

The Belgian Pediatric Clinical Research Network (BPCRN): Pediatric Trial Facilitation During and Beyond Conect4children

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Abstract

Objective

The Belgian Pediatric Clinical Research Network (BPCRN) aims to promote pediatric clinical research by enhancing collaboration among stakeholders and facilitating high-quality trials. This manuscript outlines BPCRN's growth, its role in the Innovative Medicines Initiative 2 conect4children (c4c) project, and its contributions to pediatric drug development in Belgium.

Methods

Summary of BPCRN's activities since 2018, including its role in the c4c project. Data were collected from progress reports, internal databases, and interviews with investigators. The analysis highlights BPCRN's operational activities, trial facilitation, governance structure, and collaborations with international partners.

Results

BPCRN now includes 15 pediatric study sites across Belgium, utilizing a single-point-of-contact model for efficient communication. The network supported six commercial and non-commercial trials under the c4c project and facilitated over 20 additional studies through collaborations with global partners like I-ACT for Children. A new governance framework was introduced, including an Advisory Board and Steering Committee to guide future growth and sustainability.

Conclusion

BPCRN evolved to become a key contributor to pediatric clinical research in Belgium, overcoming barriers like recruitment difficulties and methodological challenges. The network's collaborative model and strategic governance will enable its continued expansion, ensuring that children have access to innovative and safe treatments. BPCRN's success positions Belgium as a leading hub for pediatric clinical trials and addresses the unmet needs of pediatric patients.

Introduction

Therapeutics prescribed for children must demonstrate both effectiveness and safety (1). To ensure this, medicines and medical devices must undergo rigorous evaluation through well-designed and properly conducted clinical trials that include participants from all relevant age groups (2). However, conducting clinical trials in a pediatric setting poses significant challenges for all stakeholders involved. These challenges include not only methodological complexities and ethical considerations, but especially recruitment difficulties, administrative burdens, and financial constraints (3,4).

A key strategy to address the persistent inequities in access to therapeutics for children is the promotion of collaboration and capacity-building and -sharing among pediatric study sites (4). Strengthening sites enhances the feasibility and success of clinical trials, thereby facilitating the timely development and delivery of innovative, evidence-based therapies to this vulnerable population. To support the development and maintenance of the high-quality standards essential for conducting pediatric clinical trials at a local level, (inter)national networks have been established (5,6). These networks have demonstrated significant benefits across various stakeholders, including patients, investigators, study sites, regulators, governments, and sponsors.

In Belgium, the Pediatric Clinical Research Network (BPCRN) was established in 2009 as a working group within the national pediatric society, the Belgische Vereniging voor Kindergeneeskunde-Société Belge de Pédiatrie (BVK-SBP), under the auspices of the late Prof. Dr. José Ramet (7). The primary goals were to map the pediatric research landscape in Belgium and to improve communication among key stakeholders. Since 2018, the BPCRN has been an active partner in the Innovative Medicines Initiative 2 conect4children (c4c) project, a collaborative project between academic and private sectors that includes 35 academic and 10

industry partners, as well as more than 50 third parties and around 500 affiliated partners (8). During c4c, BPCRN has evolved into a fully operational and collaborative research network, focusing on the high-quality and efficient execution of pediatric clinical trials in Belgium. This report outlines BPCRN activities since 2018 and provides an early outlook on the network beyond conect4children project funding.

Methods

This manuscript provides an overview of BPCRN activities and achievements since joining the conect4children project in 2018. It highlights the operational activities that have contributed to the network's capacity building and growth into its current structure. Data for this analysis was collected from progress reports and internal databases documenting clinical trials conducted during and beyond the conect4children project funding period. Additionally, qualitative insights were obtained through interviews with investigators from the coordinating centre and participating study sites.

