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European Paediatric Translational Research Infrastructure

EPTRI SCIENTIFIC MEETING

BOOK OF ABSTRACTS

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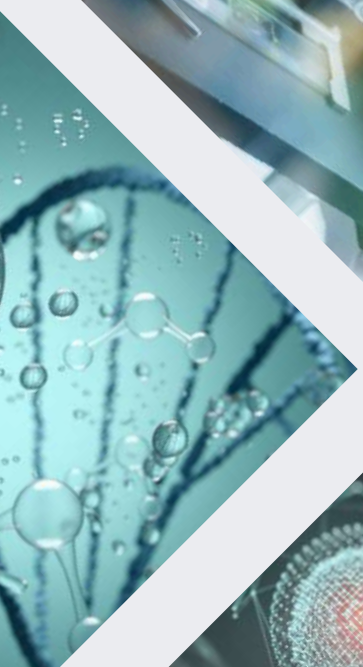

“Future Perspectives in Paediatric Research – European Networks & Infrastructures Collaboration”

SPEAKER SECTION

Speaker: Marek Migdal

Mapping Paediatric Research Needs Across the Research and Innovation Pathway: Preliminary Findings from the EPTRI Survey

Marek Migdal[1,5], Karel Allegaert[1,4], Giovanni Migliaccio[1,2], Viviana Giannuzzi[3], Donato Bonifazi[1,2]

[1] European Paediatric Translational Research Infrastructure (EPTRI AISBL), Leuven, Belgium; [2] TEDDY – European Network of Excellence for Paediatric Clinical Research, Bari, Italy; [3] Fondazione per la Ricerca Farmacologica Gianni Benzi - ETS (FGB), Bari, Italy; [4] Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium; [5] The Children’s Memorial Health Institute (CHMI), Warsaw, Poland

Paediatric research continues to face interconnected scientific, methodological and operational challenges across the research and innovation pathway. The EPTRI Paediatric Research Needs Survey was developed to capture stakeholder perspectives on current activities, unmet research and evidence needs, barriers to progress, and expectations for support and collaboration, with the aim of informing future priorities across the paediatric research ecosystem. The ongoing survey engages stakeholders from academia, clinical centres, industry, patient organisations and regulatory bodies. Most questions permit multiple responses, and preliminary findings from 129 respondents were analysed descriptively. Responses indicate activity across the full research continuum, with clinical studies and real-world data (RWD) and registries most prominent, alongside early development, biomarkers and diagnostics. Key evidence needs concerned paediatric-specific clinical evidence, RWD and registries, and validated endpoints and outcome measures. Recurring barriers included limited funding, recruitment and feasibility challenges, and regulatory and ethical complexity, with their relative importance varying across stakeholder groups. Common priorities for enabling support included data and real-world evidence, study design, multicentre coordination, and access to relevant expertise and networks. Overall, responses favoured sustained, integrated collaboration over one-off advice, while indicating that support models should reflect different stakeholder contexts. Taken together, current findings suggest a continuity gap rather than a single missing capability. Advancing paediatric research may require coordinated, long-term support connecting robust evidence generation, accessible data and feasible multicentre delivery, while incorporating stakeholder-specific needs from the outset. As the survey remains open, additional responses may further refine signals from smaller stakeholder groups.

Keywords: Paediatric research; research needs assessment; real-world evidence; stakeholder engagement; multicentre collaboration.

Speaker: Karel Allegaert

EPTRI Integrated Approach to Support Paediatric Research

Karel Allegaert[1,2], Viviana Giannuzzi[1,3], Marek Migdał[1,4], Donato Bonifazi[1,5]

[1]European Paediatric Transnational Research Infrastructure (EPTRI AISBL), Leuven, Belgium; [2]Katholieke Universiteit Leuven (KU Leuven), Leuven, Belgium; [3]Fondazione per la Ricerca Farmacologica Gianni Benzi (FGB), Bari, Italy;
[4]The Children's Memorial Health Institute (CHMI), Warsaw, Poland; [5]Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF), Pavia, Italy

The development of safe, effective, and child-centred health solutions remains a major challenge in biomedical research. Paediatric research is intrinsically complex due to age-dependent biological differences, developmental changes affecting disease mechanisms and treatment response, limited availability of validated biomarkers, small and heterogeneous patient populations, the need for age-appropriate formulations and technologies, and specific ethical and regulatory requirements for studies involving children. These challenges have historically contributed to fragmentation of expertise, limited access to specialised resources, and difficulties in translating scientific discoveries into clinical applications. To overcome these barriers, the European Paediatric Transnational Research Infrastructure (EPTRI) was established as a collaborative framework designed to integrate and coordinate multidisciplinary expertise across the entire paediatric translational research pathway. Initially launched as a Horizon 2020 INFRADEV project (Grant Agreement No. 777554) coordinated by the Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF), EPTRI has evolved into an *Association Internationale Sans But Lucratif (AISBL)* under Belgian law, headquartered at Leuven University. Today, EPTRI represents a growing European and international community, bringing together 27 members from 15 countries and involving more than 114 institutions committed to advancing paediatric research. EPTRI's added value relies on its "Hub and Spoke" organisational model, connecting a Central Management Office with distributed National Nodes and Thematic Research Platforms. This structure enables researchers, clinicians, innovators, regulators, and patient representatives to access specialised expertise, harmonised methodologies, and advanced research services, overcoming the fragmentation traditionally affecting paediatric research. By acting as a bridge between discovery science, technological innovation, clinical development, regulatory science, and patient engagement, EPTRI supports the full continuum of paediatric translational research. Its services encompass interconnected strategic areas: paediatric disease characterisation and drug development, including developmental pharmacology, innovative paediatric formulations, and integrated *in vitro*, *in vivo*, and *in silico* approaches; paediatric medical device development, supporting the design, prototyping, and evaluation of child-adapted technologies; paediatric health data management, enabling the generation, integration, and reuse of FAIR-compliant and GDPR-aligned data through digital infrastructures, bioinformatics, and artificial intelligence; and paediatric clinical research, promoting innovative trial methodologies and meaningful involvement of children, families, and patient organisations.

EPTRI demonstrates its operational capacity through the coordination of the EU4Health-funded OrphaDev4Kids project (Grant Agreement No. 101161377), where it leads a multidisciplinary consortium supporting the development of orphan and paediatric

medical devices by connecting expertise, innovation pathways, regulatory knowledge, and stakeholder engagement. EPTRI further expands its scientific and technological capabilities through collaborations with European Research Infrastructures, including INFRAFRONTIER-ERIC for juvenile disease models, Instruct-ERIC for structural biology and molecular target validation, and ELIXIR for interoperable life science data resources. Within the broader European health research ecosystem, EPTRI actively contributes to collaborative frameworks and policy discussions through engagement with initiatives such as the European Network of Paediatric Research at EMA (Enpr-EMA), the European Open Science Cloud (EOSC) Association, the EU Health Coalition, and the European Alliance for Transformative Therapies (TRANSFORM). Its strategic collaborations with complementary paediatric and rare disease initiatives, including ACT EU, c4c-Stitching, RealiseD, ERAMET, INVEST, ERDERA, European Reference Networks, and XShare, further strengthen coordination across clinical research, regulatory science, modelling and simulation, and health-data interoperability. Through this integrated and collaborative approach, EPTRI acts as a strategic catalyst within the European Research Area, creating a sustainable ecosystem where knowledge, technologies, data, and expertise can be shared to accelerate innovation for children. By reducing fragmentation and providing coordinated access to specialised capabilities, EPTRI contributes to transforming paediatric research into a more efficient, inclusive, and patient-centred endeavour, ultimately supporting the development of safer medicines and medical devices and improving health outcomes for paediatric populations across Europe and beyond.

Keywords: EPTRI; paediatric translational research; European Research Infrastructure; paediatric drug development; rare diseases; paediatric clinical research; health data management; patient engagement.

Speaker: Ricardo Fernandes

Perspectives on Enpr-EMA Strategic Plans 2026-2028

Ricardo M Fernandes[1]

[1]Enpr-EMA/conect4children, Netherlands

European paediatric research is at a critical juncture, driven by the evolving legislative, regulatory, scientific and innovation landscape. Despite progress made towards target metrics in clinical trials, challenges persist in maintaining competitiveness with other jurisdictions throughout the innovation lifecycle. Pediatric trial analytics reveal the diversity and gaps in pediatric research across age groups and therapeutic areas, with a significant proportion investigating rare diseases. Innovation opportunities extends across multiple interconnected domains, including science and development, data and digital transformation, trial design and execution, regulatory innovation, therapeutics and technologies, and patient involvement and engagement. Within this evolving landscape, European research infrastructures that support paediatric research provide complementary capabilities that differ in scope, governance, geographical footprint, operational capacities, services, user and lifecycle focus. These infrastructures exhibit varying suitability to pediatric medicines development, reinforcing the need for coordinated and fit-for-purpose support. The European Network of Paediatric Research at the European Medicines Agency, EnprEMA, has been a key “network of networks” in this field for over a

decade. Established under the Paediatric Regulation, EnprEMA has evolved to comprise 58 member networks and provide a collaborative platform for dialogue, engagement and competence building integrating research networks, sites, healthcare professionals, patient representatives, academics, medicine developers, and regulators. Through its Coordinating Group and Working Groups, it promotes stakeholder collaboration, supports the development of recommendations and best practices, and addresses strategic topics. It further liaises and and serves as an expert resource for the EMA Paediatric Committee. From its original mandate starting point, the network has delivered substantial systemic value including organizing annual multi-stakeholder workshops, developing and issuing key guidance documents and fostering community building.

As its mandate evolves and expands under the new pharmaceutical legislation, consideration must be given to this major transformation of the medicines ecosystem. There are opportunities to strengthen collaboration, leverage modern regulatory approaches and improve the efficiency and quality of paediatric medicines development. Successfully navigating this transition requires leveraging pediatric research networks towards impact and all stakeholders, to deliver child and family-centered trials and high-quality Paediatric Investigation Plans. The current EnprEMA leadership is working towards future-proofing the group's roles within the context of broader ongoing changes in structure and governance. Initial strategic actions focus on translating the opportunities into coordinated, actionable initiatives through stakeholder engagement, regulatory dialogue and generation of practical outputs, in close align with EMA and related European initiatives. Priority areas include paediatric trial platforms, recruitment and retention, patient engagement, paediatric trial assessment, methodologies supporting extrapolation and prioritisation, emerging regulatory approaches—including mechanism-of-action and adaptive Paediatric Investigation Plans—and infrastructure readiness. These activities aim to contribute to accelerating paediatric-centred, evidence-informed drug development while strengthening the preparedness of the paediatric research community and supporting the future evolution of Enpr-EMA.

Speaker: Donato Bonifazi

ACT EU as a Catalyst for Paediatric Research Innovation in Europe: How a Multi-Stakeholder Approach Can Accelerate Clinical Trials for Children

Donato Bonifazi[1], Giorgio Reggiardo[1], Mariagrazia Felisi[1], Eleonora Sarracco[1]

[1]TEDDY Network – European Network of Excellence for Paediatric Clinical Research, Bari, Italy

The Accelerating Clinical Trials in the European Union (ACT EU) initiative, launched by the European Commission, the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA), aims to create a more attractive, efficient and innovative environment for clinical research through regulatory convergence, stakeholder collaboration and methodological innovation. Its revised 2026–2027 objectives explicitly address the inclusion of under-represented populations, including children, support for non-commercial sponsors, meaningful patient involvement, capacity building and the responsible integration of digital technologies, innovative trial designs and real-world data. Paediatric clinical research represents a particularly relevant implementation domain for ACT EU because it concentrates many of the challenges the initiative seeks to overcome:

small and geographically dispersed patient populations, rare diseases, complex multinational trial execution, regulatory and operational burden, methodological constraints and the need for early involvement of children and families. At the same time, these constraints make paediatrics a powerful driver of innovation applicable to the broader clinical research ecosystem.

The presentation describes the contribution of the TEDDY Network within the ACT EU Multi-Stakeholder Platform and highlights three areas in which paediatric research networks can translate ACT EU priorities into practice. First, stronger support for academic and non-commercial sponsors is needed, including regulatory assistance, training, better access to research infrastructures and exploration of collaborative co-sponsorship models for multinational studies. Second, wider implementation of innovative methodologies, adaptive and Bayesian designs, master protocols, external controls, modelling and simulation, in-silico approaches and real-world data, can improve the feasibility and efficiency of trials in small populations. Recent initiatives such as SPIRIT-C 2026 and CONSORT-C 2026 can further strengthen the quality and transparency of paediatric trial protocols and reporting. Third, meaningful involvement of children, young people and families through KIDS (Kids Impacting Diseases through Science) and YPAG (Young Persons' Advisory) Groups, validated engagement frameworks and age-appropriate assent and consent tools can improve relevance, feasibility, recruitment and retention. Synergies with European research infrastructures, networks and initiatives, including EPTRI, Enpr-EMA, c4c, ERA4Health, ERAMET, INVENTS, PRISM, RealiseD and ERDERA, are essential to connect policy, regulatory science and operational trial delivery. In this context, paediatric research should not simply adapt to ACT EU: it can serve as a strategic test case for a more coordinated, patient-centred and methodologically advanced European clinical research system, supporting faster and more equitable access to safe and effective therapies for children.

