The RESCEU 3rd General Assembly meeting has just taken place, making available the results of two and a half years of hard work with much more to come in the second part of the project.

The meeting was held in Muntgebouw, Utrecht, on June 19th, 20th, and 21st. This year, approximately 120 participants involved in the RESCEU project and the RSV community in one way or another joined this meeting: 18 project partners and representatives of all the work packages; affiliated partners representatives; RESCEU Advisory Boards members and, among relevant stakeholders, the World Health Organization. Many European countries were represented, including the UK, Belgium, the Netherlands, Spain, Finland, Italy, Denmark, Sweden and France. In addition, there were representatives from non-European countries such as the USA and Australia.

The WP pre-meeting Day, held on the 19th of June, was for work package members to interact
with each other, to review the current status of their work, to report on the latest results and generate debates on controversial issues.

The General Assembly meeting was organized with plenary sessions to encourage the speaker/s' and the participants' interaction.

The first day started with a keynote speech from Vivek Shinde, representing Novavax. The presentation, *Phase 3 RSV maternal trial result*, focused on how the trial of the RSV prevention vaccine had progressed.

The purpose of the WP presentations was to highlight the achievements over the past 12 months and to inform the consortium members about the current status of each work package in terms of work completed, deliverables submitted and work in progress. In the case of the clinical studies WP, each centre described the next steps to conclude the investigation and achieve their objectives.

On both days, during the lunch breaks, five posters were presented by Marine van Berleere and Florian Zeevat from WP3 and Roy Zuurbier, Koos Korsten and Annfleur Lagnedijk from WP4, all Early Career Researchers.

After a long day of interesting presentations, the consortium enjoyed an excellent dinner at Paushuize, on the Pausdam, an important building in the historic city centre of Utrecht, built at the beginning of the sixteenth century. Before dinner, Dr Berent Prakken, professor of immunology and paediatrics at the Utrecht Medical Centre and chair of Research and Education of the Wilhelmina Children's Hospital, gave a speech, *RSV surveillance*, on translational science regarding publications and research findings in the medical field, and on the importance of keeping up the good work and efforts despite any potential failures.
The second day started with the presentation of four Early Career Researchers. You Li spoke about how RSV seasonality may impact future immunization program using modelling to compare maternal immunization and monoclonal antibodies approaches. Deniz Öner focused on the biomarker validation in other infant and adult cohorts’ studies. Joseph McGinley spoke about the result of acute versus convalescent RSV case sample comparison. Finally, Gulung Lin focussed his presentation on the status of 11 BC studies and 6 from infant CC study sequenced.

The Patient Advisory Board showed their commitment to raising public knowledge about RSV through the awareness campaign they are working on and invited all participants to help spread this message. Nicole Derksen introduced Inge Oliemans as PAB new communication expert.

The session on Data Management was led by Paul Peeters from Janssen, who provided a presentation based on different scenarios for data management and sustainability during and beyond the project, looking at a virtual biobank as a central information repository.

During the last day, Dr Siddhivinayak Hirve, from World Health Organization (WHO), updated the audience on WHO Global RSV Surveillance relevant topics and Mark Miller, from the International Scientific Advisory Group (ISAG), provided his feedback on RESCEU’s current developments and project results.

Overall, the meeting highlighted the great job done by each work package during the previous year and encouraged the RESCEU family to continue working to achieve the project goals.

The next RESCEU General Assembly meeting will take place on June 16th, 17th and 18th 2020 at the Royal College of Physicians of Edinburgh, hosted by the University of Edinburgh.
Older adult cohort study almost finished

During the past two winter seasons, over a thousand older adults in the Netherlands, Belgium and the United Kingdom have willingly helped us to look into the burden of disease caused by RSV. Each winter season over 500 participants were actively monitored and visited at baseline, in case of a respiratory infection and after the winter season. Just to give an impression, we have jointly performed well over 2500 study visits and completed at least 15,000 phone calls for weekly follow-up of participants during the winter months. With a range of patient between the ages of 60 and 100 we managed to get a diverse population into the study.

For the participants included in 2017 the study follow-up has already been completed last year. The current cohort included in 2018 has only one final visit left. In the months of May and June all participants of the current season complete a last “end-of-season” visit which marks their end of the study. As this is also the last year of the study, their end visit also marks the end of the entire study. This will be the first of the four prospective RESCEU study to be finished and we will be working hard in the upcoming months to make sure that the results from this study will become available.