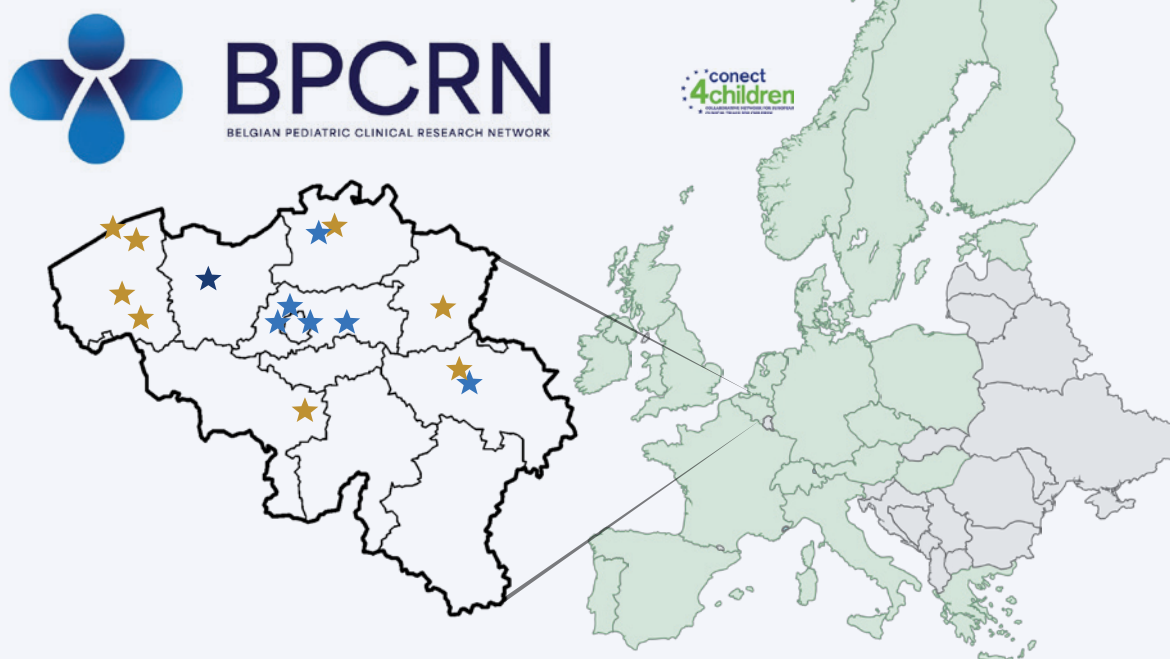
The historical context of the BPCRN, including its establishment in 2009 and activities prior to 2018, has been previously described (7).

Results

Status of the network

BPCRN comprises 15 pediatric study sites, including all seven Belgian university hospitals, seven large regional hospitals, and one pediatric rehabilitation center (Figure 1). The network is open to expanding its membership to other pediatric healthcare institutions interested in contributing to pediatric clinical research. These institutions may include academic and non-

FIGURE 1: The structure of the Belgian Paediatric Clinical Research Network (BPCRN), as developed during conect4children (c4c). Dark blue star represents the BPCRN headquarter (UZ Gent), light blue stars represent academic hospitals (CHU de Liège, Cliniques universitaires Saint-Luc, H.U.B.-HUDERF Bruxelles, UZ Antwerpen, UZ Brussel, UZ Leuven, yellow stars represent non-academic hospitals or sites (AZ Delta Roeselare, AZ Groeninge Kortrijk, AZ Sint-Jan Brugge, Clinique CHC MontLégia Liège, HUMani Charleroi, Jessa Ziekenhuis Hasselt, ZAS Paola Antwerpen, Zeepreventorium De Haan). Countries represented within c4c project are coloured in green.



academic hospitals, residential treatment centers, ambulatory clinics, and research facilities.

