REspiratory Syncytial virus Consortium in EUrope (RESCEU): Presumed risk factors and biomarkers for RSV-related severe disease and related sequelae.

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To establish biomarkers predictive of, or associated with severe infection caused by RSV in infants. This study aims to find biomarkers for disease susceptibility, disease severity and long-time sequelae following RSV infection. By extending follow-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract infections
Study type	Observational invasive

Summary

ID

NL-OMON52425

Source
ToetsingOnline

Brief title
Understanding RSV: Severe disease and the long term consequences

Condition

- Respiratory tract infections

Synonym
Respiratory Syncytial Virus, RSV, RS-virus

Research involving
Human

Sponsors and support

Primary sponsor: University Medical Center Utrecht

Source(s) of monetary or material Support: Innovative Medicine Initiative (IMI): EU/Horizon2020 en EFPIA (European Federation of Pharmaceutical Industries and Associations)

Intervention

Keyword: Biomarker, Burden of disease, Case-control, RESCEU

Outcome measures

Primary outcome

The primary endpoint is disease severity of RSV infection in the first year of life.

Secondary outcome

1. Long term sequelae of RSV disease in the first year of life.

2. RSV viral load (copies/ml) and genetic sequence.

3. Differences in immune responses between mild and severe RSV infection.

4. Transcriptomics, proteomics, metabolomics and epigenetic signatures of mild and severe RSV infection.

5. Storage of biological samples (respiratory, saliva, blood, stool and urine) in a biobank.

6. Health care utilization and costs for RSV associated ARTI and long term sequelae.

7. Applicability of found biomarkers to infants with comorbidities with RSV infection.

Extension to six years of age part:

8. To compare the incidence of asthma after RSV hospitalization with the

incidence of asthma after milder RSV infection.

9. To compare the incidence of asthma after RSV hospitalization with the

incidence of asthma after hospitalization due to other viral infections.

10. Determine the risk factors for persistent wheezing at the age of 3 and 6

years.

Study description

Background summary

The REspiratory Syncitial virus Consortium in EUrope (RESCEU) is an Innovative Medicine Initiative (IMI) effort funded by the EU and EFPIA under the H2020 framework to define and understand the burden of disease caused by human respiratory syncytial virus (RSV) infection. RSV causes severe disease in individuals at the extremes of the age spectrum and in high risk groups. It was estimated that RSV was associated with 34 million cases of acute respiratory tract infection (ARTI), 3.4 million ARTI hospitalizations and 55,000 to 199,000 deaths in children <5 years in 2005 worldwide. These estimates were based on limited data and there is a substantial gap in knowledge on morbidity and associated healthcare and social costs in Europe. New vaccines and therapeutics against RSV are in development and will soon be available on the European market.
The RESCEU case-control study is designed to investigate biomarkers for severity of disease caused by RSV. We have prioritised biomarker investigation based on key knowledge gaps that will facilitate improved understanding of the biology of RSV infection and its sequelae as well as better control and treatment of RSV infections. There is an urgent need to better define correlates of protection and we therefore prioritise analysis of potential serological biomarkers of protection in infants (using functional and total antibody assays). We will use virological sequencing and host transcriptomics to investigate phenotypic differences in each of our populations that may account for severity, susceptibility and sequelae of RSV. Findings from these analyses may identify mechanistic pathways involved in protection or the development of sequelae and provide targets for therapeutic intervention and/or monitoring in interventional treatment trials. We will also examine other key *omics* approaches to biomarker discovery including proteomics, microbiome studies, metabolomics, and epigenetic studies.

RSV infection is known to be associated with recurrent wheezing in the first year of life. It is still unclear whether RSV infection at a young age is

associated with the development of asthma at school age and the mechanisms of this possible association.

Study objective

To establish biomarkers predictive of, or associated with severe infection caused by RSV in infants. This study aims to find biomarkers for disease susceptibility, disease severity and long-time sequelae following RSV infection.

By extending follow-up to school age (6 years), we expect to gain important information on the association between RSV infection in the first year of life and the subsequent development of asthma.

Study design

Prospective observational, multicentre, multicountry case-control study.

Study burden and risks

A blood, nasal, buccal, urine and stool sample will be collected at the moment of infection and 6-8 weeks after infection. The 80 healthy controls will have only one moment (baseline) at which samples are collected. A questionnaire will be completed by the parents at baseline followed by a diary for two weeks (14 consecutive days). A yearly questionnaire up to the age of 3 years old will be completed by the parents. There are few risks of participating in the study. Blood and respiratory sampling can be associated with minor local effects, for example, discomfort, bruising or nose bleeds. There are no risks associated with collection of urine or stool samples.
There are no particular benefits to participating in this study, apart from knowing knowledge obtained from it may benefit other patients in the future.

Extension until 6 year of age
Parent of participating children will complete a questionnaire after 4, 5 and 6 years. If there has been a hospital admission due to respiratory complaints in the last year, data from this specific admission will be collected after permission from the parents. There are no direct benefits to participating. The results of the study may contribute to better knowledge about the disease burden of RSV, which is important for future treatment or implementation of prevention strategies.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

• Parent/carer of infant is willing and able to give informed consent for participation in the study.
• Male or female, and less than 12 months of age at enrolment.
• Parent has a telephone.
• Hospitalized for <48 hours at enrolment or within 96hrs of onset of illness (for those not admitted).*
• Live near enough to a participating study centre for the 6-8 week home visit/hospital appointment to be feasible.*, * not applicable for healthy control infants (group 2)

Inclusion criteria - Extension until 6 years of age
- Participants from Group 1a (previously healthy infants hopsitalized with RSV) and Group 1b (previously healthy with RSV infection that did not require

admission).
- Informed consent obtained from parents

Exclusion criteria

• History of concurrent clinically significant medical illness (not directly attributable to RSV infection) including but not limited to, cardiovascular, respiratory, renal, gastrointestinal, haematology, neurology, endocrinology, immunology, musculoskeletal, oncological or congenital disorders, as judged by the investigator*
Specifically excluded examples include, but are not limited to:
o Immunosuppressed states
o Bronchopulmonary dysplasia/chronic lung disease of infancy
o Congenital heart disease
o Down*s syndrome
• Prematurity, as defined as gestational age <37 weeks at birth.*
• History of receipt of medication to treat RSV infection (e.g. ribavirin).
• Prior exposure to an RSV investigational vaccine or medication.
• History of receipt of immunoglobulin or monoclonal antibodies (including palivizumab).
• Use of steroids or montelukast within 7 days of enrolment in the study.
• Parents not able to communicate in the local language or English.

* Inclusion criteria (and/or) for exploratory group of RSV infected infants with comorbidity (group 1c and 1d)

Exclusion criteria - Extension study until 6 years of age:
- None

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-11-2017
Enrollment:	160
Type:	Actual

Ethics review

Approved WMO Date:	20-09-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-10-2022
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL62657.041.17