Copenhaguen meeting

Copenhagen meeting on RSV-surveillance in Europe and EEA members. The meeting was hosted by SSI in Copenhagen, and co-organized with RIVM and ECDC. 30 invited participants from 17 countries, including national focal points for respiratory virus surveillance, reference laboratory representatives, academic experts from epidemiology, virology, pediatrics and infectious diseases from the RSV surveillance and research field) & RESCEU academic partners. The aim was to: discuss the technical and operational issues related to surveillance of RSV, the preliminary findings of the ongoing worldwide WHO-led RSV case definition, review developments in RSV surveillance in the EU/EEA
Region during the past decade and anticipate future developments, propose an aligned approach to national RSV surveillance system(s) within the EU/EEA region, draft a report of the workshop as a scientific manuscript co-authored by all meeting participants resulting in recommendations for alignment of national RSV surveillance systems widely within the RSV surveillance community in Europe.

Get to Know the RESCEU Team!

A series of interviews to members of the RESCEU team, where they are interviewed on their vision of RESCEU, their current position and how they contribute to the Project.

**Roy Zuurbier (UMCU)**

Roy Zuurbier is a PhD-candidate at the Spaarne Gasthuis hospital. Currently, he is working on recruitment for the birth cohort study of WP4.

Tell us about your professional career.
I am Roy Zuurbier, PhD-candidate at the Spaarne Gasthuis hospital and UMC Utrecht in the research group of Louis Bont. After graduating from medical school at the VU medical centre in Amsterdam in 2016, I started working as a resident-not-in-training at the department of paediatrics in the Spaarne Gasthuis hospital. After 4 months I applied for RESCEU’s birth cohort study as a PhD-candidate, that was going to start in June 2017 in the hospital. During my PhD I have the opportunity to improve my scientific skills and learn more about setting up and organising research. I believe, learning these things will make me a more complete physician and a better doctor, in the future. Working on RESCEU’s birth cohort study is a great opportunity to achieve these goals.

Can you please explain a bit about your role at the University of Edinburgh as part of the RESCEU project?
I am involved in RESCEU’s work package 4 (WP4). The aim of WP4 to determine the burden of RSV in risk groups for severe disease (infants, older adults and COPD patients) by means of four clinical
studies. I am working on the birth cohort study for the UMCU, under supervision of Joanne Wildenbeest, Marlies van Houten and Louis Bont. The birth cohort takes place at four other centers (UOXF/SERGAS/UEedin/TUCH). For the UCMU, all 2,000 participants are recruited at the Spaarne Gasthuis hospital. Together with the study team, I am responsible for these inclusions and active surveillance of the active cohort. In the first week after birth, I am doing a home visit to collect samples for the active cohort, amongst others blood and a nasopharyngeal swab. Participants for the active cohort are recruited during pregnancy, therefore we have a lot of contact with obstetricians and mid-wife practices. At this moment (May 2019) we have 135 participants in the active cohort and 1100 in the passive cohort. Last RSV season we have done 140 home visits at the moment of an acute respiratory tract infection (ARTI) for RSV detection. This was possible, because of really good contact with the parents of our participants. I am very proud of what we achieved, thanks to the participants and my co-workers.

How do you foresee the future of RSV infection after RESCEU project?
The RESCEU project will provide a great amount of important data, including epidemiology and biomarker analysis. Especially with the results of the birth cohort study (n = 10,000) we will be able to give an accurate estimate of the burden of disease of RSV. These data are necessary to emphasise the need for RSV vaccines and, when available, to implement future vaccines. With the biomarker analysis I hope we will be able in the future to predict whether a child has a higher risk of getting hospitalised due to RSV, for example by analysing the respiratory microbiome. Gaining more knowledge about the host pathogen interaction and human immune responses could make it easier to develop therapies for those with a severe RSV infection. This could decrease morbidity and mortality of RSV, hopefully also in lower income countries. At last, hopefully we might be able to establish a causal relationship between RSV infection during infancy and recurrent wheezing or asthma in later life.

