Patient involvement in RSV research - towards patients setting the research agenda

Nicole D. Derksen-Lazet[1], Corline E.J. Parmentier[1], Joanne G. Wildenbeest[1], Louis J. Bont[1], on behalf of the RESCEU investigators

[1] Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, the Netherlands

Running title: Patient involvement in RSV research

Corresponding author:

Prof. dr. Louis J. Bont

Department of Pediatrics, University Medical Center Utrecht

Lundlaan 6 NL-3584 EA Utrecht, The Netherlands

Tel: 088 75 555 55

E-mail: L.Bont@umcutrecht.nl

Abstract

Respiratory syncytial virus (RSV) is an important cause of childhood morbidity and mortality, and leads to a substantial disease burden among elderly and immunocompromised adults. Recognition of patient involvement in medical research is gradually increasing. Most research is being carried out without active patient involvement other than patients participating as study subjects, and most of the knowledge gained through research only partially reaches the general public. Since 2016, the RSV Patient Advisory Board has officially been involved as an advisory group in the REspiratory Syncytial Virus Consortium in EUrope (RESCEU). What started as a small single-center initiative, is now growing towards an international organization providing patient perspectives as inputs to scientists on research proposals and grants, and improving awareness of RSV among parents, professionals, and the general public. This article summarizes the history, current role, and future aims of the RSV Patient Advisory Board as an advocate to improve patient involvement in research. RSV patients and their representatives are important stakeholders in setting the global research agenda as well as educating patients, professionals, and the general public.

Key words: patient involvement, awareness, patient network, patient perspective, patient participation

Introduction

Respiratory syncytial virus (RSV) is a major cause of childhood mortality and morbidity, and the leading cause of infant hospitalization.[1] Estimates from 2015 indicate that globally roughly 33.1 million episodes of RSV-associated lower respiratory tract infection led to approximately 3.2 million hospital admissions in children younger than 5 years of age.[2] In addition, RSV-related disease results in a substantial burden among elderly and immunocompromised adults.[3,4]

There is increasing recognition of patient involvement in research.[5] Patient involvement refers to patients or others with relevant experience actively contributing to the research design, conduction and dissemination.[6] It should be distinguished from patient engagement, which is where information about research is shared with the general public.[6] Despite the increasing recognition of the importance of patient involvement, there is room for improvement. Research is mostly carried out on patients instead of with them, and research priorities are mainly set by scientific and medical experts.[7] Previous studies have demonstrated that patients' research priorities may differ markedly from those of scientists, suggesting that researchers may fall short in adequately representing the interests of patients in setting the research agenda.[8] Involvement of patients and their representatives offers scientists a unique perspective, and helps them to identify the questions with the most practical importance to those who would benefit directly from their research. It is crucial to improve the quality, credibility, impact, uptake and relevance of scientific research, and prevent it from being wasted.[7,9] Furthermore, it aligns with the democratic principle that those who are affected by a health issue have the right to have a say in the research regarding such problems.[10]

In 2013 a collaboration was started between RSV researchers and a group consisting of Dutch parents of children with a history of severe RSV infection, leading to the establishment of the RSV Patient Advisory Board (PAB). In 2016 the PAB officially became part of the governance structure of the REspiratory Syncytial Virus Consortium in EUrope (RESCEU, https://resc-eu.org/), an EU-funded Innovative Medicines Initiative (IMI) project, and received funding from RESCEU to be involved as a consultative organ in this project. Subsequently, it received funding through the ReSViNET Foundation as a participant in Preparing for RSV Immunisation and Surveillance in Europe (PROMISE, https://imi-promise.eu/), a follow-up IMI project that started in 2021. In contrast to the traditional perception of patients and their representatives having a passive role in research, the RSV PAB has a leading position in PROMISE to ensure patient-centered communication in the dissemination of results, increase RSV awareness, and facilitate the introduction of approved immunization strategies. From the beginning, the PAB has been a pioneer in the field of patient involvement in RSV research, with its unique input increasingly shaping the research agenda.

