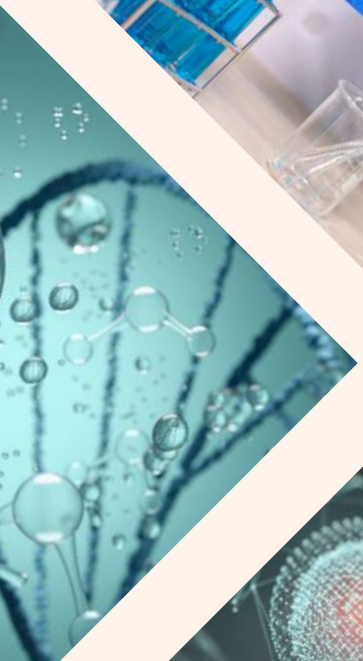
EPTRI
European Paediatric Translational Research Infrastructure

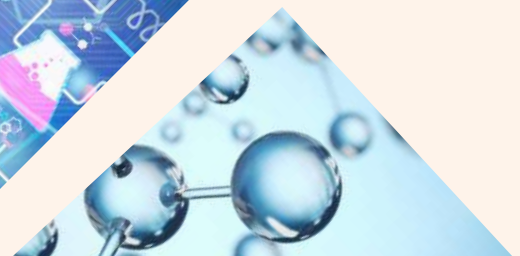
# EPTRI SCIENTIFIC MEETING

## BOOK OF ABSTRACTS

## BOLOGNA, ITALY

## 13-15 MARCH, 2025





# *“Digital Health Technologies in Paediatric Research in the Framework of Strategic Collaboration ELIXIR–EPTRI”*

## SPEAKER SECTION

### SPEAKER: CLAUDIO CARTA

### Health Data Management and FAIRification in ELIXIR: the experience of the Italian Rare Diseases Community

Claudio Carta[1,2]

1 - Istituto Superiore di Sanità, Rome, Italy; 2 - ELIXIR-Italy Local Technical Coordinator and co-lead community Rare Diseases

In the European Union, a disease is classified as rare if it affects fewer than 5 in 10.000 people, but there are more than 7.000 Rare Diseases (RDs). As a result, it is estimated that 6-8% of the world's population is affected by a RD. Due to this scenario, the diagnosis and treatment of RDs are challenging and costly and the patients' journey to reach a diagnosis is an “odyssey”.

Data on RDs, among other things, are sensitive, scarce, highly distributed across institutes and countries, gathered in different formats and, in general, with low interoperability.

We should therefore need an infrastructure to efficiently analyse data across resources and countries for more than 7.000 diseases.

There is an absolute need to combine data.

Considering also that the Vision of the International Rare DIseases Research Consortium (IRDiRC) is to “Enable all people living with a RD to receive an accurate diagnosis, care, and available therapy within one year of coming to medical attention.”

In 2016, the "FAIR guiding principles for humans and machines", were published.

The FAIR guiding principles are an IRDiRC-recognised resource and FAIR data allows us to link data from several resources in compliance with the access restrictions of the data itself.

One of the EU strategic objectives for RDs is to “enhance making rare diseases registries and data FAIR”.

As reported in the ELIXIR EU Scientific programme and priorities 2024-2028, ELIXIR EU as well as ELIXIR IT and the European and Italian RD Community of ELIXIR support Health Data Management and FAIRification of data.

Looking at the Italian RD Community, it supports FAIR priniciples and thier implementations organizing for example Bring Your Own Data hackathon and Workshops on specific topics related to Health data and FAIRification.

For example, the Rome BYOD at ISS has evolved over the years thanks to the fruitful collaboration between international experts, among whom there were, as speakers/trainers, the authors of the paper on FAIR Data guiding principles.

The Rome BYODs have been supported over the years by ELIXIR nodes, European projects and institutions and have contributed significantly to defining general steps to make a data resource FAIR.

Activities in Health Data Management and data FAIRification in the RD field were also supported by internal projects of ELIXIR: ELIXIR Commissioned Service.

In these projects funded through ELIXIR's own budget, partners of the Italian Node of ELIXIR have led or Co-Led WPs. The results of these activities and projects were presented at international conferences.