Dexter Wiseman (Imperial)
Dr Dexter James Wiseman MRCP is a PhD candidate, honorary respiratory registrar and clinical research fellow at Imperial College London. He works out of the National Heart and Lung Institute at the Brompton campus.

**Tell us about your professional career**

I am currently working at Imperial College London’s National Heart and Lung institute on the COPD cohort within the RESCEU project. I graduated with an MD from Poznan University of Medical Sciences in 2010 and undertook much of my postgraduate training in Devon, which is in the South West of England. After finishing my core medical training, I became a respiratory registrar and have held a national training number in the North West London deanery since 2015. I have been fascinated with how medical research is conducted since medical school and have been very keen to pursue a career which includes a research element. Currently I am a PhD candidate working within RESCEU, investigating the burden of RSV infections amongst COPD patients. I have a specific interest in the presence of the virus in the baseline or non-exacerbating state and the consequences thereof.

**Can you please explain a bit more about your role in Imperial as part of the RESCEU project?**

The Work Package (WP) 4 COPD arm of RESCEU is conducted out of two national centres, Imperial College London and University Medical Centre Groningen. I am involved with both WP 4 (patient cohorts) and WP 5 (biomarker studies) of the COPD arm at Imperial College in London. This is under the supervision of Professor Wedzicha who is the clinical site lead and Professor Openshaw who is joint lead for WP 5. We collaborate closely across both centres with frequent telephone conferences and emails between our team at Imperial and Dr Ben Ditz and Dr Maarten Van Den Berge at UMCG. I also work closely at Imperial with Dr Ryan Thwaites on sample analysis and we are also planning the next stages of biomarker analysis including which might be conducted in-house. With Ryan I have co-authored a systematic review of biomarkers in adult RSV infections as one part of a RESCEU deliverable.

Day to day I am involved with patient recruitment and routine study visits. I also see patients at exacerbation, where I provide medical treatment and advice as necessary. These patients are then followed up until recovery. I coordinate patient booking and ensure that the data and sample collection is of a high quality and to protocol. I often assist our lab manager Dr Shahbakhti with sample processing and storage, building up the biobank of samples that will be analysed as part of WP 5.

**How do you foresee the future of RSV infection after the RESCEU project?**

RSV causes significant morbidity and mortality across the world amongst paediatric populations. There has been growing evidence over the last couple of decades indicating the notable impact RSV has within elderly and at-risk patient groups. The RESCEU project is uniquely positioned to give a truly international perspective while thoroughly investigating RSV, its prevalence and the morbidity and mortality it causes across both groups.

Along with all the interesting data that will be coming out of RESCEU directly, this consortium will also help to forge collaborative networks across Europe and beyond. This will be invaluable in the coming years and will help ensure that the optimal amount of relevant data and research is extracted by some of the world’s leading RSV investigators and scientists. As multiple vaccines are
Currently in development this information can be utilized not only by scientists but also by health authorities in relation to direct public health needs.

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**Papers of the month**

*in collaboration with ReSViNET*

**June 2019**

**RSV and the microbiome**

Alejandro Diaz-Diaz, Cristina Garcia-Maurino, Alejandro Jordan-Villegas, Jeffrey Naples, Octavio Ramilo and Asuncion Mejias

**Summary**

Antimicrobial resistance (AMR) is one of the biggest threats to mankind. It is related to massive use of antibiotics for bacterial infection, in particular respiratory infections. Antibiotics are also used, often unnecessary in case of respiratory viral infections, including RSV infection. However, recent studies suggest that the complex interaction between the respiratory microbiome, the host’s immune response and the virus may have an impact on the pathogenesis and severity of RSV infection. In this paper Diaz-Diaz elegantly reviews the more complex role of potentially protective and pathogenic airway bacteria in patients with RSV infection. Diaz-Diaz et al summarize the current evidence regarding the epidemiologic link, the mechanisms of viral-bacterial interactions, and the associations between the upper respiratory tract microbiome and RSV disease severity. This paper shows that we need to address the complex interplay between RSV infection and the airway microbiome to optimize use of antibiotics and, thereby, improve the short-term and long-term outcome of children with RSV infection.