How an open dialogue led to partnership

In April 2013 the RSV research group of the Wilhelmina Children's Hospital, University Medical Center Utrecht, the Netherlands, approached parents of children who had experienced severe RSV infection to become involved as an advising party in clinical and translational research. An initial meeting between the research group and these parents facilitated an open dialogue between these parties to exchange experiences and current developments in the field of RSV. Researchers shared ongoing research efforts, including clinical trials as well as laboratory-based research. Parents opened up about their personal experiences, including their struggles with ongoing symptoms of stress and anxiety following their child's hospital admission and facing long-term consequences of RSV infection. Even though overlap existed between the research priorities of professionals and those of these patient representatives, this group of parents did put forward new and challenging issues. They pointed out the lack of knowledge about the impact and long-term sequelae of RSV infection among the general public, and posed questions about the psychological impact of hospital and intensive care unit (ICU) admission on children and their families. Furthermore, they made researchers acutely aware that RSV does not only have a major impact on high-risk populations, such as premature infants, but affects all children, including those without any known risk factors for severe RSV infection. To benefit from their unique point of view, a collaboration between the parents and the research team was initiated, leading to the establishment of the RSV PAB.

From single-center initiative towards an international organization

The initial activities of the PAB were focused on improving RSV research at a national level. The PAB members contributed to finding financial resources by co-authoring grant applications and writing additional letters about the importance of RSV research to potential funders. They advised researchers on the feasibility of their study proposals and encouraged them to invest in the relationship with their subjects during the conduct of a study. Researchers experienced better recruitment and retention rates, which has also been described in other studies on patient involvement in medical research.[11,12] Furthermore, they improved study recruitment by optimizing the readability of patient information forms using figures to summarize the research time schedule and providing these forms with more structure. The start of RESCEU, a major European project, gave the opportunity to bring patient involvement in RSV research to an international level. In 2016 the PAB became an integral part of the governance structure of RESCEU. Following the valuable contribution of the PAB to RSV research in the Netherlands, the international PAB was established as a consultative body in developing clinical studies, creating patient materials, and reviewing grant proposals to improve RSV research throughout Europe. Furthermore, it was assigned as manager of communications with other patient organizations. RESCEU funding was utilized to formally employ a member of the Dutch PAB as the chair of the international PAB and approach parents of RSV patients all over Europe to create a pan-European network of patient representatives. Although challenged by geographical distances, linguistic barriers, and limited amount of time, ongoing efforts led to the expansion of the PAB, which welcomed two additional mothers from Finland and the United Kingdom.

New ambitions and expanding activities

The members of the PAB were determined to put their efforts in increasing RSV awareness among the general public in addition to their consulting role in research. Initially, the Dutch PAB predominantly operated on a local level by sharing Dutch content on social media. During the second RESCEU General Assembly Meeting in 2018, the international PAB highlighted the importance of public awareness throughout Europe and the rest of the world as an instrument to draw attention from policy makers and to prevent those at risk for severe RSV infection from being unexpectedly overwhelmed by its impact. This advocacy led to receipt of financial resources from the IMI funding to the public consortium (i.e. not from the private/industrial partners in the consortium), which were used to establish a support team, consisting of a communication expert and medical students, to further expand the international PAB and increase global RSV awareness. By approaching pediatricians, members of the RSV Patient Network, and social media influencers with personal experiences with RSV across Europe, this team succeeded in finding new PAB members from Spain and the United Kingdom. These activities enabled the PAB to set up a comprehensive communication infrastructure which is essential for a professional and reliable patient organization. With the launch of “RSV Awareness Week”, the first (online) campaign in 2019, this patient organization presented itself to the outside world as “RSV Patient Network”. Ever since, this campaign week is run yearly in the second week of November, at the start of the RSV season in Europe. Beyond increasing awareness on a local level, the PAB has been focusing on improving global awareness through international social media channels and webinars for the general public. This has brought highly-motivated patient representatives from several European countries together, resulting in new international collaborations. Growth is visible in the amount followers and reach of the international social media channels. RSV Patient Network unites patients, offers them access to a support group of experienced experts, and encourages them to share their stories, thereby creating a multiplier effect to increase global awareness about RSV.