Acknowledgements

E. Capriotti, M. Roos, S. Beltran, G. Kerry, R. Cornet, M. D. Wilkinson, A. Rath, K.F. Heil, M. Hanauer, R. Casadio, P.L. Martelli, F. De Leo, A. Cestaro, A. Via, L. Licata, R. Percudani, G. Pesole, ELIXIR EU/IT Rare Diseases Community, Patient Organizations, EURORDIS, IT Trainers, FAIR Data Stewards, ELIXIR EU/IT Training Platform, RD Connect, EJP RD

## SPEAKER: MARCO VICECONTI

## Digital twins in paediatric healthcare: some examples

Marco Viceconti[1]

1 – Università di Bologna

A Digital Twin in Healthcare (DTH) is a computer model that, when fed with a specific set of information relative to a particular patient, can predict a quantity of interest that is difficult or impossible to measure but necessary to inform a clinical decision on that patient. We present two clinical applications of digital twin technologies in paediatric musculoskeletal pathologies. The first makes it possible to minimise the risk of bone fracture during rehabilitation after massive skeletal reconstruction in children due to osteosarcomas. The second uses post-mortem CT scans to create a reference database to identify abuse bone fractures in infants.

Bone tumours are prevalent in children and adolescents. They all require the surgical resection of the tumour and a large segment of a skeleton with it; being growing subjects, the skeletal gap cannot be bridged with a prosthetic device. Surgeons at the Rizzoli Orthopaedic Institute developed a biological reconstruction technique where the massive defect is bridged with a massive bone bank graft within which an autologous vascularised transplant of the proximal fibula is inserted. Plates and screws are used to ensure primary stability. The bone graft is rapidly osseo-integrated with bone stumps; the vascularised fibula eventually re-populate the dead bone with living cells, causing a complete osteointegration of the graft. After long post-operative chemotherapy, these children need to undergo aggressive physical rehabilitation; however, it is important not to overload the reconstructed bone to avoid fractures. We developed a digital twin informed by a lower body CT scan and a short gait analysis that predicts the forces transmitted to the reconstructed bone during the rehabilitation exercises. We then used the CT scan to develop a patient-specific digital twin of the reconstructed bone segment and of the contralateral health one to predict if those loads would have been sufficient to cause bone fracture (Taddei, 2003).

In a second instance, we report how a collection of post-mortem whole-body CT scans of infants was used in combination with our bone biomechanics digital twin to create a normative table for the

loading in bending and torsion required to fracture an infant long bone as a function of age or body weight (Altai, 2018). This normative information is used to decide if an infant bone fracture is consistent with the incident narrative provided by the carers or if it might be caused by abuse. In particular, with these normative data, we were able to show that self-inflicted arm fractures during rolling movements in infants were physically impossible (Altai, 2020).

Digital Twins in healthcare are a powerful medical technology in some clinical contexts. Musculoskeletal and cardiovascular diseases are an ideal target because much of pathophysiology can be explained with the laws of physics. DTHs are particularly relevant in paediatric medicine due to the extreme intersubject variability and the limitations on the type of examinations that can be ethically performed.

Altai Z, Viceconti M, Offiah AC, Li X. Investigating the mechanical response of paediatric bone under bending and torsion using finite element analysis. Biomech Model Mechanobiol. 2018 Aug;17(4):1001-1009. doi: 10.1007/s10237-018-1008-9.

Taddei F, Viceconti M, Manfrini M, Toni A. Mechanical strength of a femoral reconstruction in paediatric oncology: a finite element study. Proc Inst Mech Eng H. 2003;217(2):111-9. doi: 10.1243/09544110360579321.

Altai Z, Viceconti M, Li X, Offiah AC. Investigating rolling as mechanism for humeral fractures in non-ambulant infants: a preliminary finite element study. Clin Radiol. 2020 Jan;75(1):78.e9-78.e16. doi: 10.1016/j.crad.2019.08.026.

## SPEAKER: RITA STAGNI

## A technology-based solution for monitoring the neuro-motor developmental trajectory in high-risk infants and children from birth to adulthood.