**June 2019**

**Incidence of Respiratory Syncytial Virus Bronchiolitis in Hospitalized Infants Born at 33-36 Weeks Gestational Age Compared with those Born at Term: A Retrospective Cohort Study.**


**Summary**

A retrospective cohort study conducted in Soroka, Israel that compared the incidence rates of RSV bronchiolitis among preterm (33-36 weeks gestational age) children, and those born at term. Rate of bronchiolitis in the general population were extrapolated from the numbers collected in hospital. 374 late preterm and 2948 term infants were hospitalised with bronchiolitis throughout the course of the study, with 229 (61.2%) and 1738 (59%) of these having been tested for RSV respectively. Of these it was found that 164 (71.6%) pre-term infants and 1,266 (72.8%) term infants were positive for RSV respectively. When this was adjusted for population size mean yearly incidences per 1,000
children of RSV bronchiolitis hospitalizations of pre-term and term infants were calculated to be 35.8±13.0 and 19.6±4.1, with a mean difference in incidence ratio of 1.82 between the two groups. Pre-term infants were also found to be hospitalized for significantly longer periods (4.8±7.0) in pre-term and 3.9±4.9 in term infants.

This study shows the staggering difference in bronchiolitis rates between even late pre-term children and those born at term, and cements the importance of a treatment strategy that captures even children with severely under-developed immune systems, such as maternal vaccination. While useful, capturing this information at a single hospital in a single country limits the applicability of these data due to the large degree of variation in incidence of RSV bronchiolitis worldwide. Children with co-morbidities were excluded from this study, however it may have been useful to include them, or to perform a similar retrospective study at the same site in future to pick apart the relative contribution of different co-morbidities to the likelihood of developing severe disease.


**May 2019**


Saravanos et al provide a long term and comprehensive study of Respiratory Syncytial Virus infection in Australia.

**Summary**

This study aimed to estimate hospitalisation rates across the whole Australian population, while paying attention to factors that may influence this, such as age, race, sex, seasonality and geography. This study examined 63,814 hospitalisations in the period between 2006 and 2015, and found 94.4% of them to be in children under 5, with children under 2 months of age having the highest rate of hospitalisation within this bracket. Rates of hospitalisation were also found to be higher in those over 65, as well as in individuals of indigenous descent. Despite the majority of hospitalisations occurring in children under 5, the majority of in hospital deaths (59%) were found to occur in people over the age of 65, highlighting the difficulty of treatment in this group.


**May 2019**

Induction of Potent Neutralizing Antibody Responses by a Designed Protein Nanoparticle Vaccine for Respiratory Syncytial Virus

Jessica Marcandalli, Brooke Fiala, Sebastian Ols, Karin Loré, Laurent Perez, Neil P. King

**Summary**

Self-assembling proteins are promising inducers of a strong antibody response, because they enable multivalent antigen presentation. Jessica Marcandalli and colleagues designed such a self-
assembling protein nanoparticle vaccine, based on prefusion-stabilized RSV-F antigen. It is a computational vaccine that consists of multiple nanoparticles fused to 20 pre-F trimers, resulting in a high density of pre-F antigens. The study shows a 10 fold higher neutralizing antibody response in mice and non-human primates, compared to the response to trimeric form of RSV-pre-F protein. Marcandalli et al. hereby offer a new do-it-yourself protocol to customize RSV structure-based vaccines. With this ever expanding RSV vaccine development toolbox we are getting closer to finding a suitable RSV-vaccine every day.


**April 2019**

Global Disease Burden Estimates of Respiratory Syncytial Virus-Associated Acute Respiratory Infection in Older Adults in 2015: A Systematic Review and Meta-Analysis.

Ting Shi, Angeline Denouel, Anna K. Tietjen, Iain Campbell, Emily Moran, Xue Li, Harry Campbell, Clarisse Demont, Bryan O. Nyawanda, Helen Y. Chu, Sonia K. Stoszek, Anand Krishnan, Peter Openshaw, Ann R. Falsey, and Harish Nair, for the RESCEU Investigators

Summary

"Shi and colleagues conducted a systemic review and meta analysis of the global burden of RSV disease in adults above the age of 65, stratifying studies based on developing and industrialised regions, and taking into account community incidence, hospitalization rate, and in hospital fatality rates. This review covered a range of 44 studies from 1996 to 2018 along with 8 additional unpublished studies. There were an estimated 1.5 million cases of RSV-ARI in industrialised countries in 2015 with roughly 14.5% of these being admitted to hospitals. It was not possible to estimate these figures accurately for developing countries in isolation. It was estimated that there were approximately 336000 hospitalisations due to RSV-ARI in older adults worldwide in 2015, with about 14000 in hospital deaths in this age group. This study provides the most definitive and up to date statistics on RSV burden in this demographic and provides a companion piece to Shi and colleagues previous burden study in children published in 2017. Data for RSV-ARI burden in this demographic is lacking in developing countries, and could greatly strengthen the findings of this study."


