**Drawing a Roadmap for Wilms Research and Treatment Together: The Role of Advocacy**

Articles Reviewed

Andrews, S. M., Porter, K. A., Bailey, D. B., & Peay, H. L. (2022). Preparing newborn screening for the future: a collaborative stakeholder engagement exploring challenges and opportunities to modernizing the newborn screening system. *BMC Pediatrics*, *22*(1). <https://doi.org/10.1186/s12887-021-03035-x>

Background and objectives: Projections that 60 transformative cell and gene therapies could be approved by the U.S. Food and Drug Administration (FDA) within 10 years underscore an urgent need to modernize the newborn screening (NBS) system. This study convened expert stakeholders to assess challenges to the NBS system and propose solutions for its modernization.

Methods: NBS stakeholders (researchers, clinicians, state NBS leaders, advocates, industry professionals, and current/ former advisory committee members) participated in one of five mixed-stakeholder panel discussions. Prior to panels, participants completed a survey in which they reviewed and ranked NBS challenges generated from relevant litera- ture. During panels, participants deliberated on challenges and explored potential solutions. Pre-panel survey data were analyzed descriptively. Data from panel discussions were analyzed using a rapid qualitative analysis.

Results: Median scores of the ranked challenges (1 = most important) reveal the top three most important barriers to address: critical missing data for NBS decision-making (Median = 2), burden on state NBS laboratories (Median = 3), and the amount of time required for state-level implementation of screening for new conditions (Median = 4). Panel discussions were rooted in recurring themes: the infant’s well-being should be the focal point; the transformative therapy pipeline, although undeniably positive for individuals with rare diseases, is a threat to NBS capacity; decisions about modernizing NBS should be evidence-based; additional financial support is required but not sufficient for mod- ernization; and modernization will require participation of multiple NBS stakeholders. This final overarching theme is reported in depth, including expertise, coordination, and collaboration challenges facing NBS and novel approaches to oversight, partnership, and coordination that were suggested by participants.

Conclusions: This study engaged representatives from multiple stakeholder groups to generate potential solutions to challenges facing NBS in the United States. These solutions provide a rich starting point for policy makers and other stakeholders who desire to maximize the impact of new transformative therapies for babies, families, and society.

Asch, S., Swink, S. M., Vivar, K. L., Pickford, J., Breuning, L., Wassel, C., Hand, J. L., Milstone, L., & Castelo-Soccio, L. (2021). Use of telemedicine for ichthyosis: Patient advocacy group as conduit to expert physician advice. *Pediatr Dermatol*, *38*(1), 137-142. <https://doi.org/10.1111/pde.14460>

BACKGROUND/OBJECTIVES: Patients with rare diseases are challenged when it comes to finding physicians with expertise in their condition. The Foundation for Ichthyosis and Related Skin Types (FIRST) Tele-Ichthyosis program has provided telemedicine for patients and their families with keratinizing disorders since 2009. This study aims to characterize a decade of experience with the program. METHODS: This retrospective cohort study analyzed cases for demographics of patients and the clinicians who submitted their cases, nature of questions asked, number of expert responses, and characteristics of responses. Surveys were sent electronically to all users of the FIRST Tele-Ichthyosis service to assess experiences with the service and solicit constructive recommendations. Descriptive statistics were performed on the case review and responder surveys. RESULTS: Eighty-eight geographically diverse cases were reviewed showing increased use over time by various specialists for patients of all ages. Sixty-six percent of cases were definitively ichthyosis, and most submitters queried on diagnosis (47%) or treatment (72%). Most submitters described the service as easy to use (66.6%) and advice as timely (61.1%), clear (66.6%), and beneficial (61.1%). All submitters made suggestions for improvement (100%). Experts predominately worked with pediatric populations (70%) and reported self-motivation to volunteer and improve patients' lives (100%). Experts found technological barriers minor and provided feedback to enhance the service. CONCLUSIONS: This report highlights how a rare-disease patient advocacy group successfully supports physician collaboration and patient outcomes through secure and efficient telemedicine. Lessons learned are highly relevant in the current healthcare environment.

Backeljauw, P. F., Andrews, M., Bang, P., Dalle Molle, L., Deal, C. L., Harvey, J., Langham, S., Petriczko, E., Polak, M., Storr, H. L., & Dattani, M. T. (2023). Challenges in the care of individuals with severe primary insulin-like growth factor-I deficiency (SPIGFD): an international, multi-stakeholder perspective. *Orphanet J Rare Dis*, *18*(1), 312. <https://doi.org/10.1186/s13023-023-02928-7>

BACKGROUND: Severe primary insulin-like growth factor-I (IGF-I) deficiency (SPIGFD) is a rare growth disorder characterized by short stature (standard deviation score [SDS] </= 3.0), low circulating concentrations of IGF-I (SDS </= 3.0), and normal or elevated concentrations of growth hormone (GH). Laron syndrome is the best characterized form of SPIGFD, caused by a defect in the GH receptor (GHR) gene. However, awareness of SPIGFD remains low, and individuals living with SPIGFD continue to face challenges associated with diagnosis, treatment and care. OBJECTIVE: To gather perspectives on the key challenges for individuals and families living with SPIGFD through a multi-stakeholder approach. By highlighting critical gaps in the awareness, diagnosis, and management of SPIGFD, this report aims to provide recommendations to improve care for people affected by SPIGFD globally. METHODS: An international group of clinical experts, researchers, and patient and caregiver representatives from the SPIGFD community participated in a virtual, half-day meeting to discuss key unmet needs and opportunities to improve the care of people living with SPIGFD. RESULTS: As a rare disorder, limited awareness and understanding of SPIGFD amongst healthcare professionals (HCPs) poses significant challenges in the diagnosis and treatment of those affected. Patients often face difficulties associated with receiving a formal diagnosis, delayed treatment initiation and limited access to appropriate therapy. This has a considerable impact on the physical health and quality of life for patients, highlighting a need for more education and clearer guidance for HCPs. Support from patient advocacy groups is valuable in helping patients and their families to find appropriate care. However, there remains a need to better understand the burden that SPIGFD has on individuals beyond height, including the impact on physical, emotional, and social wellbeing. CONCLUSIONS: To address the challenges faced by individuals and families affected by SPIGFD, greater awareness of SPIGFD is needed within the healthcare community, and a consensus on best practice in the care of individuals affected by this condition. Continued efforts are also needed at a global level to challenge existing perceptions around SPIGFD, and identify solutions that promote equitable access to appropriate care. Medical writing support was industry-sponsored.

Barry, E., Walsh, J. A., Weinrich, S. L., Beaupre, D., Blasi, E., Arenson, D. R., & Jacobs, I. A. (2021). Navigating the Regulatory Landscape to Develop Pediatric Oncology Drugs: Expert Opinion Recommendations. *Paediatr Drugs*, *23*(4), 381-394. <https://doi.org/10.1007/s40272-021-00455-1>

Regulatory changes have been enacted in the United States (US) and European Union (EU) to encourage the development of new treatments for pediatric cancer. Here, we review some of the factors that have hampered the development of pediatric cancer treatments and provide a comparison of the US and EU regulations implemented to address this clinical need. We then provide some recommendations for each stage of the oncology drug development pathway to help researchers maximize their chance of successful drug development while complying with regulations. A key recommendation is the engagement of key stakeholders such as regulatory authorities, pediatric oncologists, academic researchers, patient advocacy groups, and a Pediatric Expert Group early in the drug development process. During drug target selection, sponsors are encouraged to consult the Food and Drug Administration (FDA), European Medicines Agency (EMA), and the FDA target list, in addition to relevant US and European consortia that have been established to characterize and prioritize oncology drug targets. Sponsors also need to carefully consider the resourcing requirements for preclinical testing, which include ensuring appropriate access to the most relevant databases, clinical samples, and preclinical models (cell lines and animal models). During clinical development, sponsors can account for the pharmacodynamic (PD)/pharmacokinetic (PK) considerations specific to a pediatric population by developing pediatric formulations, selecting suitable PD endpoints, and employing sparse PK sampling or modeling/simulation of drug exposures where appropriate. Additional clinical considerations include the specific design of the clinical trial, the potential inclusion of children in adult trials, and the value of cooperative group trials.

