

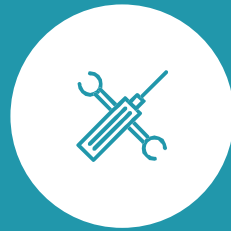
INCREASED RISK OF WHEEZING ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) IN A MULTI-COUNTRY CROSS-SECTIONAL SURVEY OF PARENT'S PERCEPTION

42nd Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), *20th - 24th May 2024, Copenhagen, Denmark*

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



Background



Methods



Results



Conclusions



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Survey context & objectives

Survey context

- RSV is a common and contagious seasonal virus. By two years of age, >90% of children will have had at least one RSV infection.
- Among infants under one year old, RSV is a leading cause of hospitalization for acute lower respiratory tract diseases such as bronchiolitis and pneumonia.
- Some studies suggest RSV bronchiolitis may be associated with an increased risk of subsequent wheezing in infants and children.
- 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)

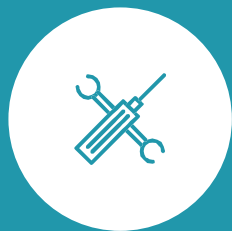
Primary and secondary objectives of the survey

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

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



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Survey methodology

Survey design

- A cross-sectional survey which included two groups of respondents: parents of children who had a past diagnosed case of RSV, parents of children who had not been infected with RSV.

Data sources

- Recruitment through Carenity platform: The Carenity community has over 500,000 members in 5 European countries and the United States. This survey targeted Carenity members aged between 25 and 40 years old and registered in the US, UK, Spanish, and Italian platforms. Carenity communities were invited to participate in the survey via emails and private messages. This recruitment channel enabled 7% of the total sample to be recruited.
- Recruitment through online campaigns and local partners: targeted online advertisements about the survey were displayed on Google and Facebook. This recruitment channel enabled 3% of the total sample to be recruited. Local partners specialised in patient studies were also used to recruit respondents (90% of the total sample).

Questionnaire

- 45 questions, including 4 open-ended text fields

Ethical Approval

- The survey design and questionnaire received IRB approval from WIRB-Copernicus.

Statistical analyses

- Comparison between groups were conducted using Chi² or Fisher's exact tests for categorical outcomes, and using Student or Wilcoxon's rank sum tests for continuous outcomes.
- Multivariable logistic regression models were used to assess the association between the presence of wheezing in children and one or more risk factors, such as a history of RSV infection.

Survey methodology

Inclusion criteria

- **Inclusion criteria applying to all respondents:**
 - Be of 18 years of age or older
 - Living in the US, UK, Spain, or Italy
 - Be parents of infant(s) or children under 6 years old
- **Inclusion criteria for the RSV group:**
 - Be parent of infant(s) or children who were diagnosed with bronchiolitis by an HCP or tested positive for RSV in the past 5 years.
 - Be parent of infant(s) or children who were diagnosed with bronchiolitis by an HCP or tested positive for RSV during their first and second year of life.
- **Inclusion criteria for the Reference group:**
 - Be parents of infant(s) or children who have never been diagnosed or hospitalised with bronchiolitis or RSV infection.
- **Fieldwork duration:** From February 10th to April 28th 2023
- **Number of respondents:** n=1,200 parents in total, including n=600 in the RSV group and n=600 in the Reference group.

				
Number of children	300	300	300	300
Incl. RSV group	150	150	150	150
Incl. Reference group	150	150	150	150



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Medical profile – Description of RSV episode

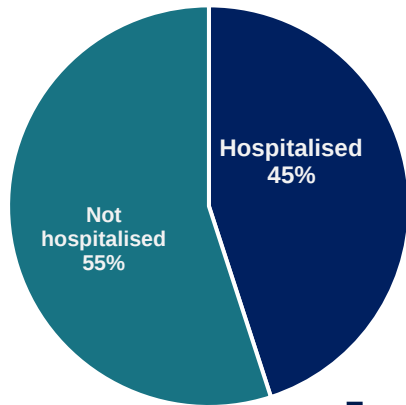
RSV-related hospitalisation

Overall, **45% of children in the RSV group were hospitalised** as a result of their RSV infection, with a median hospital stay of 5 days.

Among hospitalised children, 42% were admitted to a PICU, and 60% were placed under respiratory support.

Sample size: 600 children in the RSV group

Hospitalisation as a result of bronchiolitis or RSV infection

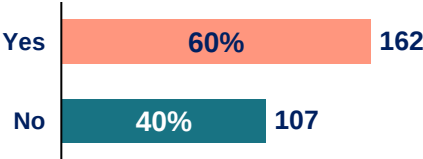


Severe RSV group
(hospitalised children)
N = 269

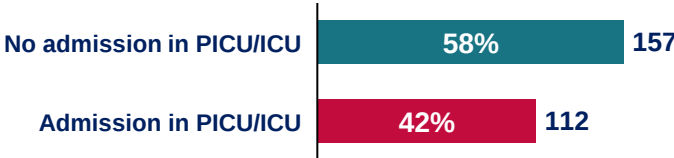
Average length of hospital stay (in days)