Keywords: ACT EU; paediatric clinical research; clinical trial innovation; multi-stakeholder collaboration; regulatory convergence; innovative trial methodologies; patient involvement; European research networks.

Speaker: Harald Schwalbe

Instruct-ERIC: Get access to advanced structural biology services

Harald Schwalbe[1]

[1]Instruct-ERIC

Instruct-ERIC is a pan-European distributed research infrastructure making high-end technologies and methods in structural biology available to users. Instruct-ERIC is comprised of 17 Member Countries and organisations: Belgium, Czech Republic, EMBL, Finland, France, Germany, Greece, Israel, Italy, Latvia, Lithuania, Netherlands, Portugal, Slovakia, Slovenia, Spain and United Kingdom. Through its 12 specialist research Centres in Europe, Instruct-ERIC offers funded research visits, training, internships and R&D awards. Instruct Centres have years of experience in providing world-class technology provision and expertise to users both in academia and industry. By promoting integrative

methods, Instruct-ERIC enables excellent science and technological development for the benefit of all life scientists [1]. More on https://instruct-eric.org/

References:

[1] Schwalbe, H., et al. (2024). The future of integrated structural biology. Structure doi: 10.1016/j.str.2024.08.014

Keywords: Structural Biology, Research Infrastructure, drug discovery

Speaker: Radislav Sedlacek

Creating Preclinical Models for Rare Diseases: RD-Factory as a Platform, Netherton Syndrome as a Case Study

Radislav Sedlacek[1]

[1]Czech Centre for Phenogenomics, Institute of Molecular Genetics of the Czech Academy of Sciences, Prague, Czech Republic

Rare diseases continue to face a major translational gap between genetic diagnosis and the availability of robust preclinical models suitable for mechanistic studies and therapy development. The RD-Factory initiative addresses this need through a structured framework for nomination, prioritization, generation and phenotypic characterization of rare disease models, with the aim of accelerating preclinical testing and strengthening the link between patient need and therapeutic strategy.

The lecture will present RD-Factory as a practical platform for rare disease model generation and will illustrate its application across multiple indications, including Angelman syndrome, SPATA5 syndrome and Netherton syndrome. Emphasis will be placed on disease selection, on model design reflecting patient-relevant pathogenic variants, and on the integration of phenotyping with downstream translational applications. Particular focus will be given to Netherton syndrome, a rare disorder caused by SPINK5 loss of function, resulting in LEKTI deficiency, dysregulated kallikrein activity, epidermal barrier disruption and systemic manifestations. Progress in this field has moved from early mouse models limited by perinatal lethality to inducible conditional Spink5-deficient models that reproduce key disease features and provide a suitable platform for therapeutic testing, including gene-therapy-based approaches.

Together, these examples illustrate how a coordinated rare disease infrastructure can support the transition from disease nomination to actionable in vivo models and translational intervention.

Speaker: Emidio Capriotti

Towards a Federated European Ecosystem for Rare Disease Research: ELIXIR Activities and Collaborative Synergies with EPTRI

Emidio Capriotti[1]

[1]University of Bologna, Italy

ELIXIR is a European distributed infrastructure that coordinates and integrates life science data, tools, and services across its member states, enabling researchers to manage and analyse genomic and other biological information at scale. Within this framework, the ELIXIR Rare Disease (RD) Community is dedicated to overcoming the inherent challenges of rare disease research, namely small patient cohorts, high phenotypic variability, and fragmented data, by establishing a robust, interoperable, and FAIR infrastructure across Europe. Our activities focus on providing foundational building blocks for multi-scale data analysis, spanning from molecular variant interpretation to systems biology and secure federated discovery. These efforts are organized in the context of the Federated Human Data community which also includes the Cancer, and Human Copy Number Variation (hCNV) communities, ensuring cross-domain alignment and the reuse of shared technical standards. To achieve this, the community leverages and promotes Global Alliance for Genomics and Health (GA4GH) standards, including the Variant Representation Specification (VRS), Categorical VRS (Cat-VRS), the Beacon Protocol for federated discovery, and the Task Execution Service (TES) for secure analysis. These standards enable harmonized variant normalisation, cross-resource querying, and privacy-preserving execution within Trusted Research Environments (TREs), ensuring sensitive genomic data remain distributed while allowing for pooled aggregate results.
Current flagship projects, such as ENIGMA and BioChef under the ELIXIR Human Data Translational Research (HDTR) initiative, are validating these frameworks. ENIGMA builds a FAIR federated framework bridging genomics and imaging, while BioChef deploys lightweight, privacy-preserving execution agents for multi-site quality control and allele frequency calculations. Complementing this, the community curates over 5,000 rare disease types, benchmarks variant interpretation tools, and develops RD-specific pathways via WikiPathways. Our roadmap (2026–2028) focuses on consolidating these services, developing a "FAIRification Toolkit" tailored to RD data, and integrating advanced AI/ML for automated re-analysis and diagnostic support. Critically, we aim to align our infrastructure with major European initiatives, including the European Health Data Space (EHDS), the European Genomic Data Infrastructure (GDI), and the European Rare Diseases Research Alliance (ERDERA).

Potential Collaboration with EPTRI: The ELIXIR RD Community sees significant synergies with the European Paediatric Translational Research Infrastructure (EPTRI). Specifically, our federated data discovery tools and privacy-preserving analytical workflows (e.g., BioChef) offer a secure, scalable model for paediatric rare disease research, where cross-border data sharing is essential but highly sensitive. Furthermore, our efforts in FAIR benchmarking sets and AI-ready datasets could directly support EPTRI's translational pipelines, enabling the standardised evaluation of tools and workflows across paediatric cohorts.

Keywords: Rare Diseases FAIR data, Federated infrastructure, GA4GH standards

“Strategic Directions in Paediatric Medical Devices Development”

SPEAKER SECTION

Speaker: Tom Melvin

Strategic Directions in Paediatric Medical Devices Development

Tom Melvin[1]

[1] Member, Medical Device Taskforce, Biomed Alliance

The translational development of paediatric medical devices is dependent on a clear clinical, technical, regulatory and business strategy. Clinical and regulatory strategies changed as a result of the Medical Device Regulation, which had consequences for both existing and new devices.

For existing devices, significant challenges in availability have been reported by 53% of respondent clinicians in Europe, with 28% of 'disappearing devices' affecting children. The introduction of a defined pathway for paediatric devices, in addition to the proposed pathways for breakthrough and orphan devices could support devices used for children, which fall outside the orphan device definition.

The off-label use of paediatric devices is vital for specialisms such a paediatric cardiology, and regulators need to increase collaboration with EMA Expert Panels to issue derogations to protect devices, whether used on or off-label at critical risk of market withdrawal when they are needed for the provision of care. There are a variety of projects active with respect to paediatric devices, development and regulation. The DeCoDe project (Developing Child and Orphan Devices) has mapped stakeholders, tools and initiatives relevant to paediatric devices, demonstrating a fragmented but valuable ecosystem of resources for developers. To improve availabilitiy and access to safe and effective medical devices for paediatrics we require continued advocacy, collaboration and shaing of experience, in addition to greater work on international harmonisation.

Keywords: Medical devices, regulation, paediatrics, rare disease

Speaker: Patrice L. (Tamar) Weiss

Participatory Co-Design of Pediatric Rehabilitation Technologies: Translating Innovation into Real-World Clinical Care

Patrice L. (Tamar) Weiss[1], Arie Melamed Yekel[2] and Naomi Gefen[3]

[1]ALYN Hospital and University of Haifa; [2]ALYN Hospital; [3]ALYN Hospital and The Hebrew University of Jerusalem, Jerusalem, Israel

Despite rapid growth in paediatric rehabilitation technologies, many innovations fail to achieve sustained clinical adoption due to limited usability, poor workflow integration, and

insufficient alignment with the lived experiences of children, families, and clinicians. This presentation introduces a clinic-embedded participatory co-design framework developed at ALYN Pediatric & Adolescent Rehabilitation Hospital to support the translation of paediatric rehabilitation technologies from concept to real-world implementation. The framework consists of five iterative stages: (1) identification of unmet clinical needs, (2) co-design and specification, (3) prototype testing and refinement, (4) implementation and adoption planning, and (5) early validation and evidence generation. The approach embeds clinicians, children, caregivers, engineers, and developers throughout the innovation lifecycle to ensure technologies remain clinically meaningful, usable, and scalable.

Two case studies illustrate the framework in practice: the Headovations head support systems (Headaloft and the 360 multidirectional support) and the Pediatric Active–Passive Trainer (P-APT). In both examples, iterative stakeholder feedback informed device refinement, usability improvements, workflow integration, and implementation planning. Families and clinicians contributed critical insights regarding comfort, accessibility, engagement, stability, caregiver burden, and participation in daily activities.

The presentation will discuss how participatory co-design aligns with implementation science, human factors engineering, and emerging regulatory expectations for paediatric medical devices. It will also highlight practical lessons regarding stakeholder engagement, usability documentation, adoption metrics, and sustainability planning. Participatory co-design is proposed as a pragmatic pathway for accelerating the safe translation of emerging pediatric rehabilitation technologies into routine clinical and community care.

Keywords: Participatory Co-Design, Paediatric Rehabilitation Technology, Implementation Science, User-Centered Design, Assistive Technology

Speaker: Kathryn Beardsall

Innovative Neonatal Technologies

Kathryn Beardsall[1]

[1]University of Cambridge, UK

Neonatal intensive care is one of the most technologically complex areas of healthcare, caring for highly vulnerable infants whose physiological and developmental needs cannot be addressed by simply adapting adult technologies. This presentation highlights how collaboration between clinicians, engineers, industry partners, families, and research infrastructures can drive the development and translation of innovative paediatric medical technologies designed specifically for newborn infants. A major challenge within neonatal intensive care units (NICUs) is the dependence on wired monitoring systems. While essential for continuous observation of vital signs, these wires tether babies to incubators and create barriers to parental contact and developmental care. Increasing evidence shows that physical contact between parents and infants improves physiological stability, supports breastfeeding, reduces parental stress, and may contribute to better long-term developmental outcomes. To address this, a multidisciplinary team has developed a family-centred wireless monitoring platform enabling continuous monitoring while reducing barriers to parent-infant interaction. Emerging work will be described including the development of intelligent observation and non-contact physiological monitoring, using

computer vision, and pose estimation technologies applied to continuous monitoring of neonatal activity and physiology. This aims to identify signs of clinical deterioration earlier than conventional assessment approaches. Particular challenges include adapting AI tools to the unique anatomy of premature infants and the complex NICU environment.

The overarching message is that babies are not small adults. Meaningful paediatric innovation requires technologies designed around the specific needs of children and families. Highlighting the need for collaborative, multidisciplinary approaches, with regulatory support to enable neonatal technologies to be translated more rapidly into clinical practice, improving care, outcomes, and experiences for babies and their families.

Speaker: Emilia Biffi

The Agilik exoskeleton for home rehabilitation in children with cerebral palsy and crouch gait: preliminary results of a randomized controlled trial

Anna Falivene[1], Mattia Chiappini[1,2], Fabio Alexander Storm[1], Eleonora Diella[1], Riccardo Riboni[1], Valentina Grasso[1], Luca Molteni[1], Roberta Nossa[1], Giorgia Malerba[1], Roberta Nicotra[3,4], Federica Pregnolato[3], Carolina Ferrante[5], Annalisa Cotardo[5], Federica Camuncoli[5], Giada Sgherri[5,6], Marco Germanotta[7], Maria Cristina Mauro[7], Alessio Fasano[7], Annalisa Sacco[7], Pietro Bondi[8], Maurizio Ferrarin[8], Anna Cavallini[8], Sabrina Giovanna Signorini[3], Giuseppina Sgandurra[5,9], Irene Aprile[7], Laura Iuvone[7], Angela Cavalagli[8], Cristina Maghini[1], Emilia Biffi[1] , on behalf of the Agilik@home Study Group

[1]Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini, Italy; [2]Department of Psychology, University of Torino, Torino, Italy; [3]Child Neuropsychiatry Unit, IRCCS Mondino Foundation, Pavia, Italy; [4]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy; [5]Department of Developmental Neuroscience, IRCCS Fondazione Stella Maris, Pisa, Italy; [6]Ph.D. Programme in Clinical and Translational Sciences, University of Pisa, Pisa, Italy; [7]IRCCS Fondazione Don Carlo Gnocchi, Firenze, Italy; [8]IRCCS Fondazione Don Carlo Gnocchi, Milano, Italy; [9]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Rationale: Crouch gait, a common motor impairment in children with spastic diplegic cerebral palsy (CP), is associated with progressive functional decline and reduced quality of life. While electromechanical devices have shown promise for gait rehabilitation, wearable exoskeletons suitable for home and real-world use in the paediatric population remain scarce. Agilik is a powered knee-ankle-foot orthosis (KAFO) tailored to the patient's anthropometric features and gait pattern, designed to enable domiciliary gait training. This study aims to fill this gap by assessing the clinical benefit of home-based exoskeleton training in children with CP.