In the last few decades, great progress has been made in developing new treatments for adult cancers. However, development of new treatments for childhood cancers has been much slower. To encourage drug companies (sponsors) to develop effective treatments for childhood cancer, authorities in the United States (US) and Europe have made new rules for drug development. Under these new rules, sponsors developing drugs for specific cancers in adults have to consider whether the target of that drug also causes cancers in children. If this is the case, sponsors have to carry out clinical studies of their drug in children who have cancer that is caused by the same drug target. In this article, we describe some reasons for why drug development for childhood cancers has been slow and the rules created to address this problem in the US and Europe. We share some recommendations to help sponsors maximize their chances of developing an effective drug in children while satisfying the new rules. Specifically, sponsors need to be aware of the differences between studying drugs in adults versus children and how these influence the way the drug is tested. We make several recommendations for each stage of the development process, beginning with what is needed even before human studies begin. Finally, we highlight some issues that sponsors need to think about during drug development, from the preclinical stage (testing drugs in cells and animals) through to clinical testing in adults and pediatric patients with cancer.

Berrios, C., McBeth, M., Bradley-Ewing, A., Schuetz, N., Campbell, A., Talebizadeh, Z., Garrett, J. R., Falicov, T., Martinez, F., Rare Voices Advisory, G., & Hurley, E. A. (2024). Developing a community-led rare disease ELSI research agenda. *Orphanet J Rare Dis*, *19*(1), 23. <https://doi.org/10.1186/s13023-023-02986-x>

BACKGROUND: Research priorities are best defined through engagement with communities who will be impacted by the research and have lived experience of the topics to be studied. We aimed to establish a pediatric rare disease community stakeholder group and empower them in (1) eliciting perspectives from affected families in the wider region and (2) synthesizing collective ideas into a research agenda focused on shared ethical, legal, and social implications (ELSI) across rare disease. METHODS: This two-year project utilized a community-centered approach to engage rare disease community members as equal partners in developing a research agenda for ELSI in rare disease. We established "Rare Voices" (RV), a 22-member stakeholder group of patients, parents, clinicians and researchers. Following capacity-building trainings, RV designed and conducted listening sessions with teen patients and parents of children with rare diseases to explore challenges, positive experiences, and ethical concerns. Listening session findings were synthesized and contextualized into research topics, which RV members further refined and prioritized. We used established measures to assess RV member engagement and satisfaction. RESULTS: From 14 listening sessions with parents (n = 52) and teen patients (n = 13), RV identified eight core research topics as most important for future rare disease research: coordinating care, communication, accessing resources and care, impact on family unit, community and support in society, mental health and identity, ethical aspects of care, and uncertainty. RV members were highly engaged throughout the two-year project and reported high levels of satisfaction with the experience and research agenda. CONCLUSIONS: Through capacity-building and authentic engagement, this project resulted in a community-led rare disease research agenda to guide future rare disease ELSI research that aligns with patients' and families' priorities. An environment of equal partnership and respect created a space for mutual learning where community members were empowered to shape the research agenda based on their collective experiences. The agenda recognizes the shared psychosocial and healthcare experiences of rare disease and offers practical areas of research to address patient and family needs.

Bronstein, M. G., Pan, R. J., Dant, M., & Lubin, B. (2019). Leveraging Evidence-Based Public Policy and Advocacy to Advance Newborn Screening in California. *Pediatrics*, *143*(2). <https://doi.org/10.1542/peds.2018-1886>

In 2016, the EveryLife Foundation for Rare Diseases, in partnership with Dr Pan, who is a pediatrician and state senator in California, launched legislation to advance and expand newborn screening. Researchers have shown that newborn screening can be cost-effective and can greatly improve health outcomes for patients with rare diseases. However, adding additional diseases in newborn screening is a long process, requiring legislative approval in addition to new state funding. Such process delays can lead to protracted diagnostic odysseys for patients, especially those with rare diseases. These delays can result in irreversible morbidity and, in some cases, early mortality for patients. To improve this process, legislation known as Senate Bill 1095 was introduced to require California to adhere to the latest federal recommendations for newborn screening within 2 years. We provide insight and describe the process of advancing state legislation, coalition building, and managing opposition. Senate Bill 1095 would become law in 2016, requiring California to screen for 2 new rare diseases by August 2018: mucopolysaccharidosis type I and Pompe disease. This case study can serve as a model for advocates looking to expand state newborn-screening programs.

Brunelle Praschberger, A., Post, A. E. M., Hermanns, S., & Graessner, H. (2022). Establishing and boosting communication in the European Reference Network for Rare Neurological Diseases (ERN-RND): the impact of offering free educational webinars. *Orphanet J Rare Dis*, *17*(1), 89. <https://doi.org/10.1186/s13023-022-02209-9>

BACKGROUND: Since it first started operating in 2017, the European Reference Network for Rare Neurological Diseases (ERN-RND) implemented a multi-channel communication strategy to effectively reach its target audience: healthcare professionals, patients, researchers, industry representatives and the general public. We first created a website containing useful and up to date information, followed by social media accounts. Here, the analytical data collected about the ERN-RND website and social media channels was compared (Twitter, Facebook, YouTube) during two periods: October 2018 to September 2019, and the year after the ERN-RND free educational webinars were launched: from October 2019 to September 2020. This allowed us to quantify the impact of offering a tangible product (webinars) on the communication strategy. RESULTS: The analytical data obtained from October 2018 to September 2019 and from October 2019 to September 2020 clearly shows a significant increase in traffic and followers since the launch of the ERN-RND webinars in November 2019. We also created a communication survey which was disseminated between February and June 2021. We collected responses from 61 people: 38 healthcare professionals, 11 scientists, 10 patients (advocates), 2 industry representatives, 1 patient association, 1 charity representative, 1 resident and 1 master student. Most respondents answered "webinars" as the number one reason when asked about which content they look for on the ERN-RND website. CONCLUSIONS: Offering a tangible product-such as the webinars presented in this report-to a specific target group (healthcare professionals) supported our communication strategy by driving traffic to ERN-RND communication channels. It has also successfully tackled ERN-RND's general aim: by enabling the flow of knowledge on rare neurological and movement disorders to the medical community in hospitals treating patients with these rare and complex conditions, patients ultimately benefit from improved and faster diagnosis, care, and treatment. We aim to set up similar strategies to effectively reach other or the same target groups. For healthcare professionals, organising eConsultations via the Clinical Patient Management System or disseminating standards of care such as diagnostic and therapeutic algorithms as well as clinical practice guidelines might offer potential. For the patient community, organising customised and multilingual webinars could also work.