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)



PICU RSV group
N = 112

Medical profile – Description of wheezing

Presence of wheezing – RSV vs. Reference group, overall and by country

Overall, the **proportion of wheezing was higher in the RSV group (61%) than in the Reference group (23%).**

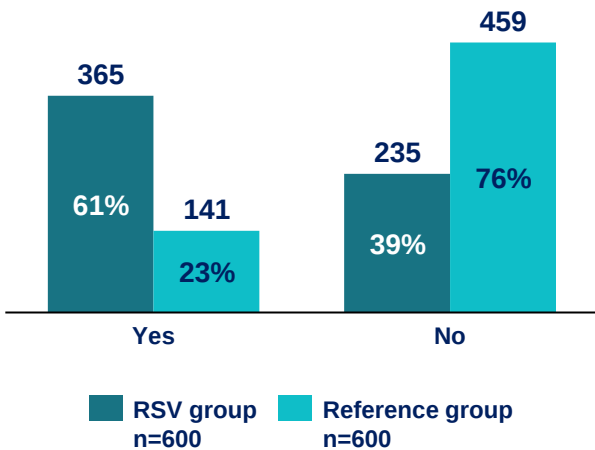
In country-specific RSV groups, the proportion of wheezing varied from 43% in Italy to 80% in the UK.

Sample size: 1200 children

Statistical comparison between groups
Chi-squared test

History of wheezing or whistling in the chest

p-value<0.001



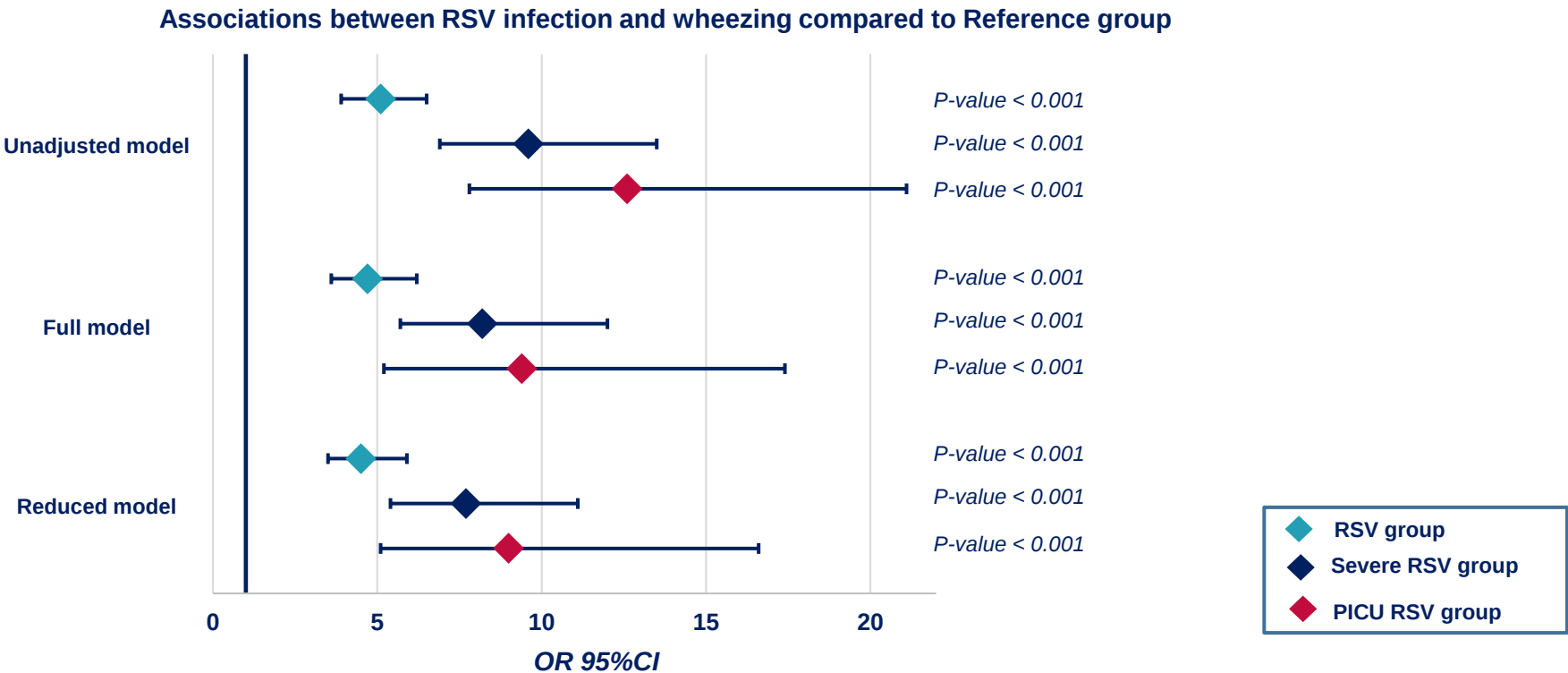
	RSV group (n=150)	Reference group (n=150)	RSV group (n=150)	Reference group (n=150)	RSV group (n=150)	Reference group (n=150)	RSV group (n=150)	Reference group (n=150)
History of wheezing or whistling in the chest	63%	27%	80%	33%	57%	21%	43%	14%
p-value	<0.001		<0.001		<0.001		<0.001	

Association between RSV and wheezing

Odds of wheezing in children in RSV, severe RSV, and PICU RSV groups

In adjusted logistic regression models, the odds of wheezing were **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** compared to the Reference group. These results suggest that RSV infection may be associated with wheezing in this cohort of children.