In addition to improving RSV research and awareness, the involvement of patient representatives in research has led to new activities with regard to education. Members of the PAB have gained an understanding of basic science, including knowledge of the molecular basis of antibodies against RSV and stages of vaccine development, by being informed by researchers who are involved in laboratory-based studies.[13] They are perfectly capable of educating patients, professionals, and the general public by combining their scientific knowledge with their personal experiences. PAB members contribute to the education of medical students, counter misinformation and answer questions about RSV on social media, and create information materials, including videos on preventive measures and symptoms of severe RSV infection.

Success factors to improve patient involvement in RSV research

Over the past 9 years, the PAB has evolved from a Dutch advisory group to an international organization improving RSV research, awareness, and education through multiple activities (Table 1). Apart from the chair, the members from the PAB all work on a voluntary basis. The history of the PAB shows several success factors regarding improving the impact of patient involvement in research. Patient representatives have been acknowledged as equal partners since the initial meeting in 2013, and time was invested by both researchers and parents to further enhance this partnership through regular meetings where parents learned about RSV research and researchers learned from the parents' perspectives on RSV. Both parties discussed expectations in these meetings, which were further clarified by the chair of the PAB, who kept close contact with both researchers and the other members of the PAB. The increasing relationship between the PAB and researchers facilitated a patient-oriented dialogue between these parties in shaping the global research agenda; PAB members alert scientists on knowledge gaps and problems that matter most to them. For example, the Utrecht RSV Research group performed a study on the psychological impact of ICU admission for RSV infection. Results from this study, which have not been published yet, showed that ICU admission of young children has an impact on the entire family, often with major stress on the relationships within the family for many weeks. Recently, the PAB was also involved in the research planning of an international drug trial, and put forward additional research questions about the effects of the particular drug that should be evaluated. Various other articles have mentioned relationship-building, clarification of duties, acknowledgement of parents as equals, and recognition of their efforts as success factors for parental involvement in research.[10] In addition to these factors, the financial independency of the PAB from industry, including pharmaceutical companies, allowed it to be a reliable and credible partner for public health and governmental stakeholders, including regulatory bodies. Finally, the establishment of a supporting organization behind the PAB and the financial resources that enabled the PAB to create a support team, were essential to take a leap in both RSV awareness improvement as well as network extension.

Barriers

Increasing patient involvement in RSV research has not been easy. Patients have a passive role in the traditional research paradigm and active patient involvement is currently an exception rather than normal practice, which can lead to unclear role distinctions and power imbalances between researchers and patient representatives. Parents and researchers are also often limited by a lack of time. Several articles on patient engagement and involvement in research have described these challenges.[10,14] Regular meetings between PAB members and researchers enabled an open dialogue about expectations and practical barriers to find solutions to prevent these challenges from leading to disengagement of parents. This led among other things to the assignment of specific tasks to specific members, with those having affinity for research design and methodology collaborating in the evaluation of study proposals, and those with an interest in raising awareness focusing on social media campaigns. Time constraints were addressed by asking for flexibility and understanding from both parties, and requests to parents were always without obligations. The expansion of the international PAB with new RSV patient representatives has been another challenge. Although some patients experience long-term sequelae, the transient nature of acute RSV infection makes it unusual for patients and their representatives to commit their time for a longer period. Additionally, linguistic, cultural, and geographical differences create a major obstacle in reaching new PAB members throughout Europe, and many potential members often lack time. Currently, the international PAB consists of 5 mothers with a lived experience of a child with RSV infection from Spain, Finland, the United Kingdom, and the Netherlands. The efforts of the support team have led to new members from countries that were previously unrepresented, but it has been especially difficult to find patient representatives from risk groups other than infants, such as immunocompromised patients and the elderly. As these groups are generally less active on social media platforms, new strategies are needed to reach these groups.