Chediak, L., Bedlington, N., Gadson, A., Kent, A., Khalek, A. A., Rosen, L., Rust, M., Shaikh, M. F., Tan, M. Y., Wiafe, S. A., Baynam, G., & Steward, C. A. (2022). Unlocking sociocultural and community factors for the global adoption of genomic medicine. *Orphanet Journal of Rare Diseases*, *17*(1). <https://doi.org/10.1186/s13023-022-02328-3>

Advances in genomic sequencing and genetic testing are increasingly transforming the diagnosis and treatment of diseases—specifically, rare diseases. However, the application and benefit of such technologies remain inequitable globally. There is a clear and urgent need to provide genomic sequencing to people across the global population, including people living in under-resourced areas and/or underrepresented populations. Financial considerations are the most obvious barriers to the adoption of genomic medicine, yet there are many other factors that are not so obvious, such as geography, language, communication, and culture. Herein, we use the lens of rare diseases and focus on firstly, selected socio-cultural factors, and in particular stigma; and secondly, empowering community factors such as education, advocacy and connectivity amongst people living with rare diseases globally. These are critical areas of need and opportunity if genomic medicine is to achieve equitable and global adoption in the patient best-interest across low- middle- and high-income country health systems. Furthermore, we touch on specific child health aspects and how they can point towards opportunities to build on specific infrastructures.

Ekins, S., & Perlstein, E. O. (2018). Doing it All - How Families are Reshaping Rare Disease Research. *Pharm Res*, *35*(10), 192. <https://doi.org/10.1007/s11095-018-2481-7>

The face of rare disease drug discovery and development is changing right before our eyes. The outliers of the past were the plucky parents who summoned up the courage to try to treat their children against all odds. Think of the rare disease focused movies 'Lorenzo's Oil' and 'Extraordinary Measures' but now accelerated to develop treatments even quicker. Parents, patient advocates and their collaborators are now capable of doing it all themselves. We think this will have profound implications for everyone from the incumbent rare disease foundations that have held sway for decades to the multibillion dollar rare disease market, BioPharma companies, VCs and angel investors that inhabit this space. The repercussions of this disruption will no doubt impact healthcare in general and ultimately influence how we develop treatments for major diseases as well. We present several lines of evidence for our viewpoint from our personal experiences interacting with many rare disease families and patient advocates in recent years.

Flegg, K., Gelkopf, M. J., Johnson, S. A., Dimaras, H., & Canadian Retinoblastoma Research Advisory Board Priority Setting Steering, C. (2020). The top 10 retinoblastoma research priorities in Canada as determined by patients, clinicians and researchers: a patient-oriented priority-setting partnership. *CMAJ Open*, *8*(2), E420-E428. <https://doi.org/10.9778/cmajo.20190221>

BACKGROUND: Retinoblastoma is a childhood cancer of the eye that can have lifelong effects on patients and families. The purpose of this study was for people affected by retinoblastoma, clinicians and researchers to jointly determine the top 10 retinoblastoma research priorities in Canada. METHODS: An adaptation of the James Lind Alliance Priority Setting Partnership (PSP) methodology was employed. People were invited to participate in any stage of the priority-setting process if they were a resident of Canada, and were a patient with retinoblastoma (or a family member or friend of someone diagnosed with retinoblastoma) or a clinician or researcher interested in retinoblastoma. Patients were full partners in study design and implementation, and result dissemination, through involvement in a national working group (1 patient and 9 nonpatients) and steering committee (4 patients and 11 nonpatients). In phase 1 of the study, participants responded to an online survey that asked, "What questions about retinoblastoma would you like to see answered by research?" In phase 2, the steering committee reviewed and refined the list of survey responses and decided on a list of 30 questions to be ranked by means of the nominal group technique in phase 3, a priority-setting workshop. RESULTS: In total, 175 retinoblastoma research questions were suggested by 59 survey participants (38 patients and 21 nonpatients). The categories with the greatest number of questions were genetics and molecular (45 [25.7%]), second cancer (29 [16.6%]) and psychosocial (27 [15.4%]). The top 10 questions as ranked by the workshop participants (10 patients and 10 nonpatients) fell into 7 categories: second cancer (2 questions), follow-up (2), psychosocial (2), treatment (1), diagnosis (1), global health (1) and miscellaneous (1). The early diagnosis of retinoblastoma was identified as the top retinoblastoma research priority in Canada. INTERPRETATION: The list of priorities will serve as a resource for advocacy groups, research teams and funding agencies that focus on retinoblastoma. The inclusion of researchers as participants was an adaptation of the James Lind Alliance PSP methodology and enriched the research prioritization process.

Härkönen, P. L., Seidlin, M., Holzman, R., Knight, P., Korf, B., Rangel Miller, V., Viskochil, D., & Bakker, A. (2017). Characterization and utilization of an international neurofibromatosis web-based, patient–entered registry: An observational study. *PLoS One*, *12*(6). <https://doi.org/10.1371/journal.pone.0178639>

The neurofibromatoses (neurofibromatosis type 1, neurofibromatosis type 2 and schwanno- matosis) are rare disorders having clinical manifestations that vary greatly from patient to patient. The rarity and variability of these disorders has made it challenging for investigators to identify sufficient numbers of patients with particular clinical characteristics or specific germline mutations for participation in interventional studies. Similarly, because the natural history of all types of neurofibromatosis (NF) is variable and unique for each individual, it is difficult to identify meaningful clinical outcome measures for potential therapeutic interven- tions. In 2012, the Children’s Tumor Foundation created a web-based patient-entered data- base, the NF Registry, to inform patients of research opportunities for which they fit general eligibility criteria and enable patients to contact investigators who are seeking to enroll patients in approved trials. Registrants were recruited through CTF-affiliated NF clinics and conferences, through its website, and by word-of-mouth and social media. Following online consent, demographic information and details regarding manifestations of NF were solicited on the Registry website. Statistical analyses were performed on data from a cohort of 4680 registrants (the number of registrants as of October 9, 2015) who met diagnostic criteria for one of the 3 NF conditions. The analyses support our hypothesis that patient-reported symp- tom incidences in the NF Registry are congruent with published clinician-sourced data. Between April 26, 2013 and July 8, 2016, the registry has been useful to investigators in recruitment, particularly for observational trials, especially those for development of patient- reported outcomes.

Hegde, D., & Sampat, B. (2015). Can Private Money Buy Public Science? Disease Group Lobbying and Federal Funding for Biomedical Research. *Management Science*, *61*(10), 2281-2298. <https://doi.org/10.1287/mnsc.2014.2107>

Private interest groups lobby politicians to influence public policy. However, little is known about how lob- bying influences the policy decisions made by federal agencies. We study this through examining lobbying by advocacy groups associated with rare diseases for funding by the National Institutes of Health (NIH), the world’s largest funder of biomedical research. Disease group lobbying for NIH funding has been controversial, with critics alleging that it distorts public funding toward research on diseases backed by powerful groups. Our data reveal that lobbying is associated with higher political support, in the form of congressional “soft earmarks” for the diseases. Lobbying increases with disease burden and is more likely to be associated with changes in NIH funding for diseases with higher scientific opportunity, suggesting that it may have a useful informational role. Only special grant mechanisms that steer funding toward particular diseases, which com- prise less than a third of the NIH’s grants, are related to earmarks. Thus, our results suggest that lobbying by private groups influences federal funding for biomedical research. However, the channels of political influence are subtle, affect a small portion of funding, and may not necessarily have a distortive effect on public science.