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.



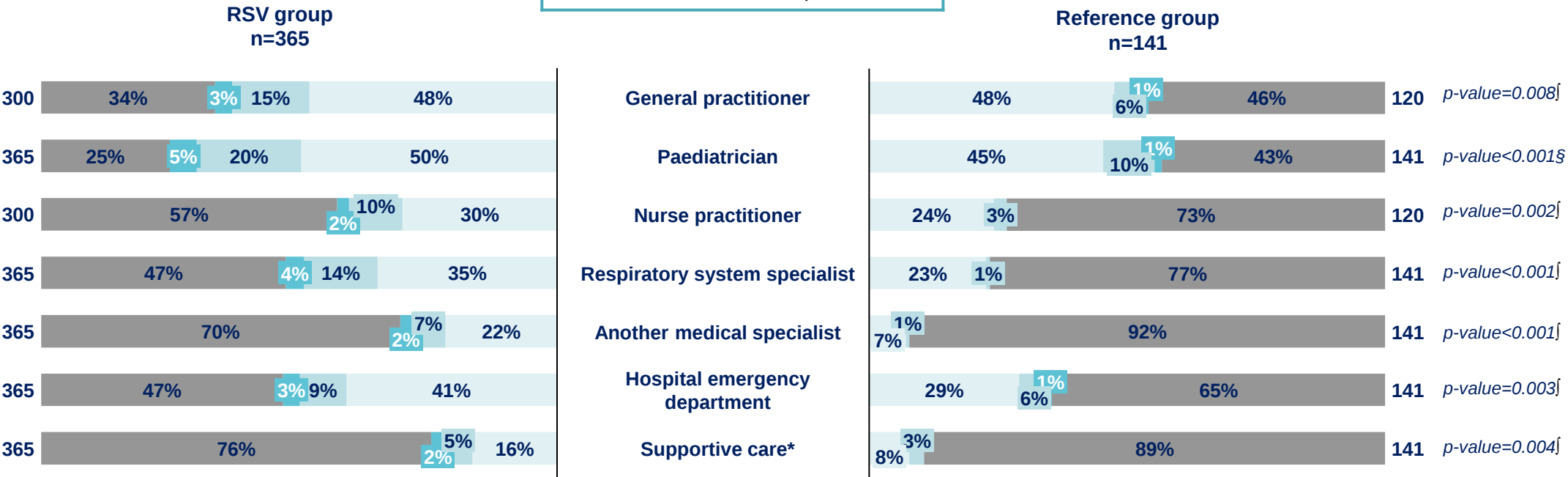
Healthcare and family cost – wheezing burden

Wheezing-related HCP visits since wheezing onset – RSV vs. Reference group

Overall, wheezing-related visits to HCPs were more frequent in wheezing children in the RSV group than in the Reference group. This trend was statistically significant for all types of healthcare assessed in the survey.

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.