The future: leadership, expansion, and research-agenda setting

With the PROMISE project building on and carrying forward the successes of RESCEU, the work of the PAB as a patient group in the context of RSV research will be taken to the next level. A sustainable RSV patient organization has been secured by the anchorage of the PAB in the non-profit ReSViNET foundation. The goals of the international PAB were extended beyond their initial tasks as advocate to improve RSV awareness and consultative body in clinical studies within the RESCEU project. In PROMISE the PAB has a leading position in facilitating future introduction of RSV immunization. Over the past years, the sole licensed RSV immunoprophylaxis has been Palivizumab, a monoclonal antibody available exclusively for high-risk infants that needs to be administered monthly during the RSV season.[15] However, several other immunization options are now within reach. These include viral vector vaccines for older adults, protein-based maternal vaccinations and vaccinations for elderly, and monoclonal antibodies for the general infant population.[15] With these vaccines and antibodies within reach, increased knowledge about RSV and these immunization strategies is crucial to ensure successful uptake among the public.[16] The PAB will organize stakeholder engagement meetings involving academia, public health agencies, policy makers, and others to discuss challenges and solutions to develop and implement novel RSV vaccines, antibodies, and therapeutics for the benefit of patients. Furthermore, the PAB will develop and conduct online surveys in several European countries to identify barriers to RSV immunization in infants, and hopes to develop a guidance document for stakeholders to facilitate future introduction of RSV immunization in Europe. Additional steps will be taken to further expand the international PAB. As the current PAB consists of parents of children who experienced severe RSV infection, the PAB will focus on expansion with representatives from other risk groups for severe RSV infection. In collaboration with the support team, they will continue to reach out to potential patient representatives in European countries that are currently not represented. This is crucial to become more involved in local research projects and initiatives to raise awareness. The input of the PAB has become increasingly involved with various areas of RSV research throughout the past years. However, patient involvement can still gain ground with regard to research-agenda setting. Patient representatives are increasingly reshaping the research agenda, but professionals are still the ones who set it. The PAB has created a vehicle to collect and bring the most important issues regarding RSV for patients and their families forward, by uniting patient representatives through the RSV Patient Network. In the coming years, the PAB will put its efforts in enhancing the patients' voice to address the research priorities of those who should benefit most from it.

Conclusions

The RSV PAB is a pioneer in the field of patient involvement in RSV research. The establishment and development of the PAB throughout a period of 9 years has demonstrated that equal partnership and commitment from both patient representatives as well as researchers are essential to benefit the unique perspective of the parents of children who have had RSV. Zero funding from industry, including pharmaceutical partners, has been a corner stone of the PAB success. Involving parents of RSV patients as partners has led towards the establishment of a reliable and independent advisory group for researchers, and many new initiatives to improve awareness about RSV among parents, professionals, and the general public. However, there are still steps that need to be taken to improve representation of the patients' perspective in research. Although patient involvement is increasingly reshaping the research agenda, scientists and medical experts are currently the ones who set it. Parents of children who have had RSV are important stakeholders in research, and involvement of these patient representatives in policy making and awareness raising should become the rule instead of the exception.

Acknowledgements

The authors would like to thank the members of the RSV Patient Advisory Board for their ongoing efforts to improve RSV research, awareness and education. We thank Lies Kriek, the current chair of the PAB, and the members of the PAB support team for their dedication in raising awareness about

RSV and finding new members for the international PAB. We thank Casper Schoemaker, Rinze Benedictus, Paul Geurts and Hester Wessels for critically reviewing this paper.

References

1. Leader S, Kohlhase K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. J Pediatr. 2003;143:S127-32.

2. Shi T, McAllister DA, O'Brien KL, et al. RSV Global Epidemiology Network. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet 2017; 390:946–58.

3. Chatzis O, Darbre S, Pasquier J, et al. Burden of severe RSV disease among immunocompromised children and adults: a 10 year retrospective study. BMC Infect Dis. 2018; 18:111.

4. Falsey AR, Hennesy PA. Formica MA, Cox C, Walsh EE. Respiratory Syncytial Virus Infection in Elderly and High-Risk Adults. N Engl J Med. 2005; 352:1749-59.

5. Boote J, Wong R, Booth A. 'Talking the talk or walking the walk?' A bibliometric review of the literature on public involvement in health research published between 1995 and 2009. Health Expect. 2015;18:44-57.

6. Holmes L, Cresswell K, Williams S, et al. Innovating public engagement and patient involvement through strategic collaboration and practice. Res Involv Engagem. 2019 Oct 21;5:30.