Javaid, M. K., Mordenti, M., Boarini, M., Sangiorgi, L., Westerheim, I., Alves, I., Skarberg, R. T., Appelman-Dijkstra, N. M., & Grasemann, C. (2021). Patients’ priorities and expectations on an EU registry for rare bone and mineral conditions. *Orphanet Journal of Rare Diseases*, *16*(1). <https://doi.org/10.1186/s13023-021-02069-9>

Background: Understanding the natural history of rare bone and mineral conditions is essential for improving clini‐ cal practice and the development of new diagnostics and therapeutics. Recruitment and long‐term participation in registries are key challenges for researchers.

Methods: To understand the user needs, the European Reference Network on Rare Bone Diseases (ERN BOND) and European Patient Advocacy Groups developed and implemented a multinational survey about the patient’s preferred database content and functionality through an iterative consensus process. The survey was disseminated by national and international patient groups and healthcare professionals. The findings were analysed using descriptive statistics and multivariate regression.

Results: There were 493 eligible responses from 378 adults, 15 children and 100 parents, guardians or carers (PGC) across 22 rare bone and mineral conditions. Osteogenesis imperfecta constituted 53.4% of responses. Contents related to improving treatment and medical services scored the highest and contents about anxiety and socializing scored less highly. Additional content was recommended by 205 respondents. Respondents preferred data entry by their Healthcare Provider (HCP). However, less than 50% of adults received followup from their specialist HCP at least annually and 29% were followed up as needed.

Conclusions: This survey of individuals, their family, guardians and carers has prioritised the key components for an EU‐based rare bone and mineral condition research database. The survey highlights issues around collecting psy‐ chosocial impacts as well as measures of HCP trust. The survey demonstrated that using only specialist centre visits for data collection, while preferred by patients, will miss a substantial number of individuals, limiting generalisability. Combined HCP and patient platforms will be required to collect representative and complete natural history data for this patient group.

Khan, T., Stewart, M., Blackman, S., Rousseau, R., Donoghue, M., Cohen, K., Seibel, N., Fleury, M., Benettaib, B., Malik, R., Vassal, G., & Reaman, G. (2019). Accelerating Pediatric Cancer Drug Development: Challenges and Opportunities for Pediatric Master Protocols. *Ther Innov Regul Sci*, *53*(2), 270-278. <https://doi.org/10.1177/2168479018774533>

Although outcomes for children with cancer have significantly improved over the past 40 years, there has been little progress in the treatment of some pediatric cancers, particularly when advanced. Additionally, clinical trial options and availability are often insufficient. Improved genomic and immunologic understanding of pediatric cancers, combined with innovative clinical trial designs, may provide an enhanced opportunity to study childhood cancers. Master protocols, which incorporate the use of precision medicine approaches, coupled with the ability to quickly assess the safety and effectiveness of new therapies, have the potential to accelerate early-phase clinical testing of novel therapeutics and which may result in more rapid approval of new drugs for children with cancer. Designing and conducting master protocols for children requires addressing similar principles and requirements as traditional adult oncology trials, but there are also unique considerations for master protocols conducted in children with cancer. The purpose of this paper is to define the key challenges and opportunities associated with this approach in order to ensure that master protocols can be adapted to benefit children and adolescents and ensure that adequate data are captured to advance, in parallel, the clinical development of investigational agents for children with cancer.

Long, K. A., Goldish, M., Lown, E. A., Ostrowski, N. L., Alderfer, M. A., Marsland, A. L., Ring, S., Skala, S., & Ewing, L. J. (2015). Major lessons learned from a nationally-based community-academic partnership: addressing sibling adjustment to childhood cancer. *Fam Syst Health*, *33*(1), 61-67. <https://doi.org/10.1037/fsh0000084>

Prolonged, intensive treatment protocols for childhood cancer disrupt family routines and daily functioning, with effects extending to all family members. Despite their unique needs, siblings of children with cancer receive limited attention from community organizations and researchers. Community-academic partnerships may foster research that effectively assesses and addresses siblings' unmet needs. In this article, "community" refers to siblings of children with cancer who participate in SuperSibs!, a national nonprofit organization for siblings of children with cancer. This article (a) describes a replicable model for successful community-academic partnerships: the Sibling Research Advisory Board (SRAB) and (b) articulates "lessons learned" from this partnership, including documenting the ability to recruit a representative sample through a community organization. Lessons emerged from an iterative process of discussion and revision that involved all SRAB members. This case study describes approaches to overcoming practical obstacles in community-partnered research planning and implementation. To meet the common goals of identifying and addressing unmet sibling needs, SRAB partners learned to establish a common language, identify each team member's unique expertise, and acknowledge differences in approach (e.g., methodology, pace of accomplishment) between research and community service. SRAB's ability to recruit a representative sample was achieved through close collaboration with SuperSibs! and implementation of active recruitment strategies to overcome barriers to research participation. Protection of community member privacy was emphasized alongside methodological rigor. Community-academic partnerships enable research with high-need, hard-to-access populations. Proactively identifying and addressing common pitfalls of community-academic partnerships promotes community engagement and acceptability and facilitates high-quality research.

Ludwinski, D., Scobie, N., & Knox, L. (2022). Role of Patients and Advocates in Cancer Therapeutics Development. In J. D. e. a. (eds.) (Ed.), *Pediatric Cancer Therapeutics Development* (pp. 123-141). <https://doi.org/10.1007/978-3-031-06357-2_9>

This chapter is dedicated to the children and young people who participate in clinical research and their families. Their bravery and contribution to advancing research are recognized and valued.

Merkel, P. A., Manion, M., Gopal-Srivastava, R., Groft, S., Jinnah, H. A., Robertson, D., Krischer, J. P., & Rare Diseases Clinical Research, N. (2016). The partnership of patient advocacy groups and clinical investigators in the rare diseases clinical research network. *Orphanet J Rare Dis*, *11*(1), 66. <https://doi.org/10.1186/s13023-016-0445-8>

BACKGROUND: Among the unique features of the Rare Diseases Clinical Research Network (RDCRN) Program is the requirement for each Consortium to include patient advocacy groups (PAGs) as research partners. This development has transformed the work of the RDCRN and is a model for collaborative research. This article outlines the roles patients and PAGs play in the RDCRN and reports on the PAGs' impact on the Network's success. METHODS: Principal Investigators from the 17 RDCRN Consortia and 28 representatives from 76 PAGs affiliated with these Consortia were contacted by email to provide feedback via an online RDCRN survey. Impact was measured in the key areas of 1) Research logistics; 2) Outreach and communication; and 3) Funding and in-kind support. Rating choices were: 1-very negative, 2-somewhat negative, 3-no impact, 4-somewhat positive, and 5-very positive. RESULTS: Twenty-seven of the PAGs (96 %) disseminate information about the RDCRN within the patient community. The Consortium Principal Investigators also reported high levels of PAG involvement. Sixteen (94 %) Consortium Principal Investigators and 25 PAGs (89 %) reported PAGs participation in protocol review, study design, Consortium conference calls, attending Consortium meetings, or helping with patient recruitment. CONCLUSIONS: PAGs are actively involved in shaping Consortia's research agendas, help ensure the feasibility and success of research protocols by assisting with study design and patient recruitment, and support training programs. This extensive PAG-Investigator partnership in the RDCRN has had a strongly positive impact on the success of the Network.