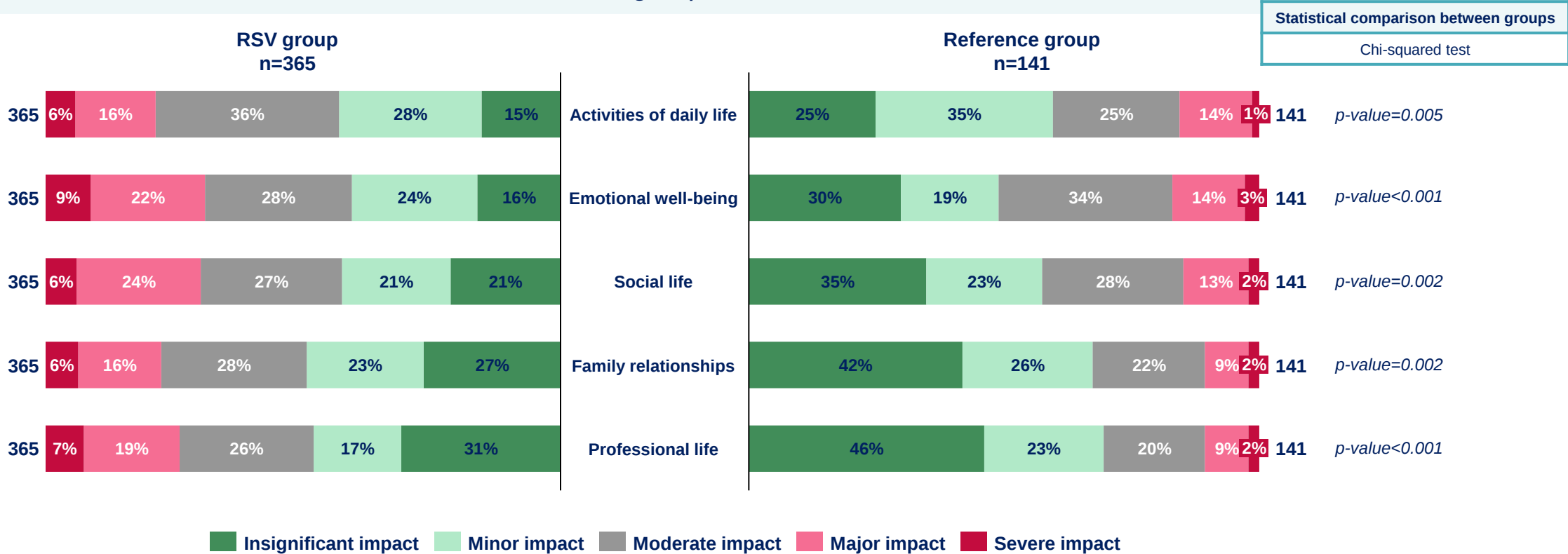
1 to 3 4 to 12 > 12 None

Impact on Quality of life – wheezing burden

Impact of wheezing on parents’ life – RSV vs. Reference group

Overall, **57% of parents** reported their child’s wheezing to have moderate to severe impact on their **emotional well-being**. Similarly, **53% reported a moderate to severe impact** on their **daily life activities and/or their social life**.

All aspects of parents’ lives assessed in the survey were more impacted by wheezing in the RSV group than in the Reference group.

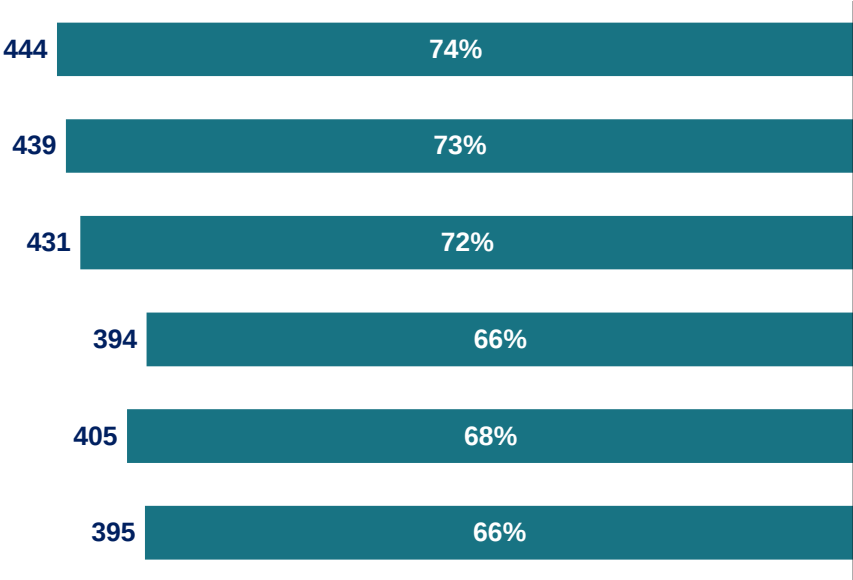


Perceived unmet public health needs

Perceived lack of knowledge about RSV

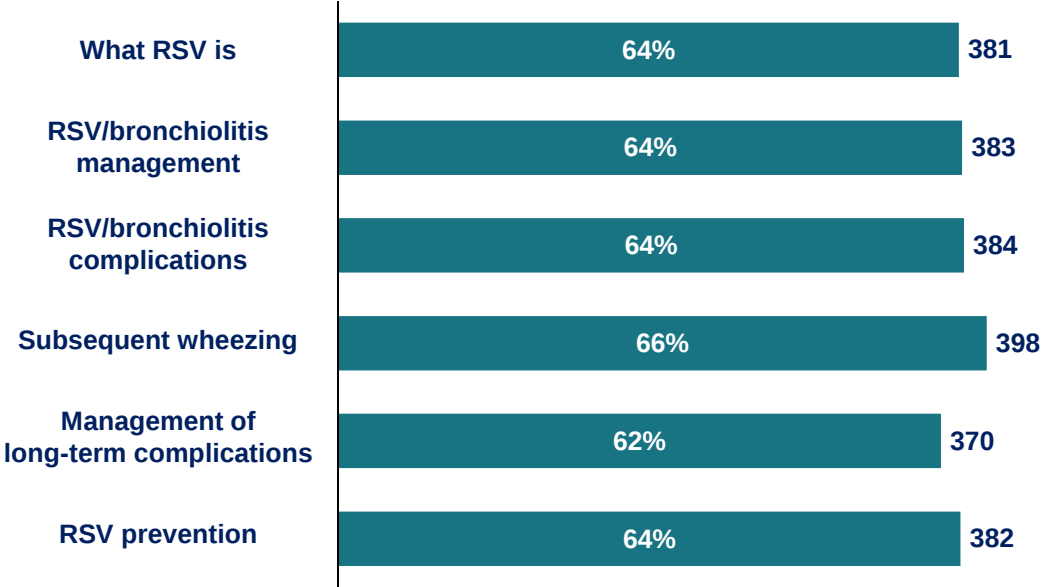
Compared to parents in the Reference group, more parents in the RSV group reported lacking knowledge about what RSV is, how to manage RSV and RSV complications.