The national coordination of BPCRN activities is managed by an Operational Team based at Ghent University Hospital, which is in close contact with the network sites through a single point of contact (SPoC) model. To underscore its nationwide scope, BPCRN has been integrated into the scientific task force of the Belgian Academy of Paediatrics (BAoP)—the national umbrella organization for pediatrics that brings together the former BVK-SBP and regional medical associations with active scientific working groups, such as the Vlaamse Vereniging voor Kindergeneeskunde (VVK) and the Groupement Belge des Pédiatres de langue Française (GBPF). Through active involvement in international initiatives and collaborations with global partners, BPCRN has established itself as a key stakeholder internationally. Accordingly, in 2024, BPCRN achieved recognition as a Category 1 European Network of Paediatric Research by the European Medicines Agency (Enpr-EMA).

Clinical trial facilitation

During the conect4children (c4c) project (2018-2025), BPCRN actively supported site identification, feasibility assessment, start-up and conduct of two academic and four industry-sponsored trials by taking up the role and responsibilities of a national coordinator (Table 1). These trials included interventional studies sponsored by academic institutions targeting pediatric populations with Kawasaki disease and preterm neonates with patent ductus arteriosus, and commercial studies recruiting patients with multiple sclerosis, chronic kidney disease and ulcerative colitis. In total, nine different Belgian sites opened for recruitment for at least one of the studies.

The network's added value was evident through its proactive communication with sponsors and study sites, facilitating site identification and streamlining feasibility assessments. BPCRN's trial support included strategies to boost recruitment, streamline trial-team coordination, pre-fill site feasibility questionnaires, and to provide guidance during the submission process. For academic trials, central and local ethical committee submissions in Belgium were executed by BPCRN. These submission packages were based on essential documents from the international sponsor and were supplemented with local documents and translations, fully supported by BPCRN. These trial support efforts relieved workload from BPCRN sites, enhanced trial efficiency, and improved feasibility outcomes.

Beyond its involvement in clinical trials under the c4c project, BPCRN established collaborations with the United States-based Institute For Advanced Clinical Trials (I-ACT) for Children, enabling further capacity building and alignment with global pediatric research efforts (9). Through collaboration with I-ACT for Children and independent direct contact with sponsors, BPCRN performed facilitation surveys for over 20 other pediatric clinical trials.

BPCRN aims to broaden its role beyond patient recruitment by providing methodological input, reviewing trial protocols, and coordinating feasibility assessments through clinical experts. While these contributions are valuable across all phases of clinical research, BPCRN particularly strives to engage with sponsors early in the trial lifecycle. In addition, the network is exploring harmonized approaches to site budgeting and contract templates, actively gathering input from both sites and sponsors to align expectations and streamline processes, with the goal of reducing start-up timelines.

Communication within and outside the network

To enhance communication and operational efficiency, BPCRN employs a single point of contact (SPoC) model for academic,

industrial, and hospital stakeholders. Site-level SPoCs consist out of (at minimum) a physician and a study coordinator. They are responsible for facilitating efficient handling of requests within their respective hospital team members or departments, ensuring reliable and timely deliverables, and providing consistent bilateral feedback to the Operational Team.

To strengthen the network, roadshow meetings were conducted in 2023 and 2024. In-person visits to the sites allowed for an in-depth assessment of network involvement, trial progress follow-up, and evaluation of site-specific needs. These equally allowed for an in-depth exploration of one of the network's key strengths, namely its multidisciplinary engagement, including the involvement of the principal investigator, research coordinator, data manager, and sub-SPoCs.

In the coming years, the Operational Team plans regular visits to existing network sites and introducing new sites involved in pediatric clinical research activities that are interested in joining the network.

In addition to gathering input from the sites, BPCRN aimed to learn from similar networks in other countries. Knowledge, skills and connections of the BPCRN have significantly increased by actively participating in meetings of the National Network of Networks (hosted by c4c) and by seeking support from networks represented in Enpr-EMA. To reflect upon common challenges, BPCRN representatives engaged in close communication with similar national networks such as PedMed-NL (the Netherlands), PEDSTART (France), DanPedMed (Denmark) and NorPedMed (Norway).