Moitra, K., Garcia, S., Jaldin, M., Etoundi, C., Cooper, D., Roland, A., Dixon, P., Reyes, S., Turan, S., Terry, S., & Dean, M. (2017). ABCC6 and Pseudoxanthoma Elasticum: The Face of a Rare Disease from Genetics to Advocacy. *Int J Mol Sci*, *18*(7). <https://doi.org/10.3390/ijms18071488>

Pseudoxanthoma elasticum (PXE) is an autosomal recessive disorder characterized by the mineralization of connective tissues in the body. Primary manifestation of PXE occurs in the tissues of the skin, eyes, and cardiovascular system. PXE is primarily caused by mutations in the ABCC6 gene. The ABCC6 gene encodes the trans-membrane protein ABCC6, which is highly expressed in the kidneys and liver. PXE has high phenotypic variability, which may possibly be affected by several modifier genes. Disease advocacy organizations have had a pivotal role in bringing rare disease research to the forefront and in helping to sustain research funding for rare genetic diseases in order to help find a treatment for these diseases, pseudoxanthoma elasticum included. Because of these initiatives, individuals affected by these conditions benefit by being scientifically informed about their condition, having an effective support mechanism, and also by contributing to scientific research efforts and banking of biological samples. This rapid progress would not have been possible without the aid of disease advocacy organizations such as PXE International.

Nguyen, C. Q., Kariyawasam, D., Alba-Concepcion, K., Grattan, S., Hetherington, K., Wakefield, C. E., Woolfenden, S., Dale, R. C., Palmer, E. E., & Farrar, M. A. (2022). 'Advocacy groups are the connectors': Experiences and contributions of rare disease patient organization leaders in advanced neurotherapeutics. *Health Expect*, *25*(6), 3175-3191. <https://doi.org/10.1111/hex.13625>

INTRODUCTION: Biomedical progress has facilitated breakthrough advanced neurotherapeutic interventions, whose potential to improve outcomes in rare neurological diseases has increased hope among people with lived experiences and their carers. Nevertheless, gene, somatic cell and other advanced neurotherapeutic interventions carry significant risks. Rare disease patient organizations (RDPOs) may enhance patient experiences, inform expectations and promote health literacy. However, their perspectives are understudied in paediatric neurology. If advanced neurotherapeutics is to optimize RDPO contributions, it demands further insights into their roles, interactions and support needs. METHODS: We used a mixed-methodology approach, interviewing 20 RDPO leaders representing paediatric rare neurological diseases and following them up with two online surveys featuring closed and open-ended questions on advanced neurotherapeutics (19/20) and negative mood states (17/20). Qualitative and quantitative data were analysed using thematic discourse analysis and basic descriptive statistics, respectively. RESULTS: Leaders perceived their roles to be targeted at educational provision (20/20), community preparation for advanced neurotherapeutic clinical trials (19/20), information simplification (19/20) and focused research pursuits (20/20). Although most leaders perceived the benefits of collaboration between stakeholders, some cited challenges around collaborative engagement under the following subthemes: conflicts of interest, competition and logistical difficulties. Regarding neurotherapeutics, RDPO leaders identified support needs centred on information provision, valuing access to clinician experts and highlighting a demand for co-developed, centralized, high-level and understandable, resources that may improve information exchange. Leaders perceived a need for psychosocial support within themselves and their communities, proposing that this would facilitate informed decision-making, reduce associated psychological vulnerabilities and maintain hope throughout neurotherapeutic development. CONCLUSION: This study provides insights into RDPO research activities, interactions and resource needs. It reveals a demand for collaboration guidelines, central information resources and psychosocial supports that may address unmet needs and assist RDPOs in their advocacy. PATIENT OR PUBLIC CONTRIBUTION: In this study, RDPO leaders were interviewed and surveyed to examine their perspectives and roles in advanced neurotherapeutic development. Some participants sent researchers postinterview clarification emails regarding their responses to questions.

Oliveira, M., Zancul, E., & Fleury, A. L. (2021). Design thinking as an approach for innovation in healthcare: systematic review and research avenues. *BMJ Innovations*, *7*(2), 491-498. <https://doi.org/10.1136/bmjinnov-2020-000428>

Design thinking has been increasingly adopted as an approach to support innovation in healthcare. Recent publications report design thinking application to various innovation

projects, across medical specialties, including paediatrics, psychiatry, radiology, gastroenterology, oncology, orthopaedics and surgery, as well as to innovation in hospital operations and healthcare management. Current literature in the area typically focuses on single case descriptions. With the recent increase in the number of cases, there is an opportunity to assess multiple cases to identify patterns and avenues for further research. This study provides a systematic review of published design thinking projects in healthcare. The aim of the study is to provide an overview of how design thinking has been applied in the healthcare sector. Data collection was based on Institute of Scientific Information (ISI) Web of Science, PubMed and Scopus databases. The systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A total of 32 original pieces of research was selected for analysis, being classified and assessed. The paper presents current status of research and practice from various perspectives, including the design thinking progression phase—inspiration, ideation, implementation—and the prevalence of design thinking tools. Avenues for further research include the need to increase focus on the inspiration phase, the opportunity for platforms for leveraging the integration of individuals in innovation projects, and the opportunity to enhance the role of lead users in healthcare innovation.

Pearson, A. D. J., de Rojas, T., Karres, D., Reaman, G., Scobie, N., Fox, E., Lesa, G., Ligas, F., Norga, K., Nysom, K., Pappo, A., Weigel, B., Weiner, S. L., & Vassal, G. (2024). Impact of ACCELERATE Paediatric Strategy Forums: a review of the value of multi-stakeholder meetings in oncology drug development. *J Natl Cancer Inst*, *116*(2), 200-207. <https://doi.org/10.1093/jnci/djad239>

In a landscape of an increasing number of products and histology and age agnostic trials for rare patient cancer, prioritization of products is required. Paediatric Strategy Forums, organized by ACCELERATE and the European Medicines Agency with participation of the US Food and Drug Administration, are multi-stakeholder meetings that share information to best inform pediatric drug development strategies and subsequent clinical trial decisions. Academia, industry, regulators, and patient advocates are equal members, with patient advocates highlighting unmet needs of children and adolescents with cancer. The 11 Paediatric Strategy Forums since 2017 have made specific and general conclusions to accelerate drug development. Conclusions on product prioritization meetings, as well as global master protocols, have been outputs of these meetings. Forums have provided information for regulatory discussions and decisions by industry to facilitate development of high-priority products; for example, 62% of high-priority assets (agreed at a Forum) in contrast to 5% of those assets not considered high priority have been the subject of a Paediatric Investigational Plan or Written Request. Where there are multiple products of the same class, Forums have recommended a focused and sequential approach. Class prioritization resulted in an increase in waivers for non-prioritized B-cell products (44% to 75%) and a decrease in monotherapy trials, proposed in Paediatric Investigation Plans (PIP) submissions of checkpoint inhibitors from 53% to 19%. Strategy Forums could play a role in defining unmet medical needs. Multi-stakeholder forums, such as the Paediatric Strategy Forum, serve as a model to improve collaboration in the oncology drug development paradigm.

Petkovic, J., Riddle, A., Akl, E. A., Khabsa, J., Lytvyn, L., Atwere, P., Campbell, P., Chalkidou, K., Chang, S. M., Crowe, S., Dans, L., Jardali, F. E., Ghersi, D., Graham, I. D., Grant, S., Greer-Smith, R., Guise, J.-M., Hazlewood, G., Jull, J., . . . Tugwell, P. (2020). Protocol for the development of guidance for stakeholder engagement in health and healthcare guideline development and implementation. *Systematic Reviews*, *9*(1). <https://doi.org/10.1186/s13643-020-1272-5>

Background: Stakeholder engagement has become widely accepted as a necessary component of guideline development and implementation. While frameworks for developing guidelines express the need for those potentially affected by guideline recommendations to be involved in their development, there is a lack of consensus on how this should be done in practice. Further, there is a lack of guidance on how to equitably and meaningfully engage multiple stakeholders. We aim to develop guidance for the meaningful and equitable engagement of multiple stakeholders in guideline development and implementation.