Materials and Methods: The Agilik@home trial is an ongoing multicentre, randomized, controlled, parallel (1:1), pragmatic interventional study conducted across four institutions (seven clinical sites) in Italy. The study aims to enrol 40 children with CP and crouch gait (target: 20 per arm). Participants are randomly assigned to the intervention group (in-clinic Agilik setting for 1 month + home-based gait training with Agilik, 30 min/day, 5 days/week, for 2 months) or the control group (standard care and daily life activities). Randomization is centralized and stratified by sex and GMFCS level. Primary endpoints are the distance walked during the 6-minute walking test (6MWT) and knee extension in mid stance (KEMS) measured via 3D gait analysis. Secondary endpoints include joint ROM, muscle length, Modified Ashworth Scale, GMFM-88, 10-meter walking test, COPM, and usability and

acceptability outcomes for the intervention group. Assessments are performed at baseline (T0), after the intervention (T1, 3 months from T0), and at follow-up (T2, 1 month after T1).

Preliminary Results: As of May 2026, 30 patients have been enrolled (21 males, 9 females; mean age 11.7 ± 3.1 years; GMFCS levels I–III) across the participating centres. In the intervention group (n=14), six patients completed home-based training with Agilik, two are currently in the training phase, three are awaiting KAFO preparation, and three dropped out due to clinical deterioration or family compliance. In the control group (n=16), ten patients completed T1 and four have undergone T0 assessment; among those, one dropped out at T1 and three at T2. Overall, adherence to the Agilik training protocol was 68% on average (range: 40–95%), with 52% of sessions meeting and 31% exceeding the prescribed 30-minute duration; 58% of sessions were performed outdoors. Patient-reported emotional experience during training was positive (VAS mean: 73.4 ± 17.1). Preliminary analysis of secondary outcomes in the intervention group showed a clinically meaningful improvement in GMFM-88 dimension D (>5%) after training, maintained at T2, and a greater increase in dimension E compared to the control group. COPM performance improved in both groups, with greater and more durable gains in the intervention group.

Conclusions: These preliminary results suggest that home-based gait training with Agilik is feasible and well-accepted by children with CP and their families. Recruitment is ongoing and needs to be accelerated to reach the target sample size within the planned timeframe. Analysis of primary outcomes will be conducted at study completion and will provide definitive evidence on the clinical effectiveness of Agilik as a tool for domiciliary gait rehabilitation in the paediatric population.

Keywords: exoskeleton, home rehabilitation, cerebral palsy

Speaker: Inês Alves

OptiTrack Feasibility for Paediatric Gait Assessment in Achondroplasia: A Rare Disease Laboratory Use Case

Inês Alves[1,2,3], Orlando Fernandes[4]

[1]ANDO Portugal; [2]Teddy Network; [3]University of Évora- CHRC; [4]University of Évora

Three-dimensional gait analysis uses synchronized motion-capture cameras, body markers, and dedicated software to generate objective reconstructions of gait and lower-limb movement (1). In children with achondroplasia, previous studies using established 3D systems with complex setups have shown that detailed gait assessment is feasible but typically dependent on highly specialized laboratory workflows (1-3). Within this context, OptiTrack is an infra-red motion-capture system that tracks passive or active markers and may represent a more adaptable and usable alternative for exploratory paediatric movement assessment in rare skeletal dysplasias, particularly in terms of marker implementation, protocol practicality, and translational usability (2-4).

Achondroplasia is a skeletal dysplasia characterized by disproportionate limb segments, altered anthropometry, joint laxity, and characteristic gait adaptations, making movement assessment technically demanding and highlighting the need for implementation strategies

tailored to condition-specific anatomy (2, 3). Evidence from paediatric gait studies shows consistent kinematic deviations and anthropometric constraints in this population, supporting careful adaptation of assessment protocols (2, 3).

This work presents a feasibility-oriented test case of an OptiTrack system in a 12-year-old girl with achondroplasia (120 cm height, 40 kg weight) using a 41-body-point marker model. The objective was to assess the usability of this optical tracking system for paediatric gait recording and its practical positioning relative to traditional 3D gait-analysis systems previously used in achondroplasia research (1-3). Marker placement followed a predefined program model and completed in 10 minutes. This presents as a potential advantages in paediatric laboratory contexts where structured marker application can be achieved with acceptable procedural burden. Such models may be particularly useful in exploratory or adapted paediatric assessments, where conventional adult-based or full-body clinical gait models may not be appropriate for children with disproportionate anatomy (2, 3). Another added value of OptiTrack is that optical tracking coordinates are not restricted to the predefined model implemented in the software and can be used to construct alternative biomechanical models, often simpler and more task-specific, to support the analysis of kinematics, kinetics, and joint forces and moments (4, 5).Nevertheless, specific paediatric models for skeletal dysplasias remain necessary, as severe short stature, body disproportionality, and frequent coexisting obesity increase the challenge of accurate anatomical landmark identification and marker placement (2-4). This proposed framework emphasizes three dimensions: feasibility of marker placement in a child with disproportionate anatomy, capacity to generate structured movement data in a controlled laboratory environment, and the need for adapted child-oriented models to improve inclusiveness and accuracy in rare-disease assessment. Compared with traditional 3D gait-analysis platforms, OptiTrack may offer a more adaptable and feasible laboratory solution for exploratory paediatric motion assessment and a relevant platform for early-stage biomechanical evaluation when supported by structured protocols, technical expertise, and local validation (5). This test case supports the value of adaptable movement-assessment platforms within innovation pathways that connect technical design, clinical relevance, and patient-centred research, and suggests that feasibility studies using alternative motion-capture systems in skeletal dysplasias may help clarify implementation options, expand access to structured biomechanical assessment, and inform the development of more condition-sensitive paediatric models and collaborative research pathways (1-5).

Keywords: Paediatric gait analysis, Achondroplasia, Optical motion capture, Feasibility study

POSTER SECTION

Clinical perspectives on wearable devices for paediatric cyanotic congenital heart disease: an expert survey to inform the early development of a multiparametric wearable biosensor

Roberta Nossa[1], Antonio Lopalco[2], Angela Assunta Lopedota[2], Małgorzata Syczewska[3], Sandra Brasil[4], Eleonora Sarracco[4], Emanuela Crea[5], Francesco La Penna[5], Rosa Conte[6], Marina Montanaro[7], Giovanni Migliaccio[7], Marek Migdal[3], Franco Bartoloni[4,6], Donato Bonifazi[4,5,7], and Emilia Biffi[1]

[1]Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini (LC), Italy; [2]Department of Pharmacy – Pharmaceutical Sciences, University of Bari Aldo Moro, Bari, Italy; [3]CMHI - The Children's Memorial Health Institute, Warsaw, Poland; [4]EPTRI - European Paediatric Transnational Research Infrastructure, University of Leuven, Leuven, Belgium; [5]TEDDY - European Network of Excellence for Paediatric Clinical Research, Bari, Italy; [6]Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus, Valenzano (BA), Italy; [7]CVBF - Consorzio per Valutazioni Biologiche e Farmacologiche, Bari, Italy

Introduction: Paediatric medical device development remains limited, particularly for rare and complex conditions such as cyanotic congenital heart disease (CCHD). Although advances in surgery and diagnostics have improved survival, continuous and non-invasive monitoring of metabolic and physiological deterioration is not available outside hospital settings. Wearable devices could address this gap, but their clinical adoption requires alignment with real-world needs, usability, and healthcare workflows. This study aimed to capture clinician perspectives to inform the early development of a wearable multiparametric biosensor for paediatric CCHD within the European OrphaDev4Kids project (EU4H-2023-PJ).

Methods: A structured, web-based anonymous survey was distributed through EPTRI channels to reach paediatric cardiology experts across Europe, including members of the OrphaDev4Kids Clinical Expert Committee. The questionnaire addressed current monitoring practices in CCHD, unmet clinical needs, usability and compliance, data integration, training requirements, and data governance. Quantitative responses were analysed using descriptive statistics, and qualitative feedback was thematically reviewed.

Results: Clinicians reported that current CCHD monitoring relies mainly on imaging and basic physiological parameters, with minimal assessment of metabolic markers and no availability of non-invasive metabolic monitoring. Infancy, both before and after heart surgery, was identified as the most critical phase for remote monitoring. Respondents strongly supported non-invasive, multiparametric wearable devices providing threshold-based alerts and longitudinal summaries rather than continuous data streams. Comfort, intuitive design, and minimal disruption to daily activities were key determinants of patient compliance, while integration with clinical workflows, training, and technical support were essential for adoption. Clinicians also emphasized the importance of secure, regulation-compliant data handling. Despite limited familiarity with advanced wearable devices, clear and consistent expectations regarding functionality and usability emerged.

Conclusions: This expert consultation identifies a clear unmet need and strong clinical support for the development of wearable, multiparametric biosensors tailored to paediatric patients with CCHD. The findings provide actionable guidance for device design and highlight the importance of combining technological innovation with human-centred design, workflow integration, and robust data governance to enable future clinical adoption.

Keywords: cyanotic congenital heart disease, paediatric medical device development, wearable devices, clinical expert survey, orphan medical devices

Identification of needs, facilitators and barriers to implement home- and community-based rehabilitation services for children with neuromotor impairments: Stakeholder Perspectives

Patrice L. (Tamar) Weiss[1], Emilia Biffi[2], Fabio Storm[2], Marta Arleo[3], Francesca Fedeli[4], Pim Valentijn[5], Olgaç Ergeneman[6] and Naomi Gefen[7]

[1]ALYN Hospital and University of Haifa; [2]Lanostra Famiglia, IRCCS Eugenio Medea; [3]ASST di Lecco; [4]Fight the Stroke; [5]Hanze University of Applied Sciences; [6]Magnes AG; [7]ALYN Hospital and The Hebrew University of Jerusalem

Emerging paediatric rehabilitation technologies increasingly enable care delivery beyond the hospital through home, school, and community-based models. However, successful implementation depends not only on technological innovation, but also on the integration of clinical, organizational, and social systems surrounding the child, family and all members of the health care team. The European project CC4C (Closer Care for Children) is addressing this challenge through a participatory co-design framework informed by the Rainbow Model of Integrated Care (RMIC), a conceptual framework that describes how person-centered, coordinated healthcare is achieved through integration across clinical, professional, organizational, functional, normative, and system levels.

This presentation focuses on the first work package (WP1) of CC4C, which aims to identify needs, facilitators and barriers to implement home- and community-based rehabilitation services for children with neuromotor impairments across more than 10 different countries. The CC4C framework recognizes that home and community-based rehabilitation cannot simply replace hospital-based services; rather, successful implementation depends on coordination across stakeholders, caregiver readiness, workforce integration, institutional collaboration, policy alignment, and integration with family routines and participation goals.

WP1 develops a multi-stakeholder co-design process to identify barriers, facilitators, and unmet needs related to decentralized paediatric rehabilitation pathways. Semi-structured interviews have been designed for four stakeholder groups: children and families, allied health professionals, healthcare administrators, and policymakers. The interview architecture translates RMIC domains into practical, stakeholder-accessible themes including person-centeredness, service coordination, professional collaboration, organizational integration, technical-functional support, and system context.

Over the coming two months, we will conduct interviews with Israeli stakeholders to further examine these perspectives and contextualize them within the local healthcare system. Preliminary findings will explore how the extent to which older children prioritize autonomy, meaningful participation, social inclusion, and therapies that fit daily life; how families emphasize communication, trust, and manageable caregiver burden; how allied health professionals identify the importance of role clarity, inter-professional coordination, workflow integration, and technical support; and how administrators and policymakers emphasize governance structures, resource allocation, interoperability, scalability, and sustainable implementation models. These data will be presented at the conference.

Building on the qualitative co-design phase, WP1 will conduct a multi-stakeholder Delphi survey to validate and refine the proposed integrated care design framework, establish consensus regarding key implementation priorities. The survey will be administered via the

REDCap platform to at least 250 respondents from over 10 countries, ensuring equitable representation across age, sex, and stakeholder group. Consensus for each item will be considered achieved if ≥70% of participants score it as 7–9 and less than 15% score it as 1–3. Delphi process will culminate in a comprehensive report identifying the specific challenges faced by children with neuromotor impairments and their families, and the barriers and facilitators experienced by healthcare workers, administrators and policymakers.

By integrating lived experience with implementation science and systems-level perspectives, CC4C consortium aims to generate actionable guidance for scalable, family-centered paediatric rehabilitation ecosystems supported by emerging technologies. The project demonstrates how participatory co-design and consensus-building methodologies can support the safe and sustainable translation of paediatric rehabilitation innovations into real-world care settings.

Keywords: Pediatric Rehabilitation, Integrated Health Care Systems, Community-Based Rehabilitation, Participatory Research, Delphi Technique

SensiVR: An Immersive Virtual Reality System for Supporting Manual Skill Development in Pediatric Neurorehabilitation — A Pilot Study

Katarzyna Koba[1]

[1]RoboKoba Katarzyna Koba

Introduction: Approximately 350 million children worldwide—about one in six—experience cognitive, behavioral, or motor disorders that can lead to significant learning difficulties and mental health challenges (UNICEF, 2021; World Health Organization, 2022). These children often exhibit deficits in manual function and visuomotor coordination, which hinder their ability to perform everyday tasks like writing, cutting with scissors, using utensils, buttoning clothes, or tying shoelaces. This also limits their participation in social activities (Schmidt & Lee, 2011; American Occupational Therapy Association, 2025).