7. van der Scheer L, Garcia E, van der Laan AL, et al. The benefits of patient involvement for translational research. Health Care Anal. 2014;25:225-241

8. Crowe S, Fenton M, Hall M, Cowan K, Chalmers I. Patients', clinicians' and the research communities' priorities for treatment research: there is an important mismatch. Res Involv Engagem. 2015;1:2

9. Caron-Flinterman JF, Broerse JE, Bunders JF. The experiential knowledge of patients: a new resource for biomedical research? Soc Sci Med. 2005;60:2575–2584.

10. Shen S, Doyle-Thomas KAR, Beesley L, et al. How and why should we engage parents as co-researchers in health research? A scoping review of current practices. Health Expect. 2017; 20:543-554.

11. Uding N, Sety M, Kieckhefer GM, et al. Family involvement in health care research: The "Building on Family Strengths" case study. Fam Syst Health. 2007;25:307–322.

12. Edwards V, Wyatt K, Logan S, et al. Consulting parents about the design of a randomized controlled trial of osteopathy for children with cerebral palsy. Health Expect. 2011;14:429–438.

13. Mazur NI, Higgins D, Nunes MC, et al. The respiratory syncytial virus vaccine landscape: lessons from the graveyard and promising candidates. Lancet Infect Dis. 2018; 18:e295-e311.

14. Flynn R, Walton S, Scott SD. Engaging children and families in pediatric Health Research: a scoping review. Res Involv Engagem. 2019; 5:32.

15. Abbasi J. RSV Vaccines, Finally Within Reach, Could Prevent Tens of Thousands of Yearly Deaths. JAMA. 2022;327:204-206.

16. Smith LE, Amlot R, Weinman J, Yiend J, Rubin GJ. A systematic review of factors affecting vaccine uptake in young children. Vaccine. 2017;35(45):6059-69.

Footnote page

Funding: The RSV PAB has received funding through RESCEU from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 116019. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation program and EFPIA. This manuscript reflects only the author's view. The European Union and IMI are not responsible for any use that may be made of the information it contains.

STUDY GROUP MEMBERS

The RESCEU investigators are as follows: Nicole Derksen-Lazet, Corline Parmentier, Louis Bont, Joanne Wildenbeest (University Medical Center Utrecht); Harish Nair (University of Edinburgh), Harry Campbell (University of Edinburgh), Philippe Beutels (Universiteit Antwerpen), Andrew Pollard (University of Oxford), Peter Openshaw (Imperial College London), Federico Martinon-Torres (Servicio Galego de Saude), Terho Heikkinen (University of Turku and Turku University Hospital), Adam Meijer (National Institute for Public Health and the Environment), Thea Fischer (Statens Serum Institut), Maarten van den Berge (University of Groningen), Carlo Giaquinto (PENTA Foundation), Michael Abram (AstraZeneca), Tin Tin Myint Kena Swanson (Pfizer), Bishoy Rizkalla (GlaxoSmithKline), Charlotte Vernhes (Sanofi Pasteur), Scott Gallichan (Sanofi Pasteur), Jeroen Aerssens (Janssen), Veena Kumar (Novavax), Eva Molero (Team-It Research).

Potential conflicts of interest: All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Table 1. Current activities of the RSV Patient Advisory Board, and the success factors and challenges for involvement of the Patient Advisory Board in RSV research.

Activities of the RSV PAB	Success factors	Challenges
Consultative body in reviewing grant proposals, clinical protocol development, and creation of patient information materials in various RSV research projects	Acknowledgement of patient representatives as equal partners Time investment to build on the relationship between	The traditional perception of patients having a passive role in research Time constraints of patients and researchers

Disseminating research findings among patients and the general public Improving awareness of RSV among the general public by organizing awareness campaigns and raising attention from the media Patient community building Educating patients, professionals, and the general public by combining scientific knowledge with personal experiences	researchers and PAB members, discuss expectations, and exchange knowledge and experiences Independent public health funding without any industry funding Establishment of an enthusiastic supporting organization to further expand the PAB	Transient nature of acute RSV infection withholding patients from committing their time for a longer period Linguistic, cultural, and geographical differences between patients and researchers from different countries

PAB: Patient Advisory Board; RSV: Respiratory syncytial virus