Supporting activities

Besides establishing and maintaining the network and facilitating clinical trials in itself, BPCRN has been able to develop various activities that have added value to conducting high-quality and meaningful research.

One of the key priorities for BPCRN has been the explicit integration of **experts** within the network to stimulate broader participation. Expert involvement remains critical, which is why this aspect will be further emphasized to encourage engagement from relevant professionals. The growing database of national experts is consultable for academic and commercial stakeholders and accessible through the BPCRN.

Another essential initiative has been the development of a **clinician-scientist platform**. This platform serves to bridge clinical practice and academic research by creating structured opportunities for shared learning, joint project development, and methodological support. As recently highlighted(10), structured clinician-scientist programs are essential to sustain translational research capacity across Europe. These programs aim to train and retain talented medical doctors by offering protected research time, strong mentorship, and clear career pathways at the interface of care and science. In addition to scientific and clinical training, they provide institutional support for long-term career development, promote interdisciplinary collaboration, and actively involve patients in the research process. BPCRN and its Dutch counterpart, PedMed-NL were among the key instigators of this initiative.

This platform serves to bridge clinical practice and academic research by creating structured opportunities for shared learning, joint project development, and methodological support. As recently highlighted in *Nature Medicine*, structured clinician-scientist programs are essential to foster sustainable careers at the intersection of care and research. These programs typically include protected research time, mentorship, dedicated infrastructure, and access to interdisciplinary collaboration, allowing clinicians to address unmet medical needs with clinically

informed research questions. BPCRN and its Dutch counterpart, PedMed-NL, were among the initiators of such an initiative within the conect4children project.

In addition, BPCRN has prioritized **patient engagement**, collaborating closely with the European Young Person's Advisory Group Network (eYPAGnet), and set up a pilot project to involve young patients in shaping research priorities, study design, and clinical trial training programs. These efforts led to the initiation of a Pediatric Nephrology Youth Advisory Council on Clinical Trials and Training which has provided valuable insights to further develop a broader and more inclusive advisory group for children (link).

Approximately 75% of **rare diseases** manifest in childhood. BPCRN has actively contributed to research exchange initiatives aimed at aligning European Reference Networks (ERNs) with c4c (11). Given that many Belgian sites demonstrate a high level of ERN participation—some achieving the highest average site involvement in Europe—this represents a significant area of contribution and ongoing efforts for BPCRN.

conect4children beyond Innovative Medicines Initiative (IMI)-funding

During the conect4children (c4c) project, BPCRN contributed to key work packages on trial execution (WP2, WP7), sustainable network models (WP3), and data standardization (WP5). As the project concludes in May 2025, BPCRN remains actively involved in advancing data integration, supporting expert panels, providing training for study teams, and coordinating the Young Investigator Community (YIC).

Following the completion of the grant, the c4c project transitioned into a nonprofit organization, c4c Stichting, administratively headquartered in the Netherlands. BPCRN played a pivotal role in providing insights from a national network perspective to support the development of this sustainable model, formally established in May 2024.

As of 2024, BPCRN continues to serve as an active member of c4c Stichting, contributing to clinical trial facilitation and expert consultations. The shared mission of both c4c Stichting and BPCRN is the advancement of better medicines for children. From a national perspective, this involves conducting the maximum number of relevant clinical trials across a well-curated selection of Belgian sites to ensure innovative treatments are accessible to the pediatric population.

While many activities during the c4c project were primarily focused on clinical drug development, BPCRN is currently exploring how, through the involvement of the same key stakeholders—along with an expansion to university and other research partners—it can also provide support for preclinical and translational research in children, including initiatives under the umbrella of the European Paediatric Translational Research Infrastructure (EPTRI). The engagement of multiple sites and their established networks represents a logical extension of the EPTRI consortium and is expected to positively impact the development of meaningful pediatric research, whether related to medicines or other health interventions.