Hand therapy plays a crucial preventive role for these children, supporting the development of fine motor skills, motor planning, and muscle tone regulation during early stages of development (Kleim & Jones, 2008; Weiss et al., 2014). However, traditional therapeutic approaches often have limitations due to their repetitive nature, reduced engagement, and lack of objective tools for monitoring progress (Ravi et al., 2017; Han & Park, 2023). Insufficient support in this area can lead to secondary emotional and behavioral difficulties, such as decreased self-confidence and reduced independence (World Health Organization, 2022).

The rapid advancement of immersive technologies, particularly virtual reality (VR), presents new opportunities to enhance preventive care, neurodevelopmental therapy, and functional rehabilitation. VR-based environments allow for engaging, repeatable, and measurable motor training tailored to the individual's needs (Riva et al., 2019; Magrini et al., 2025). Research suggests that immersive interaction based on natural movement can improve motor outcomes while also increasing user motivation and engagement (Kim et al., 2025; Steed & Lai, 2025). However, the clinical value of these technologies relies on the accuracy of motion tracking, usability, and their integration into therapeutic practice

(Drakakis et al., 2026). In response to these challenges, we developed SensiVR, a controller-free VR system designed to enhance the development of manual skills through immersive interactions. This study presents a pilot evaluation

Background: A significant number of children worldwide experience neurodevelopmental difficulties that affect their motor skills, cognitive abilities, and behavior. The limitations of traditional hand therapy—including low engagement, lack of standardization, and inadequate objective measurement—highlight the necessity for innovative approaches.

Objective: This study aimed to evaluate the usability and preliminary therapeutic potential of SensiVR, an immersive virtual reality (VR) system that utilizes controller-free hand tracking and quantitative motion analysis to support manual skill development in children.

Methods: A pilot usability study was conducted with two participants, both 8 years old, who were undergoing sensory integration therapy. The intervention included 20 VR-based sessions over four weeks. The system allowed users to interact with 3D objects through natural hand movements and recorded over 40 kinematic biomarkers. Outcome measures included the Box and Block Test (BBT), usability assessments, therapist observations, and user-reported comfort.

Results: Participants quickly adapted to the VR environment and were able to perform tasks independently, indicating high usability and an intuitive interface design. The system enabled objective measurement of movement parameters and fostered engagement through immersive interaction. Identified limitations included the need for improved hand-tracking stability, adaptive difficulty levels, and enhanced motivational features.

Conclusions: SensiVR shows promise as a complementary tool for pediatric hand therapy by offering an immersive, measurable, and scalable intervention. Further research involving larger samples and controlled study designs is necessary to validate its clinical effectiveness and long-term outcomes.

Keywords: virtual reality, pediatric rehabilitation, hand therapy, neuroplasticity, digital health

OrphaDev4Kids: Building a Paediatric-Specific Innovation Ecosystem for Orphan Medical Devices

S. Brasil[1], M. Montanaro[2], E. Sarracco[1], F. Bartoloni[1,3], B. Mascolo[1], R. Nossa[4], E. Biffi[4], E. Crea[5], A. Lopalco[6], A. Grzyb[7], M. Migdal[7], I. Mertelseder[8], AM. Weinberg[8], D. Bonifazi[1,2,5]

[1]EPTRI, University of Leuven, Leuven, Belgium; [2]Consorzio per Valutazioni Biologiche e Farmacologiche, Bari, Italy; [3]Fondazione per la Ricerca Farmacologica Gianni Benzi-ETS, Valenzano, Italy; [4]Scientific Institute, IRCCS Eugenio Medea,Bosisio Parini, Italy; [5]TEDDY European Network of Excellence for Paediatric Clinical Research, Bari, Italy; [6]University of Bari Aldo Moro, [7]The Children's Memorial Health Institute, Warsaw, Poland; [8]University of Graz

Medical device development for children lags significantly behind adult applications: paediatric populations differ from adults in size, growth, development, body composition and disease presentation, making device design more complex and commercially riskier for developers. As a result, few medical devices are specifically designed for children, with many simply readapted from adult use. OrphaDev4Kids is a 36-month project, co-funded

by the EU4Health Programme (2021–2027, Grant Agreement No. 101161377), that addresses this gap by establishing a dedicated innovation ecosystem for orphan and paediatric medical devices (MDs).

The consortium brings together eight European partners: CVBF (Consorzio per Valutazioni Biologiche e Farmacologiche, coordinator), TEDDY Network (European Network of Excellence for Paediatric Clinical Research), IPCZD (Instytut Pomnik Centrum Zdrowia Dziecka, Poland), Fondazione per la Ricerca Farmacologica Gianni Benzi - ETS, Università degli Studi di Bari Aldo Moro, IRCCS Eugenio Medea, Medizinische Universität Graz, and EPTRI (European Paediatric Translational Research Infrastructure).

The project is structured across five Work Packages. WP1 covers project management and coordination. WP2 manages access to the paediatric MD platform, connecting academia, scientific societies and users with potential manufacturers, and maintaining up-to-date financing and regulatory resources. WP3, WP4 and WP5 each develop a dedicated case study — a wearable multiplexed biosensor for cyanotic congenital heart disease, a non-invasive videocardiograph for tetralogy of Fallot, and a resorbable implant for bone fragility, respectively — spanning technology readiness levels from early-stage concept to system prototype demonstration.

Through an Open Call, OrphaDev4Kids offers academics, startups, industrial players and patient-led developers direct access to funding advice, network building, technical advice and regulatory guidance, alongside a growing regulatory and funding database and a set of Regulatory Q&As covering the applicable EU framework, clinical evidence requirements, derogations, and strategic considerations for paediatric MD research. Together, these tools and services aim to accelerate the translation of paediatric and orphan medical device innovation from concept to patient benefit across Europe.

Keywords: medical devices, orphan diseases, innovation, research

“Regulatory Challenges in Paediatric Research”

SPEAKER SECTION

Speaker: Viviana Giannuzzi

Past, Present and Future of Regulatory Science for Paediatric Medicines

Giannuzzi V[1], Ruggieri L[1], Sblano S[1], Bonifazi F[1], Ceci A.[1]

[1]Fondazione per la Ricerca Farmacologica Gianni Benzi - ETS, Italy

The European Paediatric Regulation (EC) 1901/2006, as amended, represents the 1st piece of EU legislation that requires pharmaceutical industry to develop medicines for use in a particular subset of the patient population, i.e. children. This has been issued with the main aim to improve the health of children in Europe, by facilitating the development and availability of medicines for them, by ensuring they are subject to high quality research, avoiding, at the same time, unnecessary paediatric clinical studies, and not delaying the authorisation of medicines for adults. To reach that, the EU Paediatric Regulation has issued a system of obligations, rewards and incentives to develop medicines in the relevant paediatric population subsets and measures & tools to guarantee information and transparency and is based on two pillars: the Paediatric Investigation Plan (PIP), the Paediatric Committee (PDCO).

After nearly 20 years from its entry into force, the Paediatric Regulation has led to a significant increase of PIPs and of medicines authorised for paediatric use in the EU. In line with the general trend affecting all clinical studies, the paediatric ones have decreased in Europe. In 2023, the EC reported what did not work and/or what should be improved. This consists of administrative burden of the PIP procedure, delayed conduct of paediatric studies, unattractiveness of Paediatric Use Marketing Authorisation (PUMA) and relevance of paediatric unmet needs in certain areas e.g. paediatric-only diseases, neonates.

Currently, the European pharmaceutical system is undergoing major reform through a new Regulation and a new Directive that will redefine the authorisation of medicines. Such a revision includes the Paediatric Regulation repeal: parts of the regulation will be implemented into the Regulation and other parts will be incorporated into the Directive.

The main modified paediatric-relevant provisions will be: the setup of a European Medicines Agency (EMA) working party with scientific expertise on paediatric medicinal products in place of PDCO, the introduction of the ‘initial’ PIP longer PIP procedures, deferrals capped to 5 years, involvement of Committee for Medicinal Products for Human Use (CHMP) in the PIP assessment, implementation of Mechanism of Action criteria in granting waivers, possible temporary waiver to PIP obligation during public health emergencies, deletion of lists of paediatric needs and PUMA incentive.

In 2023 EPTRI proposed amendments to the European Parliament, based on the possible effects on the future paediatric medicines development and availability, and in particular resulting in the dispersion of the PDCO’s expertise, and the weakening of PIP obligations: to establish a dedicated, permanent Paediatric Working Party at EMA; to preserve PIP obligation; to strengthen paediatric innovative and repurposed medicines development; to improve the identification of paediatric unmet needs; to secure dedicated funding. Importantly, some of EPTRI points were incorporated in the revised texts proposed by the Parliament in 2024 and by the Council of the European Union in 2025.

Despite the setback derived from these legislative changes, further commitment is required to ensure robust, mandatory paediatric regulatory pathways and prioritisation of paediatric

needs. This could be pursued through liaising with the key players in regulatory and public health, like the European Platform for Regulatory Science Research, paediatric networks, patient's organisations.

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Keywords: EU Paediatric Regulation; paediatric medicines development; Paediatric Investigation Plan; new EU pharmaceutical legislation

Speaker: Marc Dooms

Innovative Medicines for Children

Marc Dooms[1]

[1] University Hospitals, Leuven;

The European Medicines Agency (EMA) has recommended marketing authorization of 30 Advanced Therapy Medicinal Products (ATMPs) as gene therapies, cell therapies and tissue engineered medicines. Hospital Exemption is a unique European regulatory pathway that allows custom-made ATMPs to be manufactured and administrated to patients without full centralized marketing authorization. Patient access of these innovative medicines is different in all the EU Member States as the price is very high and reimbursement different in all European countries. Joint Clinical Assessment (JCA) evaluates safety and efficacy of ATMPs within the European Union and reduces redundant clinical evaluations across all the different regions. Several initiatives within some European countries have been taken to increase sustainable access to ATMPs by horizon scanning and price/reimbursement negotiations. The Biotech Act aims to stimulate research and development for these treatments and authorize market access of ATMPs by simplifying regulations and innovating randomized clinical trial (RCT) procedures. All these regulatory measures aim to improve market access of innovative medicines for children.

Keywords: Advanced Therapy Medicinal Products, Gene Therapy, Cell Therapy

Speaker: Breda Kearney

Regulatory Challenges in Paediatric Medical Devices

Breda Kearney[1], Rich Holborow[1]

[1]BSI Notified Body

Paediatric medical devices remain one of the most challenging areas within the medical device regulatory ecosystem. In clinical practice, healthcare professionals are frequently required to use devices outside of their intended purpose or off-label in paediatric populations due to the limited availability of appropriately evaluated and approved devices specifically designed for children. While these approaches may address urgent clinical need, they create significant regulatory, clinical, and ethical challenges for manufacturers, notified bodies, and clinicians alike.

This session will explore the complex realities surrounding paediatric medical devices under the Medical Device Regulation (MDR), with particular focus on the sufficiency of clinical evidence to support expanded indications and intended purposes in paediatric populations. It will examine the unique barriers that exist for manufacturers attempting to generate robust paediatric clinical data, including small patient populations, ethical limitations on clinical investigations, limited commercial incentives, and reliance on real-world clinical use and literature-based evidence.

The presentation will discuss how manufacturers can strategically transition widely accepted off-label clinical use into approved on-label indications through the development of robust evidence generation strategies. Particular emphasis will be placed on how clinical evaluation planning, literature appraisal, post-market clinical follow-up (PMCF), registry data, usability considerations, and state-of-the-art clinical practice can be integrated to support regulatory acceptance of paediatric claims.

The session will also highlight the practical challenges notified bodies face when assessing paediatric indications where traditional large-scale clinical investigations may not be feasible. It will explore how notified bodies balance regulatory requirements for clinical evidence with the realities of unmet paediatric medical need, while ensuring continued compliance with MDR General Safety and Performance Requirements. Discussion will include the use of benefit-risk determinations, clinical justification methodologies, extrapolation approaches, and the importance of transparent scientific rationale within technical documentation. In addition, the session will provide practical guidance for manufacturers preparing technical documentation submissions for paediatric indications and expanded intended purposes. Attendees will gain insight into common deficiencies observed during conformity assessment, expectations for clinical evaluation reports, and approaches for constructing strong scientific and regulatory justifications when evidence remains limited.

Ultimately, this session aims to support a more collaborative and pragmatic approach between industry, clinicians, and notified bodies to help increase the availability of safe and effective paediatric medical devices while maintaining appropriate standards of clinical evidence and patient protection.

Keywords: Medical Devices

“Advancing Paediatric Research Through Health Data, AI and Digital Technologies”

SPEAKER SECTION

Speaker: Daniel Weiss

AMIGO Proposal: A Concrete Use Case for Paediatric Innovation - From Fragmented Data to Integrated Translational Pathways

Daniel Weiss[1], Nicola Götzenberger[1]

[1]Dr. von Hauner Children's Hospital, LMU Munich

Paediatric innovation is constrained by a paradox: European children's hospitals generate valuable clinical, genomic and multi-omics data, yet these data remain fragmented across institutions, diseases, borders and consent frameworks. Children with rare, complex or undiagnosed diseases continue to experience diagnostic odysseys, while companies developing diagnostics, AI tools, sequencing technologies, drug-repurposing platforms or trial solutions lack scalable access to paediatric evidence.