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



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Limitations

- 67% of parents responded to the survey at least 1 year after their child's RSV episode so results may include a **recall bias**.
- In the survey, 45% of children were reported to have been hospitalized for their RSV infection, which reflects a higher-than-expected rate of severe RSV cases in our sample. This selection bias in favour of the most severe cases may be explained by the self-enrolment design of the survey.
- 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.

RSV infection before the age of 2 years may be associated with the presence of wheezing in children



- Parents reported that 61% of children with previous RSV infection had at least one episode of wheezing, versus 23% in the reference group.
- After adjustment for potential confounding factors, the odds of wheezing were about 5 times higher in the RSV group. This observed association increased in strength with RSV severity

Wheezing leads to increased use of healthcare resources and represents a financial burden for the family



- Unscheduled wheezing-related healthcare visits to specialist and primary care services were significantly higher in the RSV (53% and 75% reporting ≥1 visit) than in the Reference group (33% and 57%).
- Prescribed medications costs for wheezing were significantly higher in the RSV (69%) than in the reference group (55%).

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.

Authors' affiliations and 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.

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Thank you for your attention

CARENITY – Paris (FR)

1 rue de Stockholm
75008 Paris
France

pro@carenity.com

For additional information, please contact the authors
by email at laury@carenity.com



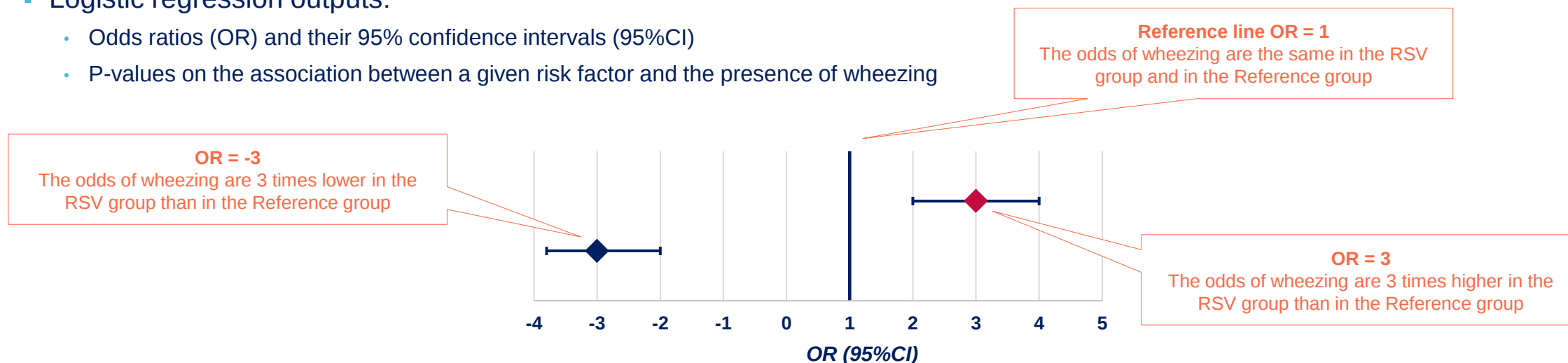
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Statistical analyses

Calculation of odds ratio & logistic regression analysis

- Logistic regression models were used to assess the association between the presence of wheezing in children and one or more risk factors, such as a history of RSV infection.
- Logistic regression analyses were conducted in three steps:
 1. A first model (called “unadjusted model”), which evaluated the odds of wheezing in children belonging to the RSV group compared to the Reference group. The same analysis was performed to compare children in the severe RSV group and those in the PICU RSV group to the Reference group.
 2. A second model (called the “full model”), which included all potential confounding factors associated with the presence of wheezing at a p-value <0.2
 3. A third model (called the “reduced model”), which derived from the full model after applying a stepwise procedure to select the statistically significant confounding factors to retain in a final model while minimising the Akaike Information Criterion.
- Logistic regression outputs:
 - Odds ratios (OR) and their 95% confidence intervals (95%CI)
 - P-values on the association between a given risk factor and the presence of wheezing