As part of the continued maturation of the network, BPCRN is exploring connections with established European research infrastructures such as the European Clinical Research Infrastructure Network (ECRIN), with the aim of strengthening its international collaboration capacity and avoiding duplication of efforts. In this context, BPCRN's expertise and site-level capacity could also contribute to initiatives focused on making network data available for the establishment of international disease registries supporting registry-based randomized clinical trials (such as the Trials Within Cohorts [TWICs] approach), or the coordinated conduct of pediatric vaccine studies—both in healthy

and immunocompromised children (e.g., through platforms such as Vaccelerate). These are high-priority areas of unmet medical need, particularly within pediatric and rare disease research, and BPCRN could serve as a valuable partner in setting up such initiatives in close collaboration with its existing stakeholders. Engaging with these European infrastructures offers an opportunity to further position the Belgian network within the broader European clinical research landscape and to contribute meaningfully to the coordination of national and cross-border pediatric trials.

BPCRN beyond conect4children

To support future collaboration and strategic growth, BPCRN proposed a new governance structure in 2024, formally introduced during a kick-off meeting held in Ghent at September 6, 2024. This restructuring led to the establishment of the BPCRN Advisory Board, comprising representatives from all network sites and relevant national stakeholders.

The Advisory Board includes voting members responsible for guiding the network's overall direction. These members represent study sites (SPoCs and heads of pediatric departments), the national pediatric organization BAoP, as well as patient advocacy groups like RaDiOrg. Non-voting members provide expert advice based on their involvement in the pediatric clinical trial ecosystem in Belgium. These include representatives from regulatory bodies (Federal Agency for Medicines and Health Products (FAGG/AFMPS)), industry associations (pharma.be, BeCRO), and pediatric associations.

The Advisory Board also endorsed the formation of a Steering Committee, comprising volunteer experts from network sites. The primary role of the Steering Committee is to oversee the activities of the Operational Team and ensure alignment with the strategic objectives of the BPCRN. This governance framework aims to foster robust collaboration, accountability, and effective management within the network.

Under the guidance of the Advisory Board, the BPCRN Steering Committee is actively pursuing both research and networking opportunities to advance the network's mission. The Steering Committee developed a BPCRN Roadmap, which outlines the network's strategic direction, including the definition of its mission and vision. This roadmap also established key principles and provided the foundational steps necessary to ensure the long-term financial sustainability of the BPCRN.

In addition to its focus on academic initiatives, BPCRN is engaging with commercial stakeholders, including (but not limited to) contract research organizations (CROs) and pharmaceutical companies. These discussions aim to identify existing gaps within the pediatric clinical trial landscape that BPCRN could address, as well as to explore potential collaborative partnerships to drive innovation, including devices, medical technologies, and diagnostics, and enhance the impact of pediatric clinical research.

Discussion and conclusion

This manuscript provides a comprehensive overview of the BPCRN, highlighting its evolution during its involvement in the c4c project and beyond. Since its participation in c4c, BPCRN has substantially enhanced its capacity to conduct pediatric clinical trials (7,9,12), thereby contributing to the broader pediatric research landscape and improving access to novel therapies and new technologies for children in Belgium.

The need for more pediatric medicines has prompted the implementation of necessary international legislation over the years. Notably, the European Union (EU) introduced the

Pediatric Regulation in 2007, aiming to promote the development and authorization of pediatric medicines (13). The regulation established the Paediatric Committee (PDCO), which determines the requirement for pediatric studies under pediatric investigation plans (PIPs) and provides incentives to support their execution. The European Commission's ten-year review of the regulation highlighted an increase in the availability of pediatric medicines; however, progress has been limited in certain areas, particularly for rare diseases and conditions that primarily affect children (14–16). Despite these efforts, up to 50% of pediatric clinical trials do not achieve successful completion, highlighting the enduring challenges within the field of pediatric research (17–20). Moreover, several of these initiatives at the European level may be at risk due to upcoming regulatory changes. It is evident that emerging European regulations will further shape the current landscape, underscoring the importance of having stable national actors to ensure the continuity of clinical studies in Belgium.