AMIGO – Advanced Medical Intelligence for Guiding Omics-based Medicine – is proposed as a concrete use case for overcoming this fragmentation. Importantly, AMIGO is not intended to become one proprietary product, one exclusive platform or one in-house software project. Its role is to create a trusted federated environment in which companies, academic groups and clinical partners can contribute existing products, algorithms, infrastructure and expertise. AMIGO acts as an enabling ecosystem: hospitals keep data locally, while innovators bring validated tools to the data under transparent governance and privacy-preserving rules.

The scientific ambition is to move from isolated datasets to integrated paediatric disease models. Within participating hospitals, longitudinal clinical data, phenotypes, lab values, WES and WGS, transcriptomics and proteomics can be harmonised and linked through standards such as HPO, OMOP, SNOMED CT and LOINC. A clinical knowledge graph connects genes, proteins, pathways, phenotypes and trajectories, enabling gene prioritisation, clustering of unsolved patients around solved cases, pathway-level interpretation, biomarker discovery, cohort feasibility and research-only decision support.

The operational principle is that algorithms travel to the data, not the other way around. Federated machine learning, secure execution environments and privacy-preserving analytics allow technology providers to deploy solutions inside controlled hospital environments. Raw clinical and omics data remain under hospital control; outputs can be limited to aggregate results, model-performance metrics or privacy-controlled insights. This allows multiple companies to participate without competing for exclusive access to data. Sequencing providers, AI companies, decision-support developers, knowledge graph specialists, privacy-enhancing technology providers, EHR innovators and pharmaceutical partners can each contribute complementary capabilities.

A central argument of AMIGO is that federated (gen)omics data use is not only a technical and ethical necessity, but also the basis for a new economic ecosystem in paediatric innovation. AMIGO proposes a pre-competitive model in which hospitals are active data and knowledge partners rather than passive data suppliers, and companies are not forced into an exclusive vendor relationship. They can test, improve and demonstrate products in

a governed European paediatric setting, while respecting local control, consent, GDPR requirements and clinical responsibility.

This model addresses a market failure in paediatrics: single institutions and rare disease subgroups are often too small to attract sustained commercial investment, yet centralised data pooling is constrained by law, ethics and trust. By making federated analysis operational, AMIGO can lower the entry barrier for SMEs and industry partners, create opportunities for in-kind contributions and translational collaborations, and generate a fairer value proposition for hospitals.

For EPTRI, AMIGO illustrates how paediatric translational infrastructure can connect clinical care, multi-omics research, digital health, industry collaboration and regulatory-grade real-world evidence. Its impact is a scalable framework for turning fragmented hospital data into shared translational capability: privacy-preserving, clinically meaningful, economically sustainable and open to many contributors rather than dependent on a single solution provider.

Keywords: Multi-Omics Data; Knowledge Graph; Public-Private Ecosystem

Speaker: Christophe Maes

Unlocking the Potential of Real-World Health Data for Paediatric Clinical Research: From Data Fragmentation to Evidence Generation

Christophe Maes[1]

[1]Board member European Institute for Innovation through Health Data ; Co-founder eSource Taskforce – i~HD

Paediatric clinical research faces persistent challenges arising from small patient populations, rare diseases, geographically dispersed cohorts, and complex recruitment requirements. These factors contribute to prolonged study timelines, protocol amendments, increased costs, and delayed access to innovative therapies. Although healthcare systems routinely generate large volumes of real-world health data (RWD) through electronic health records (EHRs), registries, laboratory systems, and digital health applications, the full value of these data remains unrealised because of fragmentation, heterogeneity, limited interoperability, and poor reusability.

RWD has the potential to support the entire clinical research continuum, including protocol design, study feasibility assessment, patient identification, recruitment, trial execution, long-term follow-up, and real-world evidence generation. In paediatric research, where every eligible participant is particularly valuable, the use of interoperable health data can improve understanding of disease populations, optimise inclusion and exclusion criteria, reduce screen failure rates, facilitate site selection, and enhance recruitment efficiency. Integration of healthcare and research data workflows through eSource and EHR-to-EDC approaches can further reduce duplication of data entry, improve data quality, decrease administrative burden, and accelerate study execution.

The European Health Data Space (EHDS) establishes an unprecedented regulatory and governance framework for the secure sharing and reuse of health data across Europe. By enabling cross-border interoperability and secondary use of health data, the EHDS creates new opportunities for multinational paediatric research, particularly in rare diseases where

access to sufficiently large and representative cohorts remains a major challenge. However, realising these benefits requires significant improvements in data quality, semantic interoperability, infrastructure readiness, governance mechanisms, and stakeholder trust. Stakeholder consultations consistently identify poor data quality and the repeated curation of the same data for different research purposes as major barriers to value creation.

Emerging European initiatives are addressing these challenges from complementary perspectives. The Horizon Europe AIDAVA project explores AI-assisted data curation, semantic interoperability, and Personal Health Knowledge Graphs to transform heterogeneous and often unstructured clinical information into reusable, research-ready assets. By supporting a "curate once, use many times" paradigm, AIDAVA aims to improve data quality at source while enabling multiple downstream uses across healthcare, research, innovation, and policymaking.

In parallel, the xShare project demonstrates how interoperable patient-controlled health data can facilitate patient empowerment, self-identification for clinical studies, federated feasibility assessments, and the secure reuse of healthcare data during clinical trial conduct. Such approaches offer new mechanisms for connecting patients, healthcare providers, and researchers, while preserving transparency, consent, and trust. They may prove highly valuable for paediatric and rare disease populations, where eligible participants are difficult to identify and recruit.

The convergence of EHDS, interoperable health data infrastructures, AI-enabled data quality technologies, and patient-mediated data sharing models offers a unique opportunity to transform paediatric clinical research. Establishing a connected evidence ecosystem in which health data can be securely reused across care and research has the potential to accelerate innovation, improve trial efficiency, strengthen European competitiveness in clinical research, and improve outcomes for children and young people.

Speaker: Cosimo Altomare

AI-Based Digital Platforms for Early Drug Repurposing Studies in Paediatric Diseases

Cosimo Damiano Altomare[1], Caterina Deruvo[1], Modesto de Candia[1], Marco Catto[1], Orazio Nicolotti[1]

[1]University of Bari Aldo Moro, Bari, Italy

Matching novel natural and synthetic compounds to putative drug targets or repurposing old drugs for new therapeutic indications are crucial for reducing the drug discovery attrition rate, by saving time and costs. This goal could be achieved by employing effective in-silico target fishing approaches with the aim of prioritizing novel compounds towards desirable targets, ranking the endpoints for in-vitro testing and preclinical studies.

In this framework, an easy-to-use drug discovery web platform, named PLATO (the acronym stands for Polypharmacology pLATform prediction),1 has been developed with a two-fold objective: (i) to fish putative protein drug targets and (ii) to forecast the bioactivity values of small molecules. The predictions are made by using a multifingerprint similarity algorithm

based on ligand-based screening of the ChEMBL database (v.35). Besides PLATO, other web platforms dedicated to assessing the risk of developmental toxicity of new chemicals, namely TIRESIA and TISBE, have been developed based on an explainable artificial intelligence approach.2

Herein, two case studies related to applications of the above-mentioned platforms will be presented and discussed. The first one deals with the computer-aided repurposing of drugs for treating the Lafora disease, an ultrarare recessively inherited condition causing progressive myoclonic epilepsy and decline in cognition and motor function of young people.3 The second one pertains application of AI-based approaches to identify drugs to treat autosomal recessive polycystic kidney disease (ARPKD), a rare genetic disorder in pediatric nephrology associated with altered vasopressin V2 receptor (V2R) responses [4]. In both cases, combining in-depth computational investigations and functional studies, some drugs were prioritized for being repurposed.

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Keywords: Drug repurposing, digital platforms, target fishing, artificial intelligence

POSTER SECTION

Time-Dependent Pattern of Liver Injury Biomarkers in Neonates with Hypoxic-Ischemic Encephalopathy Undergoing Therapeutic Hypothermia

Jannes Warlop[1,*], Noor Borloo[1,*], Hemananda Muniraman[2,3], Barbara Michniewicz[4], Kata Kovacs[5], Pieter Annaert[6,7], Gozdem Kayki[8], Paul Clarke[2,9], Dawid Szpecht[4], Miklos Szabo[5], Steffen Fieuws[10], Nadir Yalcin[11], Anne Smits[1,12,**], Karel Allegaert[11,13,14,**,***]

[1]Neonatal Intensive Care Unit, University Hospitals Leuven, Leuven, Belgium; [2]Neonatal Intensive Care Unit, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, Norfolk, United Kingdom; [3]Neonatal Intensive Care Unit, Los Angeles General Medical Center, Los Angeles, United States of America; [4]Department of Neonatology, Poznan University of Medical Sciences, Poznan, Poland; [5]Department of Neonatology, Pediatric Centre, Semmelweis University Budapest, Hungary; [6]Drug Delivery and Disposition, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium; [7]BioNotus CommV, Niel, Belgium; [8]Division of Neonatology, Department of Pediatrics, Hacettepe University, Ankara, Turkiye; [9]Norwich Medical School, University of East Anglia, Norwich, United Kingdom; [10]Interuniversity Centre for Biostatistics and Statistical Bioinformatics, Department of Public Health, KU Leuven, Leuven, Belgium; [11]Department of Clinical Pharmacy, Faculty of Pharmacy, Hacettepe University, Ankara, Turkiye; [12]Department of Development and Regeneration, KU Leuven, Leuven, Belgium; [13]Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium; [14]Department of Hospital Pharmacy, Erasmus MC, Rotterdam, The Netherlands.

Purpose: Hypoxic-ischemic encephalopathy (HIE) often results in multi-organ damage. Liver injury following HIE is typically characterized by time-dependent altered patterns of alanine aminotransferase (ALT), aspartate aminotransferase (AST) or total bilirubin (TB) concentrations. This study aims to describe age-dependent patterns of liver injury biomarkers during and after therapeutic hypothermia (TH).

Methods: Liver injury biomarkers (ALT, AST, TB) over the first 10 days of postnatal age (PNA) from six cohorts, including 428 neonates with moderate-to-severe HIE treated with TH were pooled. Statistical modelling with linear mixed models and quantile regression was applied to assess trends and correlations with HIE severity, gestational age, and birth weight.

Results: ALT and AST concentrations were highest on PNA day 1 (median [IQR]: 37.5 [18.75-85.50] U/L), and 154 [79-345 U/L], respectively) and declined thereafter. ALT and AST values were both associated with HIE severity ($p<0.001$). The AST/ALT (De Ritis) ratio remained >3.0 throughout PNA days 1-10. TB exhibited a biphasic pattern, highest at PNA day 3 (median [IQR] 4.5 [3.1-6.2]mg/dL) and PNA day 8 (4.95 [2.10-9.52] mg/dL).

Conclusion: We compiled age dependent reference values of liver injury biomarkers in HIE neonates treated with TH. Along with PNA, HIE severity has a strong association with liver biomarkers, while the De Ritis ratio reflects ischemic hepatic injury throughout PNA (day 1-10). These age-dependent reference values can be used to assess intra- and interpatient variability, or to explore other causes of hepatic toxicity like drug-induced liver injury, preferably following external validation.

Keywords: liver injury; biomakers; asphyxia; newborn; physiology-based pharmacokinetics; pharmacovigilance

Embedding-Based Semantic Matching for OMOP CDM Vocabulary Harmonization in a Multilingual Pediatric Environment: A Comparative Evaluation of Sentence Embedding Models

Stefan Marynowicz[1,2], Elżbieta Birgiel[1], Rafał Bartczuk[1]

[1]Paediatric Regional Centre for Digital Medicine, The Children's Memorial Health Institute, 04-730 Warsaw, Poland; [2]Institute of Fundamental Technological Research, Polish Academy of Sciences, Pawinskiego 5B, Warsaw, 02-106, Poland

Background: The harmonization of clinical terminology to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM) represents a critical bottleneck for non-English-speaking healthcare institutions seeking to participate in international observational research networks such as Data Analysis and Real World Interrogation Network (DARWIN EU). In multilingual settings, local terms require translation prior to vocabulary standardization, adding complexity to the mapping process. Established tools such as Usagi, which is based on Term Frequency-Inverse Document Frequency (TF-IDF) string matching, are not designed to address this challenge. The problem is particularly relevant in p aediatric referral centers, as their measurement vocabularies include rare disease biomarkers, subspecialty-specific abbreviations, and local naming conventions rarely represented in general-purpose biomedical ontologies. Additionally local vocabulary is not defined and therefore duplicates exist. As a result, real-world data (RWD) from

paediatric hospitals remain underused in international observational research, despite their significant scientific value.

Methods: We developed a multi-stage semantic normalization pipeline for harmonizing terms in the OMOP Measurement domain at the Children's Memorial Health Institute (CMHI) in Warsaw, Poland – a national paediatric referral center with over 562,000 patient records. The pipeline comprised automated Polish-to-English translation using the DeepL API model, abbreviation detection and canonicalization using a regex-based classifier with manual expert validation and embedding-based semantic matching against OMOP standard vocabularies. A total of 3,625 unique measurement terms were processed, including 691 laboratory abbreviations expanded using a large language model and subsequently reviewed by experts. Three sentence embedding models were evaluated – all-mpnet-base-v2, S-BioBERT, and BAAI/bge-large-en-v1.5 – across three vocabulary configurations (LOINC, SNOMED CT, and combined LOINC + SNOMED CT), resulting in nine experimental conditions. Performance was assessed using mean cosine similarity and compared against Usagi as the baseline.