Rita Stagni[1], Maria Cristina Bisi[1], Arianna Aceti[2], Duccio Maria Cordelli[2]

1 – DEI, University of Bologna; 2 – DIMEC, University of Bologna

Neurodevelopmental disorders (NDDs) encompass a group of heterogeneous clinical conditions with onset in early life, associated with abnormalities of development. In western countries, more than 1 in 10 children are thought to be affected by NDDs of different severity (Halfon et al. 2012). NDDs have multifactorial etiology, involving both genetic and environmental factors (De Felice et al, 2015), and affecting multiple domains of development (Cioni et al, 2016).

Despite the advances in understanding the etiology, pathogenetic pathways, and biological underpinnings of NDDs, diagnosis often occurs many months after the first clinical signs are observed, thus delaying prompt intervention (Novak et al, 2017). Early detection of NDDs is one of the major challenges, with the highest odds of producing ground-breaking changes in child healthcare (Novak et al, 2017), since the response to intervention is more significant the earlier the therapy is initiated (Johnston et al, 2009; Heckman, 2008).

In the first months of life, a careful neurodevelopmental assessment combined with specific technical tools such as neuroimaging, neurophysiological tests, and genetic tests, provide important information to support the early detection of atypical development. Unfortunately, this level of clinical accuracy is only possible in a minority of the cases, namely in the presence of significant risk factors that identify infants at very high risk of NDDs (e.g. preterm birth, birth asphyxia, syndromes, neonatal seizures). Clinical screening tools generally show very low predictive value and reliability, particularly in the phase of emergence and establishment of the first clinical signs (Lee et al, 2015). Advances in technology have been shown to significantly improve medical care of patients, however,

there is a lack of integration of available technology into the assessment of infant development from birth to adult age.

Based on these premises, we have developed an unobtrusive technological approach for the quantitative assessment and longitudinal monitoring of biomarkers of neuro-motor-development in children from birth to adulthood. The proposed approach is designed to support and integrate the traditional assessment of milestones of motor development (i.e. general movements, sitting, horizontal displacement, standing, walking, handling), as well as to provide a deeper insight in the underlying control.

The acquisition protocol was designed to be easy to implement, child friendly, and require little time, to guarantee applicability and acceptance, while guaranteeing the reliability of the extracted biomarkers. In particular, videos from a commercial camera for general movements and motion data from wearable inertial sensors for other tasks are recorded by clinicians or carers during routine ambulatory assessment at programmed time-points. Quantitative metrics are extracted from video and kinematic signal processing as biomarkers of biomechanical performance, variability, fluidity, and coordination of motion, as well as complexity and automaticity of motor control (Bisi et al, 2019; Bisi et al, 2020), providing a characterization of the neuro-motor development that integrates clinical assessment.

The longitudinal implementation of the full approach allows to track the developmental trajectory from birth to adult age, but modular implementation of the full protocol is possible to target a specific population and/or research question.

The proposed assessment in currently applied to children:

- born preterm from birth to 36 months (video- and sensor-based assessment);

- affected by severe neurologic/rare disorders from 5 to 18 years (only normal gait in Mowat-Wilson, Dravet, and Chiari syndrome);

- affected by minor musculoskeletal deformities from 5 to 16 from 5 to 18 years (normal and tandem gait in scoliosis, flat foot, club foot);

- during pre-school and school age from 4 to 18 years (posture, normal and tandem gait, object handling).

## SPEAKER: LUCA SANGIORGI

## Wearable Sensors for Monitoring Osteogenesis Imperfecta in Children: A Pilot Study.

Marina Mordenti[1], Alice Moroni[1], Manila Boarini[1], Giulia Rogati[1], Roberto Ramaglia Amadasi[1], Francesca Gurioli[1], Marta Calzolari[1], Alberto Leardini[1], Luca Sangiorgi[1]

1 – IRCCS Istituto Ortopedico Rizzoli

Osteogenesis imperfecta (OI) is a rare bone disorder causing fractures, deformities and short stature due to bone fragility. OI typically progresses during childhood, with partial stabilization in adulthood, and has significant clinical and genetic variability.

Long-term OI management requires a multidisciplinary approach, including rehabilitation. Technological advancements are improving patient care, with Inertial Measurement Units (IMUs) becoming increasingly used as wearable sensors. Despite some limitations, IMUs offer a cost-

effective alternative to lab-based gait analysis and support rehabilitation and daily exercise, providing step-by-step, game-based guidance.