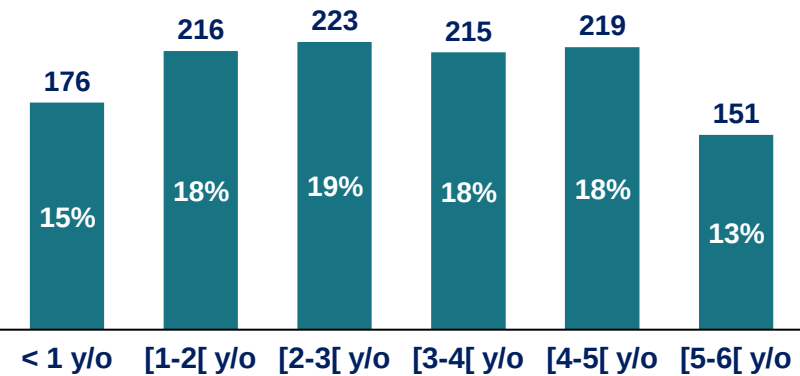
Socio-demographic profile

Children’s profile

Children included in the survey were 2.9 years old in average. Their age was similarly distributed across 1-year age categories from 0 to 6 years, and similar proportions of them were born in the Spring-Summer or in the Autumn-Winter seasons. Finally, the survey included a similar proportion of male and female children.

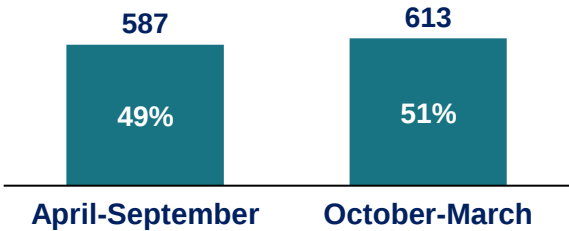
Sample size: 1200 respondents

Children’s age



Estimator	Age (in years)
Mean	2.9
95% CI	[2.8; 3.0]
Standard Deviation (SD)	1.6
1 st quartile (25%)	1.5
Median	2.9
3 rd quartile (75%)	4.3

Children’s month of birth



Children’s sex*



* n = 3 answered “prefer not to say”

Medical profile – Description of RSV episode

Age at RSV diagnosis and month of birth

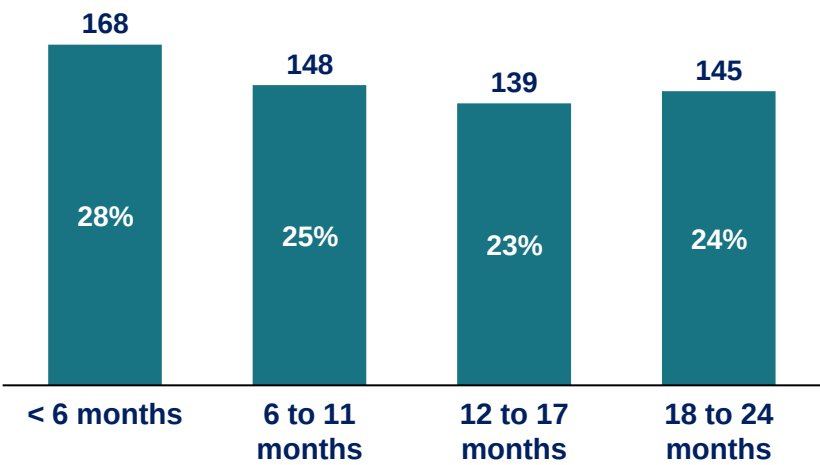
Overall, the distribution of children’s age at diagnosis was consistent across 6-month increment categories and was similar in all countries. In addition, children’s month of birth was similar in between the RSV and Reference groups. In particular, **children were born during and outside of RSV season in similar proportions.**