Results: BAAI/bge-large-en-v1.5 achieved the highest mean cosine similarity across all conditions (range: 0.756–0.788), outperforming S-BioBERT (0.656–0.700) and all-mpnet-base-v2 (0.616–0.667). All three embedding models substantially outperformed Usagi across all vocabulary configurations (Usagi: 0.463–0.541). The combined LOINC + SNOMED CT vocabulary configuration yielded the highest scores for each model. LOINC consistently produced more precise candidate matches for quantitative laboratory parameters than SNOMED CT alone.

Conclusions: Retrieval-optimized sentence embedding models may improve candidate term retrieval for OMOP Measurement vocabulary harmonisation in multilingual clinical settings compared with TF-IDF-based matching. The proposed pipeline reduces manual curation effort while maintaining mapping quality and is transferable to other non-English institutions undertaking OMOP CDM harmonization.

Keywords: OMOP CDM, semantic concept mapping, sentence embeddings, multilingual NLP, pediatric health data

Transforming paediatric hospital EHR data to the OMOP Common Data Model: ETL implementation and data quality assessment in Polish national referral center

Elżbieta Birgiel[1], Stefan Marynowicz[1,2], Aleksander Wiśniewski[1], Rafał Bartczuk[1]

[1]Paediatric Regional Centre for Digital Medicine, The Children's Memorial Health Institute, 04-730 Warsaw, Poland; [2]Institute of Fundamental Technological Research, Polish Academy of Sciences, Pawinskiego 5B, Warsaw, 02-106, Poland

Background: The increasing adoption of the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM) enables large-scale observational research through standardized data harmonization. However, hospital data are typically stored according to local rules and terminologies and are only partially standardized, limiting interoperability between institutions. Despite these limitations, such data contain valuable information on disease progression, treatments, medications, laboratory tests, and patient outcomes.

The Children's Memorial Health Institute (CMHI) represents this challenge. Although its internal systems, data models, and governance rules are well defined locally, they cannot directly support large-scale international studies. To facilitate interoperability and cross-institutional collaboration, the adoption of a common data model with standard vocabularies is required.

One initiative addressing the harmonization of clinical data across institutions, including pediatrics, is the Data Analysis and Real World Interrogation Network (DARWIN EU), which aims to provide reliable evidence on medicines across the European Union (EU).

Methods: We implemented an extract-transform-load (ETL) workflow to transform data from the CMHI Hospital Information System (HIS) into OMOP CDM v5.4 using an Oracle Database Management System. Standard vocabularies were retrieved from the Athena platform, while locally used HIS terminology was extracted, cleaned, and normalized to establish mappings to standard concepts.

The Conditions and Procedures domains were mapped directly using OHDSI vocabulary relationships, as the local terminology already relied on ICD-10 and ICD9Proc codes. The Drugs domain required substantial normalization and cleaning to achieve consistent mapping to standard concepts. Data quality was assessed using OHDSI tools, including the Data Quality Dashboard, CdmOnboarding, and DashboardExport.

Results: The ETL workflow populated the following OMOP CDM domains: Visits (3,625,977 records), Conditions (1,839,061), Procedures (1,379,759), Person (568,724), Drug Exposure for administered drugs (197,697) and prescribed drugs (536,205), Observation Period (572,404), and Provider (1,362). The earliest mapped records dated back to January 2008.

Visit data included outpatient, inpatient, and emergency room encounters. In total, 6,035 condition source codes, 2,696 drug source names, and 844 procedure codes were processed.

Conclusions: The main OMOP CDM domains were successfully mapped and populated. Source codes were mapped to standard concepts with a high level of conformance. In the Data Quality Dashboard, the Conformance category showed that on average 0.06% of records did not conform to standards or data model integrity rules for the currently loaded tables. However, additional verification and clinician consultations are still required for unmatched or uncertain mappings, particularly where local naming conventions are poorly defined. The Measurements domain also requires separate processing and standardization, as no locally defined vocabulary currently exists and NLP-based approaches may be necessary.

Keywords: OMOP CDM, ETL, RWD, clinical data standardization, pediatric health data

Machine Learning-Driven Quality by Design Framework for Predicting Dose Recovery in Enteral Feeding Tube Administration

Anthony Chan[1], Smita Salunke[2*], Esmerald Hermans[3], Tina Arien[3], Maarten Vliegen[3]

[1]University College London School of Pharmacy / KU Leuven; [2]University College London, School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, UK; [3]Johnson & Johnson Innovative Medicine, Turnhoutseweg 30, 2340 Beerse, Belgium

*Corresponding author

Introduction: Enteral feeding tubes (EFTs) are widely used in paediatric care to deliver essential medicines to children with a compromised swallowing function. However, ensuring effective drug delivery via EFTs is challenging, as outcomes depend on a complex interplay of tube characteristics, formulation properties, and administration conditions. Quality by Design (QbD) frameworks aim to address this complexity by defining design spaces that link these variables to key delivery outcomes, such as dose recovery. Nonetheless, establishing design spaces using traditional experimental approaches remains labour-intensive and time-consuming. Hence, this pilot study evaluates the feasibility of using machine learning (ML) to predict dose recovery and clogging risk, ultimately supporting the development of a design space to guide EFT formulation design.

Methods: For data collection, fifteen glycerol-polymer formulations of varying viscosity range were prepared using xanthan gum (XG), carbopol (CBP), and hydroxypropyl cellulose (HPC). These formulations and three marketed solutions (Benylin® Dry Cough & Sore Throat Syrup, Furoped® Oral solution, and Dafalgan® Paediatric Syrup) were characterised for viscosity, flow behaviour, and in-vitro gravimetric dose recovery in 4, 6, and 8 Fr tubes. The obtained glycerol-polymer data was subsequently used for ML model training and the marketed oral solutions for model validation. Four ML classification models (Logistic Regression (LR), Decision Trees (DT), Random Forests (RF), Extreme Gradient Boosting (XGB)) were tested to predict EFT administration risk based on a predefined dose recovery threshold (90%), and evaluated using PR-AUC, macro-F1, and balanced accuracy.

Results: Three models (LR, RF, and XGB) showed strong discrimination between formulations with a low- and high-risk for EFT administration, with RF providing the most robust performance (macro-F1 = 0.78, balanced accuracy = 0.81, PR-AUC = 0.78). Subsequent RF SHAP-analysis revealed that highly viscous and strongly shear-thinning solutions were associated with a higher risk of administration failure, consistent with our in-vitro observations. The predicted failure risk probabilities of the RF model were visualised into practical decision boundary heatmaps, illustrating how ML could guide formulation design space development through risk-based decision-making.

Conclusion: Overall, this study demonstrated the feasibility of integrating experimental data and ML within a QbD framework to support EFT formulation design. By enabling data-driven formulation decisions, this ML-based QbD framework has the potential to reduce experimental burden and accelerate formulation development.

Keywords: Paediatrics, Machine Learning, QbD, Formulation Development

SPEAKER SECTION

Speaker: Marios Phylactides

Gene Therapy for α-Thalassaemia: Towards an In Utero Therapeutic Approach

Marios Phylactides[1], Charis Constantinou[1], Carsten Lederer[1], Petros Patsali[1], Panagiota Papasavva[1], Michael Antoniou[2], Panicos Shnagaris[2], Nicoletta Psatha[3]

[1]The Cyprus Institute of Neurology and Genetics; [2]King's College London; [3]Aristotle University, Thessaloniki

In utero genome editing (IUGE) has the potential to transform the treatment of severe congenital disorders by correcting disease before irreversible pathology develops. Unlike postnatal therapies, prenatal intervention exploits the unique biology of the developing foetus, including an immature immune system that promotes immune tolerance, rapidly expanding haematopoietic stem cell populations, lower therapeutic dose requirements due to small foetal size, and the opportunity to prevent rather than reverse disease. These advantages make IUGE particularly attractive for disorders with prenatal onset, such as α-thalassaemia major.

A universal gene therapy platform for α-thalassaemia is being developed as a foundation for future prenatal therapy. A series of lentiviral vectors derived from the clinically validated GLOBE platform has been engineered, incorporating novel erythroid regulatory elements to maximise α-globin expression while maintaining lineage-specific expression.

Translation of these advances to the prenatal setting is being pursued through intrahepatic foetal delivery in a murine α-thalassaemia model. Emerging technologies, including targeted lipid nanoparticle delivery, base editing and prime editing, are expected to further improve the precision, safety and clinical applicability of prenatal gene therapy. Together, these developments highlight the potential of IUGE to provide curative treatment for α-thalassaemia before birth and establish a therapeutic framework for a broad range of severe developmental-onset genetic disorders.

Keywords: Alpha Thalassaemia, Gene therapy, *In utero*

Speaker: Nicolas Deconinck

Disease-Modifying Therapies in Rare Pediatric Neuromuscular Diseases: Where Do We Stand?

Nicolas Deconinck[1]

[1]Department of Pediatric Neurology and Neuromuscular Reference Center, Hôpital Universitaire des Enfants Reine Fabiola (HUB), Université Libre de Bruxelles, Brussels, Belgium

Rare pediatric neuromuscular diseases represent a heterogeneous group of severe inherited disorders characterized by progressive muscle weakness, disability, multisystem complications, and significant impact on quality of life and survival. Over the past decade, major advances in molecular genetics, biomarker discovery, and a deeper understanding of the underlying pathophysiological mechanisms—such as motor neuron degeneration, membrane instability, fibrosis, inflammation, impaired muscle regeneration, and

neuromuscular junction dysfunction—have profoundly transformed the therapeutic landscape of these conditions. This improved knowledge has enabled the development of innovative disease-modifying strategies, including gene replacement therapies, exon skipping, RNA-targeted approaches, genome editing, and precision pharmacological interventions. As a result, disorders previously considered untreatable, such as Spinal Muscular Atrophy (SMA) and Duchenne Muscular Dystrophy (DMD), have entered a new therapeutic era, while promising pipelines are emerging for other rare disorders including Limb-Girdle Muscular Dystrophies (LGMD) and Charcot-Marie-Tooth diseases (CMT).

This presentation will provide an overview of the current state of disease-modifying therapies in rare pediatric neuromuscular diseases, highlighting both established therapeutic successes and future perspectives. Particular attention will be given to the pathophysiological rationale supporting these therapeutic developments, illustrating how advances in disease mechanisms have directly guided the emergence of targeted treatments. The lecture will also address key translational and clinical challenges, including optimal timing of treatment, clinical trial design, identification of sensitive outcome measures, long-term efficacy and safety monitoring, regulatory pathways, and equitable patient access.

To illustrate these developments, the lecture will also present data and experience from our research group, particularly in the field of innovative endpoints and translational clinical research. Examples will include gait analysis as a functional outcome measure in Duchenne Muscular Dystrophy and swallowing assessment as a clinically meaningful endpoint in Spinal Muscular Atrophy. In addition, results from international collaborative studies and publications involving our group in SMA and DMD will be discussed, providing practical insight into how academic research networks contribute to therapeutic progress in rare neuromuscular diseases.

Keywords: Advanced therapies, Neuromuscular Diseases, Gene Therapy, Translational research, Precision Medicine

Speaker: Pablo Ruiz

Gait analysis in Duchenne Muscular Dystrophy: a functional, selective tool for evaluating gene therapy?