Methods: This will be a multi-stage project. The first stage is to conduct a series of four systematic reviews. These will (1) describe existing guidance and methods for stakeholder engagement in guideline development and implementation, (2) characterize barriers and facilitators to stakeholder engagement in guideline development and implementation, (3) explore the impact of stakeholder engagement on guideline development and implementation, and (4) identify issues related to conflicts of interest when engaging multiple stakeholders in guideline development and implementation.

Discussion: We will collaborate with our multiple and diverse stakeholders to develop guidance for multi-stakeholder engagement in guideline development and implementation. We will use the results of the systematic reviews to develop a candidate list of draft guidance recommendations and will seek broad feedback on the draft guidance via an online survey of guideline developers and external stakeholders. An invited group of representatives from all stakeholder groups will discuss the results of the survey at a consensus meeting which will inform the development of the final guidance papers.

Our overall goal is to improve the development of guidelines through meaningful and equitable multi-stakeholder engagement, and subsequently to improve health outcomes and reduce inequities in health.

Pintér, D. G. (2016). Public Self-Demolition in Practise: The Conclusions of the Crisis Communication of the Children Cancer Foundation from the Perspective of Public Relations. *Periodica Polytechnica Social and Management Sciences*, *24*(1), 41-51. <https://doi.org/10.3311/PPso.8472>

By 2014 the revenue of the Hungarian Children Cancer Foun- dation Non-Proit Organisation deriving from the 1% offer- ings of citizens’ personal income taxes dwindled to less than a third of the rates in former years, which was due to a series of scandals relating to one of Hungary’s largest nonproit com- panies that lasted several months. This article focuses on the press conference organised by the president of the Children Cancer Foundation, which was supposed to clear him and the institution of the accusations received, and besides, to spread further information aiming to tackle problems regarding the general operation of the institution. There are two hypothe- ses that serve as the basis of my analysis; on the one hand, I argue that via the media even an insigniicant event may turn into an issue of nationwide attention if it lacks an appropriate interpretation and has undeined contents. On the other hand, it is illustrated that failing to identify the different natures of the accusations received by the brand and its employees may have a negative impact on the judgement of the crisis situa- tion and the reputation of the institution by the public. Fram- ing is essential to my analysis, which may be observed in the changes of the public opinion regarding people’s responsibility and attitude to certain issues. Although the press featured such opinions relating to the Hungarian Children Cancer Founda- tion that belong to the domain of politics, the present analysis is not intended to adjudicate the activities of the organisation at all. On the contrary, the actions of the institution are inves- tigated only through crisis communicative aspects.

Pinto, D., Martin, D., & Chenhall, R. (2016). The involvement of patient organisations in rare disease research: a mixed methods study in Australia. *Orphanet J Rare Dis*, *11*(1), 2. <https://doi.org/10.1186/s13023-016-0382-6>

BACKGROUND: We report here selected findings from a mixed-methods study investigating the role of Australian rare disease patient organisations (RDPOs) in research. Despite there being many examples of RDPOs that have initiated and supported significant scientific advances, there is little information - and none at all in Australia - about RDPOs generally, and their research-related goals, activities, and experiences. This information is a pre-requisite for understanding what RDPOs bring to research and how their involvement could be strengthened. METHODS: We reviewed 112 RDPO websites, conducted an online survey completed by 61 organisational leaders, and interviewed ten leaders and two key informants. Quantitative and qualitative data were analysed using basic descriptive statistics and content analysis, respectively. RESULTS: Although most are small volunteer-based groups, more than 90% of the surveyed RDPOs had a goal to promote or support research on the diseases affecting their members. Nearly all (95 %) had undertaken at least one research-related activity - such as providing funding or other support to researchers - in the previous five years. However, RDPO leaders reported considerable challenges in meeting their research goals. Difficulties most frequently identified were insufficient RDPO resources, and a perceived lack of researchers interested in studying their diseases. Other concerns included inadequate RDPO expertise in governing research "investments", and difficulty engaging researchers in the organisation's knowledge and ideas. We discuss these perceived challenges in the light of two systemic issues: the proliferation of and lack of collaboration between RDPOs, and the lack of specific governmental policies and resources supporting rare disease research and patient advocacy in Australia. CONCLUSION: This study provides unique information about the experiences of RDPOs generally, rather than experiences retrospectively reported by RDPOs associated with successful research. We describe RDPOs' valuable contributions to research, while also providing insights into the difficulties for small organisations trying to promote research. The study is relevant internationally because of what it tells us about RDPOs; however, we draw attention to specific opportunities in Australia to support RDPOs' involvement in research, for the benefit of current and future generations affected by rare diseases.

Rahimzadeh, V., Wolfert, S., Buenger, V., Campbell, C., French, R., Ludwinski, D., Weinstein, A., & Barrett, C. (2022). A systematic literature review to identify ethical, legal, and social responsibilities of nonprofit organizations when funding clinical trials in pediatric cancer. *Pediatr Blood Cancer*, *69*(9), e29854. <https://doi.org/10.1002/pbc.29854>

Nonprofit organizations (NPOs) play critical roles as funding sources, research partners, and disseminators of drug developments in pediatric cancer. Yet the literature provides limited guidance about ethical best practices when NPOs make trial funding decisions in this space. We conducted a systematic review of the literature indexed in PubMed and Web of Science to identify the ethical, legal, and social responsibilities of NPOs to four key stakeholder groups in funding pediatric cancer trials: (i) patients/families, (ii) researchers, (iii) industry sponsors, and (iv) donors. We applied the lifecycle framework for patient engagement in drug research and development proposed by Geissler and colleagues to analyze themes related to NPOs' responsibilities across 54 articles that met our inclusion criteria. Emergent themes included transparency surrounding conflicts of interest, the rigor of scientific review, and communication with patients/communities about trial progress. Our research identified critical gaps in best practices for negotiating research partnerships, managing competing research priorities, and pursuing alternative financing models including venture philanthropy. Results from our review informed a set of best practices to guide NPOs in making trial funding decisions that align with stakeholder values and interests.

Rodriguez-Laguna, L., Davis, K., Finger, M., Aubel, D., Vlamis, R., & Johnson, C. (2022). Mapping the PIK3CA-related overgrowth spectrum (PROS) patient and caregiver journey using a patient-centered approach. *Orphanet J Rare Dis*, *17*(1), 189. <https://doi.org/10.1186/s13023-022-02338-1>