Sample size: 600 children in the RSV group

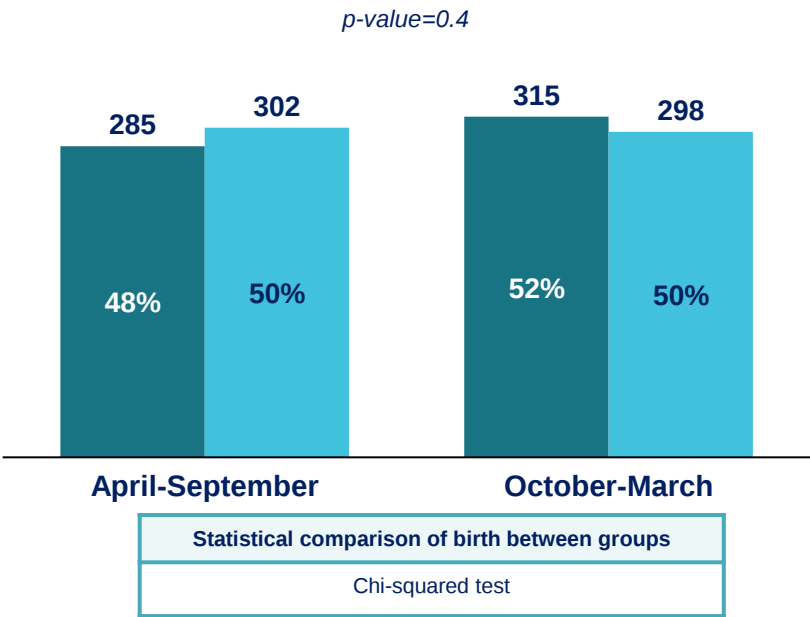
RSV group
n=600

Reference group
n=600

Age at RSV diagnosis



Children’s month of birth

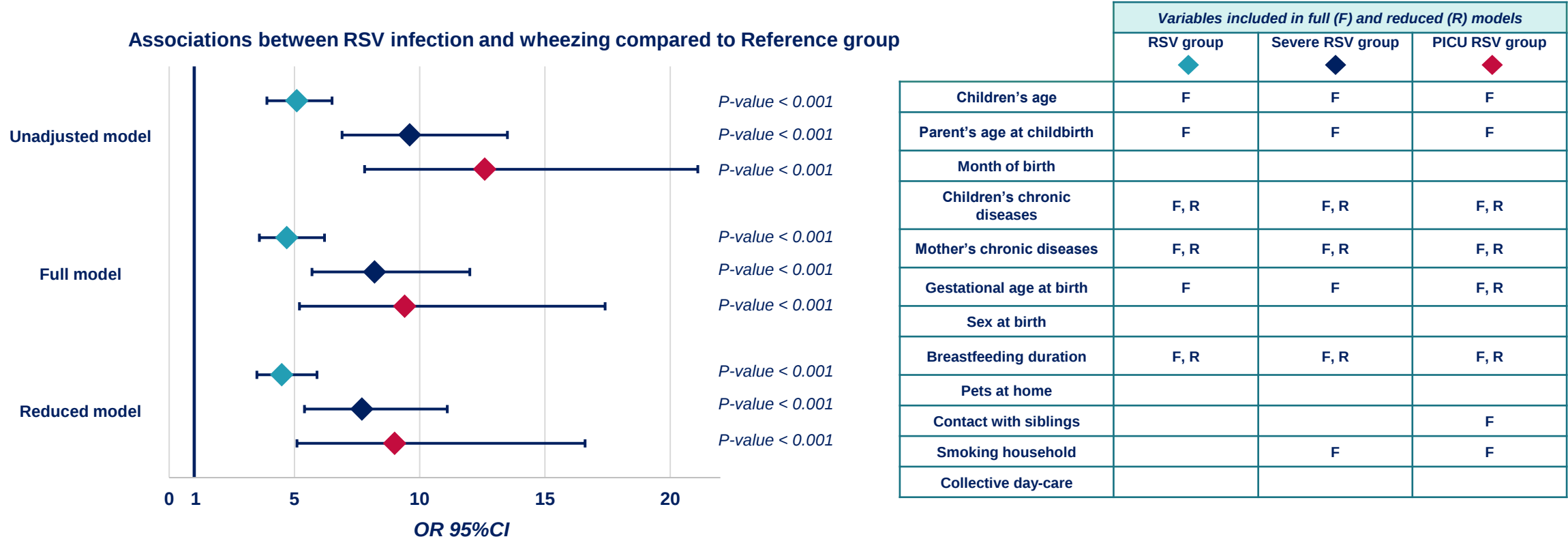


Association between RSV and wheezing

Odds of wheezing in children in RSV, severe RSV, and PICU RSV groups

In adjusted models after reduction (reduced models), the odds of wheezing were 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 compared to the Reference group. These results suggest that RSV infection may be associated with wheezing in this cohort of children.

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.



Healthcare and family cost – healthcare utilization

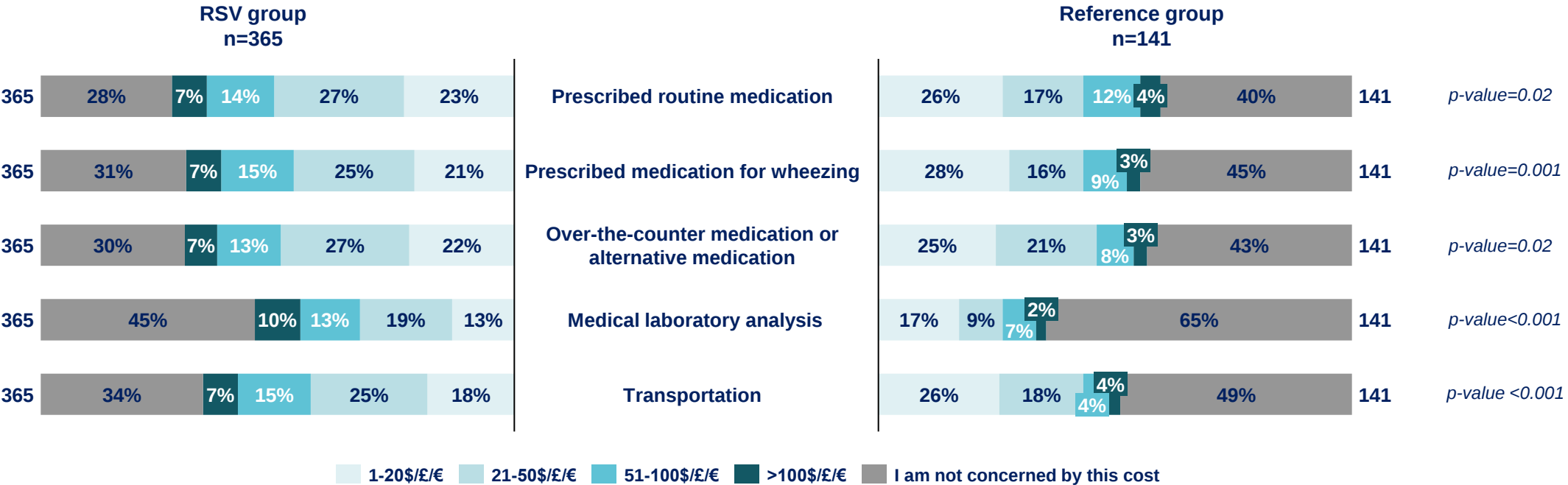
Wheezing-related healthcare costs since wheezing onset – RSV vs. Reference group