Pablo Ruiz[1], Cheron Guy[1], Tahon Valentine[2], Cebolla Ana Maria[1], Deconinck Nicolas[1,2,3]

[1]NeuroMove, Laboratory of Movement Neurophysiology, Université Libre de Bruxelles, Brussels; [2]UZ Gent, Neuromuscular Reference Center NMRC, Ghent; [3]Department of Pediatric Neurology and Neuromuscular Reference Center, Hôpital Universitaire des Enfants Reine Fabiola (HUB), Université Libre de Bruxelles, Brussels, Belgium

Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder marked by early motor decline. The absence of functional dystrophin protein leads to progressive degeneration of skeletal muscles. Gene-modifying therapies, including exon skipping and gene therapy for DMD, aim to restore or replace dystrophin to slow disease progression. Although functional assessments such as the Nord Star Ambulatory Assessment, Ten-Meter Walk Test (10MWT), and Time to Stand (TTS) are commonly used to track disease progression, they provide limited information on qualitative changes in ambulatory

function. Instrumented gait analysis may better capture these changes through detailed kinematic parameters, which, in the context of emerging gene-modifying therapies, have not been provided. This study first described longitudinal gait changes in boys with DMD who were followed at two Belgian centers (HUDERF and UZ Gent) and all received standard corticosteroid therapy (CS) from age 5 years. Second, it explored whether spatiotemporal parameters and the Gait Profile Score (GPS), a single gait index, could discriminate disease progression in a subgroup additionally receiving gene-modifying therapies (RGM). In parallel, NSAA and TTS were assessed. Thirteen boys with genetically confirmed DMD (mean baseline age 6.8 ± 1.44 years; n = 8 RGM, n = 5 CS only) underwent 39 gait analyses (2–4 assessments/patient, approximately annually) using a VICON system. Longitudinal changes in spatiotemporal parameters and GPS data were analyzed using a linear mixed-effects model that included participant-level random effects and baseline age, time between sessions, interaction baseline time, and treatment group as fixed effects. According to the results by linear mixed models, GPS was estimated to increase by 0.23 points/year across groups (n = 13, 95% CI: -0.17 to 0.64), with a mean GPS of 8.73 in the CS-only group at 8.17 years of age (n = 5, 95% CI: 7.51 to 9.94). This increase was driven primarily by greater pelvic tilt, hip flexion, and hip external rotation. Patients receiving RGM had GPS values 1.98 points lower than those receiving CS only (n = 8; 95% CI: -3.52 to -0.43; t = -2.50; p = 0.026). For normalized step length (NSL), normalized step width (NSW), and normalized walking velocity (NWV), no between-group differences were observed. However, NSW stabilized between ages 7 and 10, whereas NSL and NWV continued to decrease. For the functional assessments, NSAA was estimated to decrease by -0.09 points/year across groups (n = 13, 95% CI: -1.17 to 0.99), and the Baseline time interaction was -1.39 (points baseline)/year across groups (n = 13, 95% CI: -2.18 to -0.60). The mean NSAA in the CS-only group was 20.32 (n = 5, 95% CI: 16.90 to 23.76), while the group receiving RGM had 6.77 points higher than those receiving only CS (n = 8; 95% CI: 2.57 to 10.98; t = 3.16; p = 0.007). TTS was estimated to increase by 0.72 seconds/year across groups (n = 13, 95% CI: 0.14 to 1.31), and the Baseline time interaction was 0.45 (points*baseline)/year across groups (n = 13, 95% CI: 0.03 to 0.83). The mean TTS in the CS-only group was 5.81 seconds (n = 5, 95% CI: 4.14 to 7.48), while the group receiving RGM had 2.046 seconds less than those receiving only CS (n = 8; 95% CI: -4.09 to 0.00; t = -1.96; p = 0.07). These findings suggest that functional tests, particularly NSAA, in conjunction with GPS, may be a gait-sensitive marker of DMD progression and provide evidence of stabilization of key kinematic impairments in patients receiving RGM.

Keywords: Duchenne Muscular Dystrophy, gait analysis, gene therapy, functional assessments, children

Speaker: Kun Shi-van Wielink

The Challenge Is Not the Therapy, it's the Population – An industry perspective on pediatric evidence generation beyond ATMPs.

Kun Shi-van Wielink[1]

[1]Santen SA

Advanced Therapy Medicinal Products (ATMPs) have brought renewed attention to the challenges of pediatric drug development, including small patient populations, ethical considerations, long-term follow-up requirements, and evidence generation for regulatory and reimbursement decision-making. While many of these challenges are frequently discussed in the context of ATMPs, they are not unique to advanced therapies.

This presentation will explore the broader question of whether some of the most persistent barriers in pediatric development arise primarily from the therapy itself, or from the realities of generating evidence in children. Drawing on industry experience across clinical development, medical affairs, and health economics and outcomes research (HEOR), the session will highlight challenges that extend beyond ATMPs and affect a wide range of pediatric interventions.

Using pediatric ophthalmology as an illustrative example, the presentation will discuss how evidence generation can remain challenging even in relatively common childhood conditions. Unlike many rare disease or ATMP settings, care is often delivered in outpatient and community-based environments, where patient identification, longitudinal follow-up, data collection, and outcome assessment can be difficult. Large patient populations do not necessarily translate into accessible evidence. Fragmented care pathways, evolving physiology, caregiver involvement, and the need to demonstrate long-term outcomes may create barriers comparable to those encountered in more specialized therapeutic areas.

The presentation will examine the burden on evidence generation in paediatric indications, including chronic and long-term study settings, with focus on feasibility, patient recruitment and retention, endpoint selection, collection of patient-centered outcomes, generation of long-term evidence, and the growing role of real-world data and real-world evidence. Particular attention will be given to the disconnect that can exist between the availability of patients and the availability of meaningful, decision-relevant data.

Finally, the session will discuss potential enabling pathways that may benefit both ATMP and non-ATMP pediatric programs, including collaborative research networks, disease registries, digital data collection approaches, pragmatic evidence generation strategies, and greater alignment among regulators, HTA bodies, clinicians, patients, and industry.

By broadening the discussion beyond technology platforms, this presentation aims to highlight a common challenge across pediatric development: the difficulty is often not finding patients, but generating the evidence needed to improve outcomes and support decision-making throughout the healthcare system.

Keywords: industry perspective

Speaker: Sean Kilbride

Industry Perspective on Paediatric Rare Disease Development

Seán Kilbride[1]
[1]Senior Director, Regulatory Affairs – Regeneron Ireland DAC

Regeneron is a leading biotechnology company that discovers and develops transformative medicines for people with serious diseases. Drawing on Regeneron's experience across development phases and therapeutic areas, this presentation offers an industry perspective on developing novel medicines for paediatric patients with rare and ultra-rare conditions in Europe. It will also discuss specific examples that illustrate how the European paediatric regulatory system can provide flexibility in some situations while in others it causes significant procedural challenges for sponsors. Recent changes in EMA guidance and evolving requirements from EU regulatory bodies are considered in this context. For example, CHMP Scientific Advice on paediatric clinical trials cannot provide EMA agreement that a clinical programme is appropriate to meet the requirements for registration; this must be addressed through the PIP procedure, where details of the clinical trial designs, including full statistical plans must be specified. Indeed, until recently CHMP Scientific Advice was not available to sponsors if the advice related to paediatric developments. The impact of the requirements are particularly relevant for paediatric rare disease development, where conventional randomised controlled trials and routine statistical success criteria may not be feasible. While CHMP Scientific Advice can provide a shorter and more focused route to feedback on complex clinical trial questions, the PIP procedure can require multiple rounds of interaction and may result in legally binding key elements before study initiation. This can delay the conduct of paediatric studies in the EU while detailed statistical nuances are debated. Additionally, unresolved PIP key elements that require submission of additional data can also be difficult to address through subsequent lengthy PIP modifications.

Overall, paediatric rare disease development in the EU would benefit from more constructive, consistent, coherent, and timely regulatory feedback. Greater alignment between PDCO and CHMP expectations, clearer guidance on statistical success criteria, and sufficient flexibility to reflect the scientific, methodological and ethical realities of clinical development in small paediatric populations are needed. By identifying procedural barriers and opportunities for improvement, the EU can support earlier and more equitable access to innovative medicines for children with rare diseases.

Keywords: Industry, rare diseases

“Innovations In Paediatric Clinical Research and Translational Science”

SPEAKER SECTION

Speaker: Sergiu Siminiuc

AI-Powered Clinical Trial Navigation for Dystrophinopathies: Empowering Patients, Families and Clinicians

Sergiu Siminiuc[1], Elvina Sakellariou[1], George Paliouras[1,2]

[1] Duchenne Data Foundation; [2] National Center for Scientific Research "Demokritos”

The Duchenne Data Repository (DDR) and Duchenne Map (DM) form a digital ecosystem designed to empower people living with dystrophinopathies to identify and access appropriate clinical trial opportunities. Built using open-source technologies and FAIR principles, the DDR continuously integrates curated disease information with up-to-date clinical trial data from public registries, providing a reliable foundation for intelligent trial discovery. As part of its data processing pipeline, the DDR applies artificial intelligence (AI)-assisted metadata enrichment to analyze publicly available clinical trial protocols and automatically extract key eligibility criteria, including targeted exons, mutation-specific requirements and other clinically relevant characteristics. By transforming complex trial information into structured, searchable metadata, the DDR creates an enriched dataset that supports precision trial discovery while reducing the manual effort traditionally required to interpret clinical trial registries. Building these AI-enriched data, the Duchenne Map provides an intuitive, patient-centered interface that combines intelligent filtering with interactive geospatial visualization of clinical trial sites. Patients and families can search for studies using clinical and genetic characteristics while identifying recruiting centers geographically, allowing them to locate potential trial sites near their place of residence and better understand travel requirements. For clinicians, the platform serves as a practical decision-support tool that facilitates identification of suitable studies, streamlines referral pathways, and supports informed discussions with patients regarding available research opportunities. Together, the DDR and Duchenne Map demonstrate how AI-assisted data enrichment, structured clinical knowledge, and intelligent geospatial navigation can transform complex clinical trial information into meaningful, actionable knowledge. Rather than functioning solely as trial registries, they empower patients and families to navigate research opportunities with greater confidence while enabling clinicians to identify appropriate studies more efficiently and facilitate timely trial referrals. This patient-centered, AI-enabled approach offers a scalable and transferable model for improving clinical trial accessibility, precision recruitment and patient engagement across rare and pediatric diseases.

Keywords: Duchenne muscular dystrophy Clinical Trial matching AI-assisted metadata enrichment FAIR data principles Geospatial visualization

Speaker: Jan Přibyl

From Molecules to Disease Models: Correlative Microscopy Approaches and Integrated Structural Biology for Multiscale Phenotyping of Fibrosis, Tissue Mechanics, and Cardiac Organoids

Jan Přibyl[1], David Vondrášek[2], Daniel Hadraba[2,3], Markéta Jiroušková[4], Martin Gregor[4], Šárka Jelínková[5,6], Martin Pešl[5,6], Vladimír Rotrekl[5,6], Petr Skládal[1]

[1]CEITEC, Masaryk University; [2]Institute of Physiology of the Czech Academy of Sciences; [3]Czech-BioImaging; [4]Institute of Molecular Genetics of the Czech Academy of Sciences; [5]Masaryk University; [6]International Clinical Research Center, St. Anne's University Hospital Brno

Background: Pediatric diseases often arise from molecular lesions that manifest across cells, tissues, and organs, yet conventional phenotyping captures only a fragment of this multiscale pathology.

Aim: To demonstrate how correlative microscopy-biomechanics workflows can quantify structural and mechanical disease signatures in limited patient samples and in human pluripotent-stem-cell (hPSC)-derived models.

Methods: We combined polarization microscopy, second- and third-harmonic generation (SHG/THG) imaging, and atomic-force microscopy (AFM) nanoindentation. In surgically obtained tissue from relapsed congenital clubfoot, medial and lateral sections were analyzed for Young's modulus, collagen density (SHG), adipose content, and collagen crimp (polarization). A separate AFM-polarization protocol was applied to human liver biopsies spanning early- to late-stage fibrosis. The same pipeline was used on hPSC-derived cardiomyocytes and cardiac organoids modeling Duchenne muscular dystrophy (DMD) cardiomyopathy.

Results: • Medial clubfoot tissue displayed a 34 % increase in Young's modulus ($p < 0.001$), +22 % SHG-derived collagen signal, -15 % adipose area, and a more pronounced collagen crimp compared with the lateral side, indicating that altered extracellular-matrix tension sustains relapse [1].

• In liver samples, AFM-polarization mapping revealed stepwise stiffening of collagen-rich septa (2 kPa → 8 kPa, $p < 0.01$) and pronounced biomechanical heterogeneity across fibrosis stages [2].

• DMD-derived cardiac organoids recapitulated calcium-handling defects, reduced contractile force, brady-arrhythmias and blunted β-adrenergic response, all quantitatively resolved by the correlative workflow [3, 4].

Conclusion: Integrated structural-biophysical workflows provide pediatric researchers with quantitative, multiscale read-outs from scarce biopsies and stem-cell models, facilitating mechanistic insight and drug-response testing from molecules to organoids.

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Keywords: Correlative microscopy; Disease models; Tissue biomechanics; Cardiac organoids; Integrated structural biology

Speaker: Oksana Degtjarik

Cryo-EM for Paediatric Disease Research at Leeds Instruct Centre

Oksana Degtjarik[1], Yehuda Halfon[1], Csaba Zoltan Kibedi Szabo[1], Martin Fuller[1], Tom O'sullivan[1], Charlie Lovatt[1]

[1]University of Leeds

Cryo-electron microscopy (cryo-EM) has transformed structural biology by enabling the visualisation of biological macromolecules at near-atomic resolution, providing unprecedented insights into disease mechanisms and supporting the development of novel therapeutics. As an Instruct-ERIC Centre, the Electron Microscopy Facility at the University of Leeds provides researchers with access to state-of-the-art cryo-EM instrumentation, specialist expertise, and training, enabling projects that address important challenges in paediatric and rare disease research.

This presentation will showcase how cryo-EM has been applied to study proteins implicated in inherited and childhood diseases. Case studies will include the first cryo-EM structure of glycogen synthase in complex with a therapeutic candidate currently in clinical trials for Pompe disease, revealing a previously uncharacterised drug-binding site with implications for the treatment of glycogen storage disorders. We will also present cryo-EM studies of cardiac myosin that enable the structural mapping of mutations associated with inherited early-onset cardiomyopathies, providing new insights into disease mechanisms and supporting future therapeutic development.

Together, these examples demonstrate how access to advanced cryo-EM infrastructure through Instruct-ERIC enables researchers to answer clinically relevant biological questions and accelerates the translation of structural discoveries into potential treatments for paediatric and rare diseases.