BACKGROUND: PROS disorders are driven by somatic, gain-of-function mutations in PIK3CA that result in hyperactivation of the phosphatidylinositol-3-kinase (PI3K) signaling pathway. PROS encompasses a broad spectrum of overlapping phenotypes (including overgrowth and vascular malformations) that vary significantly in their severity; every case is unique, leading to different, complex experiences. Here, we aim to describe the PROS experience from the patients' and caregivers' points of view, from onset to diagnosis to treatment and support. RESULTS: The PROS patient journey was developed using a literature review, an ethnography study, health care professional (HCP) research, and social listening. It was then validated with patients, caregivers, and patient advocates. Physician research included 94 PROS centers and other vascular anomaly centers throughout the United States and Europe. Ethnographic research included 24 patients, caregivers, and/or advocates; selected data from 223 patients were reviewed. Key priority areas of need were identified, along with barriers to and potential enablers of quality care. Visual mapping of the PROS patient and family journey was developed to identify key personal health and system issues, and opportunities for improvements throughout patients' lifespans. Maps were also developed for 3 specific conditions: Klippel-Trenaunay syndrome (K-T); congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal anomalies (CLOVES) syndrome; and megalencephaly-capillary malformation syndrome (M-CM). Overall, most patients with PROS conditions and their families struggle with a long path to diagnosis, access to genetic testing, and finding qualified specialists. Following diagnosis, patients and families are frequently challenged with major medical events, comorbidities, unpredictability, frequent hospitalization, impact on school and work, the need for multidisciplinary care, unwanted attention, adverse impact on mental and emotional health, and financial pressures. Lack of effective pain management emerged as a substantial issue. Challenges and barriers to quality care shift throughout patients' lifespans; transition from pediatric to adult care can be especially difficult. CONCLUSIONS: This patient journey in PROS was created in collaboration with patients, caregivers, and advocates as key partners. This novel methodology, which could be applied elsewhere, can more accurately identify areas of unmet need, barriers to care, education topics, and assist HCPs to understand the patient and family perspective.

Stein, S., Bogard, E., Boice, N., Fernandez, V., Field, T., Gilstrap, A., Kahn, S. R., Larkindale, J., & Mathieson, T. (2018). Principles for interactions with biopharmaceutical companies: the development of guidelines for patient advocacy organizations in the field of rare diseases. *Orphanet J Rare Dis*, *13*(1), 18. <https://doi.org/10.1186/s13023-018-0761-2>

BACKGROUND: Rare diseases are a global public health concern, affecting an estimated 350 million individuals. Only 5% of approximately 7000 known rare diseases have a treatment, and only about half have a patient advocacy organization. Biopharmaceutical companies face complex challenges in developing treatments for rare diseases. Patient advocacy organizations may play a major role by positively influencing research and development, clinical trials, and regulations. Thus, collaboration among patient advocacy organizations and industry is essential to bring new therapeutics to patients. METHODS: We identified an unmet need for guidelines on day-to-day decision-making by rare disease patient advocacy organizations when working with biopharmaceutical partners. We convened an Independent Expert Panel experienced in collaborations between patient advocacy organizations and biopharmaceutical companies (April 2017) to develop consensus guidelines for these relationships. The guidelines were based on an original version by the International Fibrodysplasia Ossificans Progressiva Association (IFOPA). The Expert Panel reviewed and broadened these to be applicable to all patient advocacy organizations. Comments on the draft Guidelines were provided first by Panel participants and subsequently by six independent experts from patient advocacy organizations and industry. RESULTS: The Panel comprised four experts from the rare disease community who lead patient advocacy organizations; three leaders who perform advocacy functions within biopharmaceutical companies; and two facilitators, both having leadership experience in rare diseases and industry. The finalized Guidelines consist of four main sections: Identification and Engagement With Companies, Patient Engagement and Patient Privacy, Financial Contributions, and Clinical Trial Communication and Support. The Guidelines address the daily considerations, choices, and consequences of patient advocacy organizations as they engage with biopharmaceutical companies, and offer recommendations for volunteer/paid leaders of the organizations on how to interact in a thoughtful, responsible, ethical way that engenders trust. CONCLUSIONS: These Guidelines recommend best practices and standards for interactions between patient advocacy organizations and industry that will ultimately have a positive effect on the development of novel treatments. Patient advocacy organizations will be provided free access to these Guidelines to help bring clarification to day-to-day decision-making around their interactions, and for use as a living document with the potential for regular revisions and updates.

Taccone, M. S., Baudais, N., Wood, D., Bays, S., Frost, S., Urquhart, R., Graham, I. D., & Takacs, J. (2023). Co-creation of a patient engagement strategy in cancer research funding. *Res Involv Engagem*, *9*(1), 86. <https://doi.org/10.1186/s40900-023-00501-x>

BACKGROUND: As research teams, networks, and institutes, and health, medical, and scientific communities begin to build consensus on the benefits of patient engagement in cancer research, research funders are increasingly looking to meaningfully incorporate patient partnership within funding processes and research requirements. The Canadian Cancer Society (CCS), the largest non-profit cancer research funder in Canada, set out to co-create a patient engagement in cancer research strategy with patients, survivors, caregivers and researchers. The goal of this strategy was to meaningfully and systematically engage with patients in research funding and research activities. METHODS: A team of four patient partners with diverse cancer and personal experiences, and two researchers at different career stages agreed to participate as members of the strategy team. Ten staff members participated in supportive roles and to give context regarding different departments of CCS. The strategy was co-developed in 2021/2022 over a series of 7 workshops using facilitation strategies such as ground rules and consensus building, and methods such as Design Thinking. The strategy was subjected to 3 rounds of validation. RESULTS: The co-creation and validation process resulted in a multi-faceted strategy with actionable sections, including vision, guiding principles, engagement methods, 13 prioritized engagement activities spanning the spectrum of research funding, and an evaluation framework. The experience of co-creating the strategy was captured using the Patient and Public Engagement Evaluation Tool and revealed a positive, supportive experience. CONCLUSIONS: Lessons learned included the value of an emphasis on a co-creation process from day one, the utility of facilitation techniques such as ground rules for dialogue, consensus building and Design Thinking, and the importance (and challenge) of designing for and incorporating equity when drafting the strategy. Future work will include implementation and evaluation of the strategy, as well as an examination of further ways to meaningfully and systematically engage diverse voices in research and research funding.As researchers and healthcare providers see benefits of patient engagement in cancer research, research funders are also looking to engage with patients in their funding processes and research activities. The Canadian Cancer Society (CCS), the largest non-profit cancer research funder in Canada, set out to co-create a patient engagement in cancer research strategy with patients, survivors, caregivers and researchers. The goal of this strategy was to meaningfully and systematically engage with patients in research funding and research activities. Four patient partners and two researchers were supported by ten CCS staff members to co-create the strategy in 2021/2022 over a series of 7 workshops. They used facilitation strategies such as ground rules and consensus building, and methods such as Design Thinking. The strategy was then validated. Co-creation resulted in an easy-to-use strategy with actionable sections, including vision, guiding principles, engagement methods, 13 prioritized activities, and an evaluation framework. The experience of co-creating the strategy was captured using a well-regarded evaluation tool and revealed a positive, supportive experience. Lessons learned during the process included making sure the co-creation process started on day one, the usefulness of facilitating the process, and the importance of considering issues of equity when drafting the strategy.