**April 2019**

The repertoire of maternal anti-viral antibodies in human newborns.


Summary

Virscan is a novel diagnostic tool to measure antibodies against >1000 viral strains. It shows previous
viral exposures of an individual person. Christian Pou and colleagues used Virscan to get understand antibody transfer from mothers to their infants. The authors compared the antibody repertoire against RSV, amongst other viruses, of preterm and term infants. Despite a higher IgG concentration in term infants, both groups had the same antibody repertoire. Furthermore, the RSV-neutralizing capacity in plasma of preterm and term infants did not differ. This is surprising because it’s generally accepted that maternal antibody transfer occurs in the third trimester, and that extremely premature children lack this passive immunity and therefore are more prone to develop RSV. It’s fascinating that preterm infants would have the same repertoire and functionally active RSV-antibodies as term infants. Nevertheless, it leaves us with the question what the precise role is of maternal RSV antibodies in RSV immunity in preterm infants. As the number of participants in this complex study was low, future research should aim to confirm these findings and help us understand transfer of specific vaccine-induced antibodies.

Abstract on PubMed.

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**Upcoming major RSV/respiratory meetings**

**WP2 RSV SURVEILLANCE MEETING ON THE DEVELOPMENT OF A HARMONIZED RSV SURVEILLANCE SYSTEM IN EUROPE**

As previously announced, we are on the eve of the Surveillance Meeting, where WP2 team is gathering experts from Public Health agencies and academic bodies to discuss and develop a suggested framework for an RSV surveillance protocol in Europe, basing discussions on the 2017 ECDC RSV surveillance survey. In this occasion, RESCEU partners, SSI, RIVM, UEDIN, PENTA, and Affiliated Partners, NIPH (N), THL (FIN), NIVEL (NL), will meet representatives of ECDC - updating on RSV Atlas and ECDC perspective on RSV surveillance -, WHO - giving updates on ongoing RSV pilot surveillance project -, and many more National Health institutes in Europe.

Updates on feasibility assessments for various surveillance systems, framework design and further strategical content, after the meeting.

**MARCH 20 – 21, 2019**

**COPENHAGEN, DENMARK**

**IMMUNOLOGICAL ASSAYS AND CORRELATES OF PROTECTION FOR NEXT GENERATION INFLUENZA VACCINES**

The Conference on Immunological assays and Correlates of Protection for Next Generation Influenza Vaccines, taking place in Siena (IT) in the end of March, will gather scientists from academia, industry, and government public health, standardisation and regulatory agencies that develop and evaluate seasonal and pandemic influenza vaccines, to focus on relevant steps to develop next-generation
influenza vaccines. More information, agenda are available on the website and registration is possible till the 21st of March.

MARCH 31 - APRIL 2, 2019
SIENA, ITALY

10TH EDITION OF THE OPTIONS FOR THE CONTROL OF INFLUENZA IRSV CONFERENCE
The 10th edition of the ISRV Conference on Options for the Control of Influenza, will be held between the 28th of August and the 1st of September in Singapore. This is the largest international conference exclusively dedicated to influenza prevention, control and treatment, including seasonal flu and pandemic preparedness. Highlights of the meeting include: new tracks on influenza co-infections with other viral pathogens and key issues for policy making - special sessions to showcase the latest developments in Chinese-speaking countries - pre-conference workshops on a wide variety of topics including technology, mathematical modelling and bioinformatics. Registration are opening soon. See website.

AUGUST 28 - SEPTEMBER 1, 2019
SINGAPORE

List of recent RSV papers

June


https://mailchi.mp/b6e9cae9cea9/newsletter-10-general-assembly-meeting-2019-special-issue


May


April


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For more information, visit us at www.resc-eu.org
Sign up for RESCEU-Newsletter here! Next issue in June.

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