Keywords: Cryo-electron microscopy (cryo-EM), Structural biology, Paediatric diseases, Rare diseases, Instruct-ERIC

Speaker: Antonio Lopalco

Advances in Paediatric Medicine Development through Direct Powder Extrusion 3D Printing

Nunzio Denora[1], Antonio Lopalco[1], Angela Assunta Lopedota[1], Giuseppe Francesco Racaniello[1]

[1]University of Bari;

The development of age-appropriate paediatric medicines remains a major challenge due to the need for flexible dosing, acceptable dosage forms, and rapid adaptation to individual patient requirements. Among emerging additive manufacturing technologies, Direct Powder Extrusion (DPE) three-dimensional (3D) printing has gained considerable attention as a versatile platform for the production of personalised pharmaceutical dosage forms. Unlike conventional fused deposition modelling (FDM), DPE eliminates the need for intermediate filament fabrication and enables the direct conversion of powder blends into printed medicines in a single manufacturing step. This approach broadens formulation design, reduces processing time and material waste, and can minimise thermal stress on active pharmaceutical ingredients.

Recent advances in DPE have demonstrated its ability to address key unmet needs in paediatric drug development. By enabling precise adjustment of dose, geometry, and drug-release characteristics, DPE facilitates the manufacture of patient-specific medicines tailored to age, body weight, and therapeutic requirements. Formulation strategies involving suitable polymers, plasticisers, and excipients have been developed to ensure powder flowability, printability, mechanical integrity, and reproducible performance. In addition, DPE has shown particular value for poorly soluble drugs through the generation of amorphous solid dispersions and enhanced drug dissolution profiles.

Applications reported for Biopharmaceutics Classification System (BCS) Class II and IV compounds, including niclosamide, budesonide, clobetasol propionate, lidocaine, carvedilol, and furosemide, highlight the broad potential of this technology. DPE has been successfully used to produce personalised tablets, mucoadhesive systems, and orodispersible films with tunable drug loading and release kinetics. Such dosage forms can improve treatment adherence in children by offering easier administration, improved palatability, and dose flexibility that are difficult to achieve with conventional manufacturing methods.

Overall, DPE 3D printing represents a scalable, solvent-free and highly adaptable manufacturing platform capable of accelerating pharmaceutical development while enabling true medicine personalisation. Continued advances in formulation science, process optimisation, and regulatory frameworks are expected to further support the translation of DPE-based technologies into clinical and hospital settings, where they have the potential to transform the preparation of paediatric medicines and improve therapeutic outcomes.

Keywords: Paediatric, Medicines, 3D printing, personalisation, direct powder extrusion

POSTER SECTION

The distorted, noncoding logic of a paediatric brain cancer

Pietro Laneve[1], Alessandro Belvedere[2], Paolo Tollis[3], Monica Ballarino[2], Alessia Grandioso[1]

[1]Institute of Molecular Biology and Pathology, National Research Council of Italy (CNR-IBPM); [2] Department of Biology and Biotechnologies, Sapienza University of Rome; [3]Center for Life Nano- & Neuro-Science, Istituto Italiano di Tecnologia, Rome;

Background and objectives. Group 3 is among the most aggressive molecular subgroups of medulloblastoma (MB), the most common malignant brain tumour of childhood, and is frequently associated with metastatic dissemination, poor clinical outcome, and activation of MYC-dependent oncogenic programmes. Although MYC is a central driver of tumours' aggressiveness, its broad and pleiotropic roles in proliferation, differentiation, cell-state maintenance, and metabolism, together with its intrinsically disordered and largely undruggable structure, make direct therapeutic targeting particularly challenging. This promptes the search for more disease-restricted vulnerabilities within regulatory layers associated with, and functionally required by, MYC-driven tumour states. In this context, long noncoding RNAs (lncRNAs) represent attractive candidates, as they can display tissue- and disease-specific expression and may contribute to the organisation of subgroup-specific regulatory programmes. Despite extensive -omic characterisation of Group 3 MB, the functional contribution of lncRNAs to its phenotype remains insufficiently explored (Laneve et al., 2020).

Methodology and results. Building on our previous identification of MYC-regulated lncRNAs in Group 3 MB cells (Rea et al., 2021), we prioritised lncMB1 and lncMB3 as candidates for functional, mechanistic, and translational investigation.

LncMB3 emerged as a pro-survival factor, as its depletion induces apoptosis in Group 3 MB cells. Mechanistically, lncMB3 modulates the TGF-β pathway through RNA-RNA interactions involving HMGN5, thereby reshaping a photoreceptor-like transcriptional programme linked to apoptotic control. This mode of action has recently been defined, together with translational efforts aimed at combining lncRNA targeting with chemotherapy and nanocage-based RNA drug delivery (Grandioso et al., 2025). In parallel, steric-blocking antisense oligonucleotides are being developed to disrupt pathological lncRNA-dependent complexes in Group 3 MB cells.

LncMB1 is transcribed antisense to RHOT1, a key regulator of mitochondrial (MT) trafficking. Its depletion reduces RHOT1 mRNA and protein abundance, downregulates gene sets associated with MT metabolism, and causes fragmentation and redistribution of the MT network. Ongoing RNA pulldown/RNA-seq, mass spectrometry, and untargeted

metabolomics analyses aim to define the molecular basis through which lncMB1 preserves MT homeostasis.

Conclusions. Our findings identify lncMB3 and lncMB1 as disease-relevant lncRNAs controlling complementary hallmarks of Group 3 MB aggressiveness: apoptotic resistance and MT dynamics. These results support the concept that the noncoding transcriptome contributes functionally to paediatric tumour biology and may expose RNA-based therapeutic vulnerabilities in the most aggressive MB subgroups.

References:

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Keywords: Brain cancer, long noncoding RNAs, RNA therapy

Cytoskeletal defects disrupt nuclear architecture, heterochromatin organization and genome stability in Drosophila models of microcephaly

Maria Patrizia Somma[1], Laura Ciapponi[2], Claudia Pellacani[1], Marta Marzullo[2]

[1]IBPM-CNR; [2]Università Sapienza, Roma

Autosomal recessive primary microcephaly (MCPH) is a neurodevelopmental disorder frequently associated with mutations in centrosomal and microtubule-related genes, including ASPM and CENPJ. The Drosophila orthologs, asp and Sas4, are known regulators of centrosome biogenesis and spindle organization; however, their contribution to interphase nuclear organization remains poorly understood. Here, we investigated how loss of Asp or Sas4 affects cytoskeletal organization, nuclear architecture, chromatin state, and genome stability in developing Drosophila larval brains.

We found that asp and Sas4 mutant neuroblasts display microtubule disorganization in interphase. These defects are accompanied by abnormal distribution of the LINC complex component Klarsicht, reduced Lamin levels, and nuclear envelope invaginations. Mutant cells also exhibit altered heterochromatin organization, including reduced centromere clustering and significant decreases in H3K9me2, H3K9me3, H3K27me3, and HP1α levels, together with increased H3K4me3. Pharmacological inhibition of demethylases restores H3K9me3 and nuclear morphology defects, supporting a functional link between chromatin state and nuclear architecture.

Importantly, asp and Sas4 mutant brains accumulated endogenous DNA damage and showed hypersensitivity to X-ray-induced double-strand breaks, with delayed γH2Av resolution and increased chromosomal aberrations. Comparable phenotypes were also detected in spd2 mutants, suggesting that centrosome and microtubule dysfunction broadly impact chromatin organization and genome integrity.

Overall, our findings reveal an unexpected role for centrosome-associated proteins in maintaining the functional coupling between the cytoskeleton, nuclear envelope, and heterochromatin. We propose that disruption of this axis contributes to epigenetic instability and defective genome maintenance during neurodevelopment, providing new insight into the cellular mechanisms underlying MCPH pathogenesis.

Keywords: MCPH, Epigenetics, Microtubule, Cytoskeleton, Nuclear lamina, model organism

From Patient Voices to Clinical Study Design: TEDDY KIDS Network and the Patients Advisory Board (PAB) in Gabapentin in Paediatric Pain - GAPP study

Donato Bonifazi[1], Emanuela Crea[1], Claudia Pansieri[1], Francesco Lapenna[1], Eleonora Di Campi[1], Ana Muke[1]

[1]TEDDY Network

In recent years, clinical research has evolved towards models that are increasingly focused on the patient. In this context, TEDDY Network[1] plays a crucial strategic role in the advancement of paediatric research, promoting the active involvement of young people through initiatives coordinated by the Working Group on Engagement and Advocacy[2] and the TEDDY KIDS Network[3].

The aim is to demonstrate the value of the structured engagement model for children, young people and adolescents, developed within the TEDDY Network and codified in the TEDDY Charter[4], in supporting the integration of patient-centred research principles into clinical and scientific processes, as illustrated by the case study from the GAPP study.

In the GAPP study, TEDDY engages patients via a Patient Advisory Board (PAB), including young patients from the TEDDY KIDS Network. The Working Group on Engagement and Advocacy supports the implementation of activities, ensuring an inclusive and methodologically structured approach. The GAPP study case demonstrates how the integration of PAB, the TEDDY KIDS Network and the TEDDY Working Group provide a framework for implementing a patient-centred approach.

The PAB is involved in all stages of the study, performing a key advisory role and contributing to decision-making processes, ensuring that methodological and organisational decisions are in line with patients' needs, through continue dialogue with all stakeholders. Young patients participate in the review and co-design of the study and its documents.

TEDDY's model highlights how structured patient involvement addresses some of the key challenges in paediatric research, such as limited recruitment and the off-label use of medicines.

1. https://www.teddynetwork.net/
2. https://www.teddynetwork.net/areas-of-interest/#ChildrenEngagement
3. https://www.teddynetwork.net/network/teddy-kids-network/
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Keywords: Patient-centred research; Paediatric clinical research; Patient Advisory Board (PAB); TEDDY KIDS Network; Gabapentin in Paediatric Pain (GAPP)

Use of synthetic control arms in clinical trials as a promising approach for generating evidence

Donato Bonifazi[1,2], Giorgio Reggiardo[1], Viviana Giannuzzi[3,1], Claudia Pansieri[1], Mariagrazia Felisi[2,1], Adriana Ceci[3]

[1]TEDDY Network; [2]Consorzio per le Valutazioni Biologiche e Farmacologiche (CVBF); [3]Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus (FGB)

Context: Synthetic Control Arms (SCAs) represent an innovative approach for accelerating drug development, particularly for paediatric and rare diseases. By replacing traditional control groups with realworld or historical data, SCAs streamline trial logistics and address key ethical barriers reducing recruitment time, cost, and allowing patients quicker access to potentially life-saving treatments. Regulatory recognition of SCAs, began roughly 25 years ago but has accelerated significantly in 2020. The European Medicines Agency is actively working on a reflection paper for SCAs, with a draft planned in late 2026 (EMA/CHMP/225255/2025). The objective of this analysis was to quantify the use of SCAs in clinical trials and evaluate the methods used to create them.

Methods: We searched the EU Clinical Trials Register (EUDRACT) to identify single-arm trials referring to a synthetic control arm analysis. EUDRACT is the database for all interventional clinical trials on medicinal products conducted in the European Union between 1 May 2004 and 30 January 2025. The search strategy included standardized keywords: “single-arm” AND “completed” AND “trials with results”. Data on the study design, intervention, and number of patients included in the SCA were extracted from the published summary results. The source of real-world data, methodological aspects in the construction of the SCA, and clinical outcomes were analysed. The presence of sensitivity analyses was also evaluated. If an advanced statistical modelling was used to generate the SCA, the external data sources (historical or real-world data) was evaluated. The search was conducted on 31 December 2025.

Results: The EU Clinical Trials Register currently displays 44.366 clinical trials, of which 21.237 were completed and the trial results were available. Studies with a single-arm design are 654, of which 14 incorporate a SCA using real-world and/or historical data to create the virtual cohort. None recruited children. The most common method used in 11 studies to generate a SCA was the propensity score matching. These scores were generated using multivariable logistic models that took into account baseline patient demographic and clinical characteristics. After obtaining propensity scores, specific weighting methods were applied to create a virtual balanced dataset, effectively making the investigational arm and the SCA more comparable by adjusting for differences in patient characteristics (covariates) that influence treatment assignment, thus reducing bias in treatment effect estimation. The designs were supported by a rigorous methodology (such as target trial emulation, pre-specification, robust statistical methods) to manage bias and confounding factors, ensuring credible evidence.

Discussion: SCAs have been introduced as a pragmatic approach which can improve the interpretation of single-arm trial results and reduce the bias due to the lack of randomization. A criticism of SCAs is called unknown confounding, this means some difference in baseline characteristics between the investigational arm and the SCA. To

minimize this confounding, EMA emphasizes a robust statistical matching approach. The external data must be of high quality, and the "synthetic" cohort of patients must be closely matched to the treatment group using advanced statistical methods like propensity score matching or Bayesian models. Our analysis shows that SCAs can offer a promising alternative in certain clinical trial scenarios, providing a balance between ethical considerations, efficiency, and scientific rigor. SCAs could allow reducing the number of children to enrol in clinical trials by replacing or supplementing traditional control groups with a virtual cohort of patients but currently this approach is underused.

Keywords: Synthetic Control Arms, Real-World Data, Single-Arm Clinical Trials, Propensity Score Matching, Paediatric Drug Development