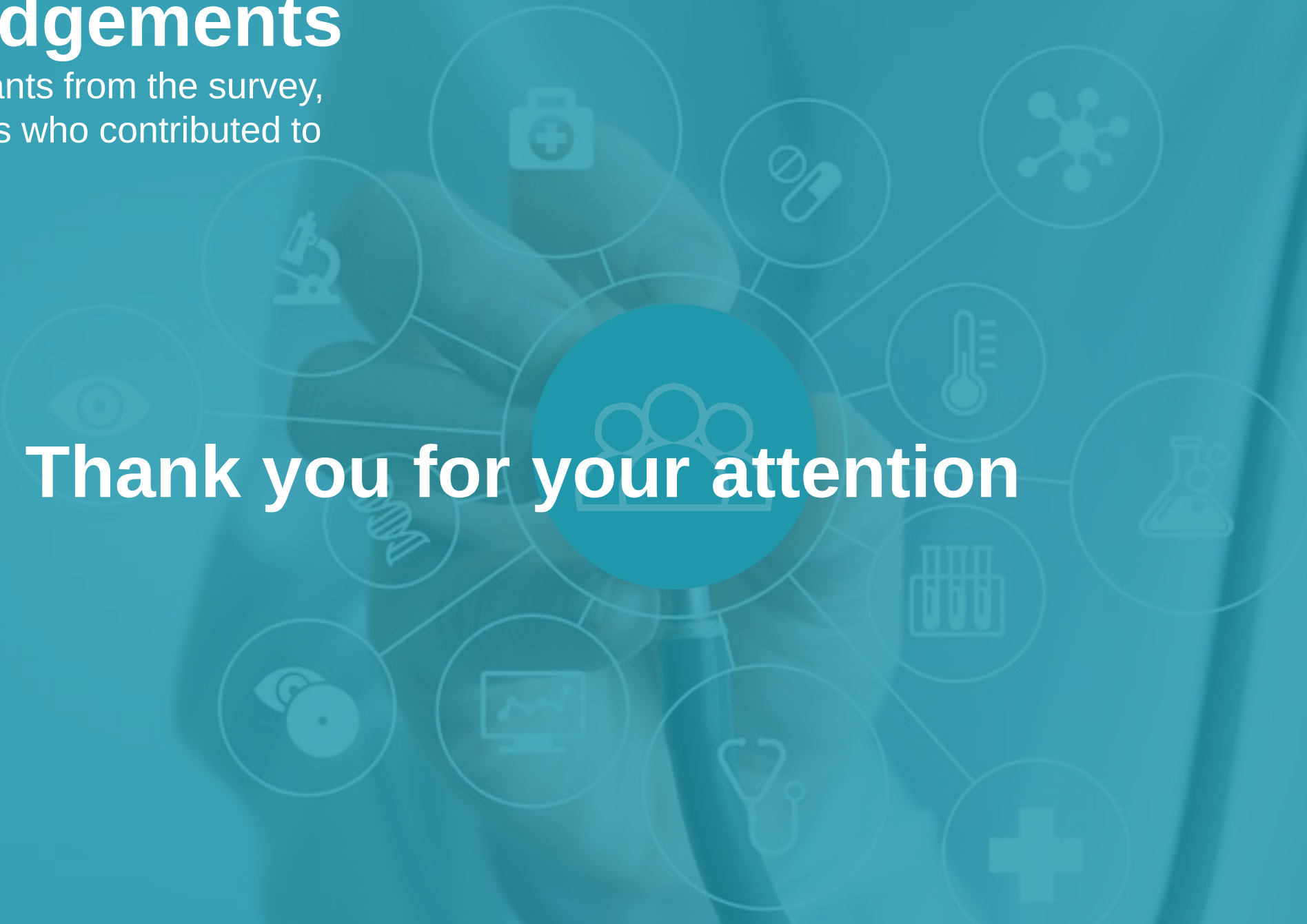
- More than half of parents reported their child's wheezing to have moderate to severe impact on their emotional well-being, daily and/or social life activities.
- 64% of parents reported moderate to severe impact of wheezing on child's quality of sleep.

RSV is surrounded by a lack of knowledge and insufficient support for parents

- Over 60% of parents feel they lack knowledge about RSV.
- Overall, 30% of parents do not feel sufficiently supported in the management of wheezing.

Acknowledgements

We thank all participants from the survey, along with the experts who contributed to this project.

A hand holding a magnifying glass over a network of medical icons. The background is a solid teal color. In the center, a hand holds a magnifying glass. The lens of the magnifying glass is positioned over a central blue circle containing a white icon of three people. Radiating from this central circle are several lines, each connecting to a smaller white circle. Each of these smaller circles contains a different medical or scientific icon: a first aid kit, a pill, a virus, a thermometer, a flask, a test tube rack, a stethoscope, a plus sign, a monitor with a graph, a CD/DVD, an eye, a DNA helix, a microscope, and a speech bubble. The overall theme is healthcare and research.

Thank you for your attention