Overall, **wheezing-related healthcare costs were higher in wheezing children in the RSV group** than in the Reference group. This trend was statistically significant for all types of healthcare assessed in the survey.

Sample size: 506 children who have experienced wheezing

Statistical comparison between groups

Chi-squared test

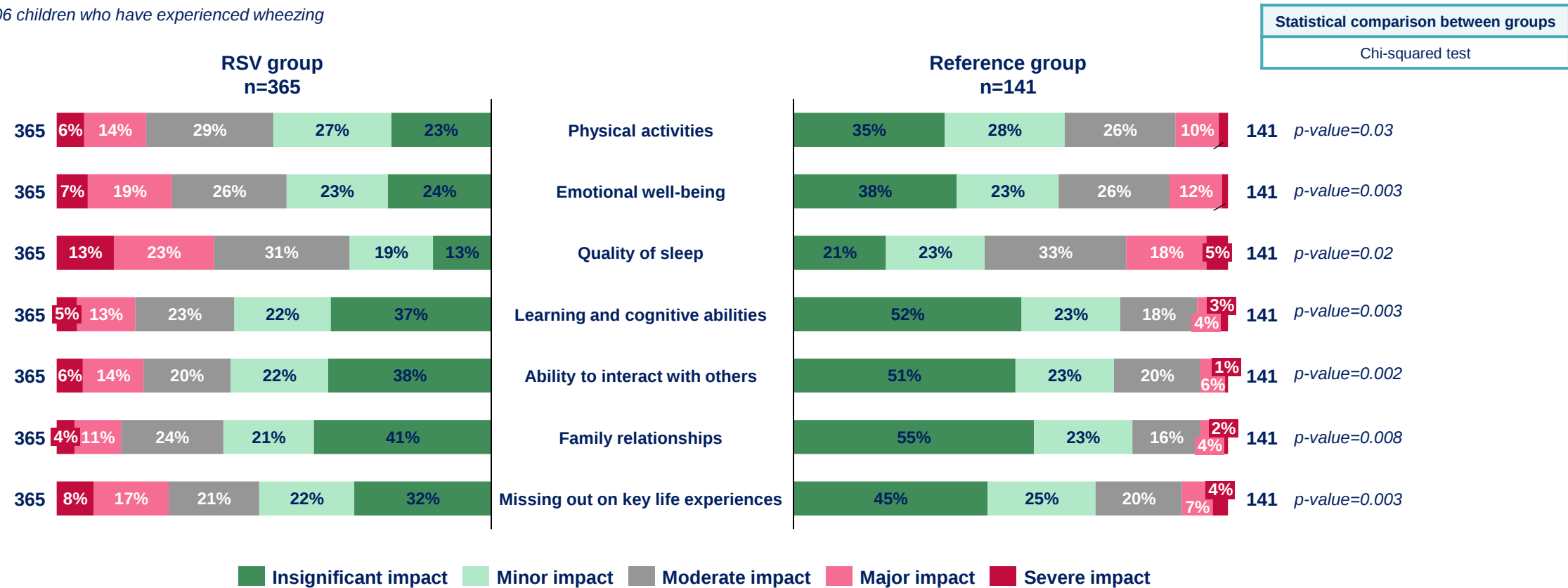


Healthcare and family cost – wheezing burden

Impact of wheezing on children’s life – RSV vs. Reference group

64% of parents reported moderate to severe impact of wheezing on child’s quality of sleep and 49% and 46% reported a moderate to severe impact on their children’s emotional well-being and physical activities.
Overall, all aspects of children’s lives assessed in the survey were more impacted by wheezing in the RSV group than in the Reference group.

Sample size: 506 children who have experienced wheezing



Perceived unmet public health needs

Unmet support for wheezing management

More than half of parents of wheezing children did not receive advice to handle feeding, information on how to prevent wheezing exacerbations, information on the risk for asthma, or psychological support.
Only 4% of parents did not receive any of the listed support options for their child’s wheezing.

Sample size: 506 parents of children who have experienced wheezing

I received this

I did not receive this, and I would not have found it useful

I did not receive this, but would have found it useful

I don't remember/Not relevant