BPCRN's collaborative approach has significantly contributed to overcoming barriers to pediatric clinical trials. By supporting site identification, streamlining site initiation processes, enhancing recruitment strategies, and improving coordination among study sites, BPCRN has demonstrated the advantages of national networks in addressing key challenges in pediatric research. Moreover, BPCRN's efforts in data standardization, integration of real-world data, and building of an expert network database have strengthened the quality and efficiency of pediatric clinical trials, ensuring consistency across studies and facilitating data sharing among stakeholders. A concrete outcome of these efforts is the availability of a specific CDISC Pediatric User Guide (21), which is now online and ready for use. Additionally, BPCRN has established a broad network of experts who can be consulted for pediatric clinical and trial-associated inquiries, further supporting the development and execution of high-quality pediatric research.

Through its national SPoC structure and regular operational contacts, BPCRN collaborates closely with clinical trial units embedded in university hospitals and regional centers, promoting harmonization of processes and fostering knowledge exchange. From the perspective of participating sites, the national expert network coordinated by BPCRN is available for consultation, enabling access to targeted clinical and methodological expertise. Other potential benefits for sites include streamlined feasibility procedures, support in ethics and regulatory submissions, opportunities for training and capacity building, as well as increased visibility for national and international study opportunities.

The success of BPCRN can largely be attributed to its robust partnerships with academic institutions, medical associations, industry, and regulatory bodies. A key development in this regard has been the establishment of a governance framework, which includes an Advisory Board and a Steering Committee. This structure has enabled BPCRN to align its objectives with the network's long-term strategy, ensuring transparency, accountability, and effective decision-making. The BPCRN Roadmap, developed by the Steering Committee, outlines strategic priorities, including securing sustainable funding and fostering relationships with commercial partners to ensure continued growth and innovation. These novel developments were presented and approved by the Advisory Board at the BPCRN kick-off meeting in Ghent at Sept 6th, 2024.

Despite these accomplishments, several challenges remain. Recruitment, particularly for rare diseases, continues to be a major obstacle, as do methodological complexities, such as the design of age-appropriate studies and adherence to ethical guidelines (4). Cross-disciplinary collaboration is essential, not only between centers but also among EU-recognized ERN units within Belgium and across broader EU infrastructures, such as ERDERA. While rare diseases affect both pediatric and adult populations, Belgium currently lacks a dedicated BPCRN counterpart for adult

patients, representing a critical unmet need. Additionally, a major emerging challenge in clinical trials is the increasing regulatory requirements set by the European Medicines Agency (EMA) for medical devices in children. Addressing these regulatory demands will be crucial to ensuring continued innovation and accessibility of pediatric medical technologies.

Addressing these challenges requires ongoing optimization of clinical trial planning, recruitment strategies, involving patients and public, and site coordination. Additionally, financial constraints remain a significant barrier to expanding the network and ensuring the sustainability of pediatric clinical trials. As such, continued collaboration with industry and securing both public and private funding will be crucial for the network's long-term viability. Clear agreements with private partners and internal stakeholders are essential to ensure that industry funding never compromises the integrity of the network—a principle that will ultimately benefit all parties in the long run.

The future success of BPCRN will depend on its ability to expand both local and international collaborations. Strengthening these partnerships, alongside efforts to secure long-term financial support, will be critical to sustaining the network's growth. As BPCRN continues to evolve, its role in advancing pediatric drug development and improving access to novel treatments for children in Belgium and beyond will remain indispensable.

Conclusion

BPCRN's progress in conducting pediatric clinical trials and its commitment to collaboration have significantly advanced pediatric clinical research in Belgium. While challenges persist, BPCRN's robust governance model, strategic partnerships, and ongoing capacity-building efforts will aid to firmly establish Belgium as a leading hub for pediatric clinical trials. In doing so, BPCRN will help address the unmet needs of pediatric patients by enhancing access to safe and effective therapies for children.

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