Tonetto, L. M., da Rosa, V. M., Brust-Renck, P., Denham, M., da Rosa, P. M., Zimring, C., Albanti, I., & Lehmann, L. (2021). Playful strategies to foster the well-being of pediatric cancer patients in the Brazilian Unified Health System: a design thinking approach. *BMC Health Serv Res*, *21*(1), 985. <https://doi.org/10.1186/s12913-021-07018-7>

BACKGROUND: Cancer care can negatively impact children's subjective well-being. In this research, well-being refers to patients' self-perception and encompasses their hospital and care delivery assessment. Playful strategies can stimulate treatment compliance and have been used to provide psychosocial support and health education; they can involve gamification, virtual reality, robotics, and healthcare environments. This study aims to identify how playfulness, whenever applicable, can be used as a strategy to improve the subjective well-being of pediatric cancer patients in the Brazilian Unified Health System. METHODS: Sixteen volunteers with experience in pediatric oncology participated in the study. They were physicians, psychologists, child life specialists, and design thinking professionals. They engaged in design thinking workshops to propose playful strategies to improve the well-being of pediatric cancer patients in the Brazilian Unified Health System. Data collection consisted of participatory observations. All activities were video recorded and analyzed through Thematic Analysis. The content generated by the volunteers was classified into two categories: impact of cancer care on children's self-perception and children's perceptions of the hospital and the care delivery. RESULTS: Volunteers developed strategies to help children deal with time at the hospital, hospital structure, and care delivery. Such strategies are not limited to using playfulness as a way of "having fun"; they privilege ludic interfaces, such as toys, to support psychosocial care and health education. They aim to address cancer and develop communication across families and staff in a humanized manner, educate families about the disease, and design children-friendly environments. Volunteers also generated strategies to help children cope with perceptions of death, pain, and their bodies. Such strategies aim to support understanding the meaning of life and death, comprehend pain beyond physicality, help re-signify cancer and children's changing bodies, and give patients active voices during the treatment. CONCLUSIONS: The paper proposes strategies that can improve the well-being of pediatric cancer patients in the Brazilian Unified Health System. Such strategies connect children's experiences as inpatients and outpatients and may inform the implementation of similar projects in other developing countries.

Vassal, G., Zwaan, C. M., Ashley, D., Le Deley, M. C., Hargrave, D., Blanc, P., & Adamson, P. C. (2013). New drugs for children and adolescents with cancer: the need for novel development pathways. *Lancet Oncol*, *14*(3), e117-124. <https://doi.org/10.1016/S1470-2045(13)70013-5>

Despite major progress in the past 40 years, 20% of children with cancer die from the disease, and 40% of survivors have late adverse effects. Innovative, safe, and effective medicines are needed. Although regulatory initiatives in the past 15 years in the USA and Europe have been introduced, new drug development for children with cancer is insufficient. Children and families face major inequity between countries in terms of access to innovative drugs in development. Hurdles and bottlenecks are well known-eg, small numbers of patients, the complexity of developing targeted agents and their biomarkers for selected patients, limitations of US and EU regulations for paediatric medicines, insufficient return on investment, and the global economic crisis facing drug companies. New drug development pathways could efficiently address the challenges with innovative methods and trial designs, investment in biology and preclinical research, new models of partnership and funding including public-private partnerships and precompetitive research consortia, improved regulatory requirements, initiatives and incentives that better address these needs, and increased collaboration between paediatric oncology cooperative groups worldwide. Increased cooperation between all stakeholders-academia, parents' organisations and advocacy groups, regulatory bodies, pharmaceutical companies, philanthropic organisations, and government-will be essential.

Woodward, L., Johnson, S., Walle, J. V., Beck, J., Gasteyger, C., Licht, C., Ariceta, G., & a, H. U. S. R. S. A. B. (2016). An innovative and collaborative partnership between patients with rare disease and industry-supported registries: the Global aHUS Registry. *Orphanet J Rare Dis*, *11*(1), 154. <https://doi.org/10.1186/s13023-016-0537-5>

BACKGROUND: Patients are becoming increasingly involved in research which can promote innovation through novel ideas, support patient-centred actions, and facilitate drug development. For rare diseases, registries that collect data from patients can increase knowledge of the disease's natural history, evaluate clinical therapies, monitor drug safety, and measure quality of care. The active participation of patients is expected to optimise rare-disease management and improve patient outcomes. However, few reports address the type and frequency of interactions involving patients, and what research input patient groups have. Here, we describe a collaboration between an international group of patient organisations advocating for patients with atypical haemolytic uraemic syndrome (aHUS), the aHUS Alliance, and an international aHUS patient registry (ClinicalTrials.gov NCT01522183). RESULTS: The aHUS Registry Scientific Advisory Board (SAB) invited the aHUS Alliance to submit research ideas important to patients with aHUS. This resulted in 24 research suggestions from patients and patient organisations being presented to the SAB. The proposals were classified under seven categories, the most popular of which were understanding factors that cause disease manifestations and learning more about the clinical and psychological/social impact of living with the disease. Subsequently, aHUS Alliance members voted for up to five research priorities. The top priority was: "What are the outcomes of a transplant without eculizumab and what non-kidney damage is likely in patients with aHUS?". This led directly to the initiation of an ongoing analysis of the data collected in the Registry on patients with kidney transplants. CONCLUSION: This collaboration resulted in several topics proposed by the aHUS Alliance being selected as priority activities for the aHUS Registry, with one new analysis already underway. A clear pathway was established for engagement between a patient advocacy group and an international research network. This should ensure the development of a long-term partnership which clearly benefits both groups.

Yohe, M. E., Heske, C. M., Stewart, E., Adamson, P. C., Ahmed, N., Antonescu, C. R., Chen, E., Collins, N., Ehrlich, A., Galindo, R. L., Gryder, B. E., Hahn, H., Hammond, S., Hatley, M. E., Hawkins, D. S., Hayes, M. N., Hayes-Jordan, A., Helman, L. J., Hettmer, S., . . . Langenau, D. M. (2019). Insights into pediatric rhabdomyosarcoma research: Challenges and goals. *Pediatr Blood Cancer*, *66*(10), e27869. <https://doi.org/10.1002/pbc.27869>

Overall survival rates for pediatric patients with high-risk or relapsed rhabdomyosarcoma (RMS) have not improved significantly since the 1980s. Recent studies have identified a number of targetable vulnerabilities in RMS, but these discoveries have infrequently translated into clinical trials. We propose streamlining the process by which agents are selected for clinical evaluation in RMS. We believe that strong consideration should be given to the development of combination therapies that add biologically targeted agents to conventional cytotoxic drugs. One example of this type of combination is the addition of the WEE1 inhibitor AZD1775 to the conventional cytotoxic chemotherapeutics, vincristine and irinotecan.

Young, A., Menon, D., Street, J., Al-Hertani, W., & Stafinski, T. (2017). Exploring patient and family involvement in the lifecycle of an orphan drug: a scoping review. *Orphanet Journal of Rare Diseases*, *12*(1). <https://doi.org/10.1186/s13023-017-0738-6>

Background: Patients and their families have become more active in healthcare systems and research. The value of patient involvement is particularly relevant in the area of rare diseases, where patients face delayed diagnoses and limited access to effective therapies due to the high level of uncertainty in market approval and reimbursement decisions. It has been suggested that patient involvement may help to reduce some of these uncertainties. This review explored existing and proposed roles for patients, families, and patient organizations at each stage of the lifecycle of therapies for rare diseases (i.e., orphan drug lifecycle).

Methods: A scoping review was conducted using methods outlined by Arksey and O’Malley. To validate the findings from the literature and identify any additional opportunities that were missed, a consultative webinar was conducted with members of the Patient and Caregiver Liaison Group of a Canadian research network.

Results: Existing and proposed opportunities for involving patients, families, and patient organizations were reported throughout the orphan drug lifecycle and fell into 12 themes: research outside of clinical trials; clinical trials; patient reported outcomes measures; patient registries and biorepositories; education; advocacy and awareness; conferences and workshops; patient care and support; patient organization development; regulatory decision-making; and reimbursement decision-making. Existing opportunities were not described in sufficient detail to allow for the level of involvement to be assessed. Additionally, no information on the impact of involvement within specific opportunities was found. Based on feedback from patients and families, documentation of existing opportunities within Canada is poor.

Conclusions: Opportunities for patient, family, and patient organization involvement exist throughout the orphan drug lifecycle. However, based on the information found, it is not possible to determine which opportunities would be most effective at each stage.