The present pilot study on OI children aims to investigate the impact of IMU technology on remote monitoring.

The study, supported by the project 4FRAILTY, funded by Italian Ministry of Education, University and Research - PON R&I grant ARS01_00345, CUP B76G18000220005 - was conducted at IRCCS Istituto Ortopedico Rizzoli, an OI reference center, and aimed to enroll OI "walking" children to undergo a kinematic analysis via an IMU-based motion tracking system.

Patients were equipped with 5 IMUs (Euleria srl, Rovereto, Italy) secured to specific anatomical segments using adjustable bands. They performed motor tasks representative of daily living activities (e.g. walking) and selective joint exercises (e.g. knee flexion/extension). The study also aimed to assess patients' health-related quality of life via EuroQoL-5-Dimensions Young version (EQ-5D-Y) and balance confidence in performing activities via the Activities-specific Balance Confidence Scale (ABC Scale). A patient satisfaction questionnaire was used to evaluate the IMU approach.

The study enrolled 10 children with OI type I according to Sillence classification (7M, 3F, mean age 11.8 years). Two of them performed a subset of motor tasks due to non-OI-related issues.

In a preliminary analysis on 4 patients, the seated knee extension exercise resulted in an average range of motion of 94.9 ± 10.8 deg, while the standing hip extension and abduction exercises yielded 29.8 ± 13.5 and 23.8 ± 7.5 deg, respectively.

The EQ-5D-Y showed that no participants reported problems with mobility, self-care, or usual activities. However, difficulties were reported in the pain/discomfort (40%) and anxiety/depression (80%) dimensions. The mean EQ VAS score was 87/100 (IQR 65–100), indicating a generally high self-rated health status, and confidence in performing daily activities without experiencing unsteadiness using the ABC scale was 83/100 (IQR 74–90), indicating a high level of self-perceived balance and stability.

All participants reported good/high feasibility of the motor tasks and exercises in the satisfaction questionnaire. In addition, 80% said they would be willing to use the IMUs if they were available in local clinics and for domestic use.

This pilot study shows that IMU's game-based approach is an innovative tool to promote exercise in rare children. While OI children reported good overall health and functional independence, many experienced pain/discomfort and emotional distress. The high ABC scale scores indicate confidence in balance and stability during daily activities, despite physical and psychological challenges. These findings highlight the need for targeted interventions to address pain and mental well-being in this population.

IMUs are an easy-to-use, accessible alternative to gait analysis in fully equipped laboratories, encouraging local healthcare providers to adopt these systems for easier, more widespread monitoring. Only patients needing in-depth assessment will be referred to hub hospitals, optimizing resource allocation and care. Furthermore, remote digital communication lets clinicians advise and assess patient from a distance, reducing the need for patient journeys to centers of expertise, which can be complex and expensive.

## SPEAKER: CHEMS HACHANI

### Optimizing Pediatric Clinical Trials: Leveraging Milo AI for Efficient Recruitment and Data Management in Assessing Hypertonic Inhalation.

Chems HACHANI[1]

1 – Eclevar Medtech

Pediatric clinical trials require efficient recruitment and data management. This 4-week, prospective, open-label, randomized, multicentric, parallel-arm study evaluates the performance and safety of HYPERTONIC INHALATION (3%, 6%, 7% sodium chloride) in infants, children, and adults with cystic fibrosis (CF) or non-CF bronchiectasis (NCFB). Conducted by [Confidential Manufacturer] with Eclevar MedTech at UK sites, the trial utilizes the Milo AI platform to enhance participant selection and data handling. Milo captures clinical audio from patient visits, interprets it, and integrates summaries into its electronic data capture (EDC) system. This EHR-to-EDC process auto-populates case report forms, with human oversight ensuring precision. In a 360-patient cohort, Milo boosted recruitment efficiency and data integrity. This approach underscores AI's ability to optimize clinical trials, providing robust evidence of device performance and safety per EU MDR 2017/745 standards

# POSTER SECTION

### The Impact of Digital Technology on Cognitive and Emotional Development in Children: A Narrative Review.

Sergii Tukaiev[1], João Miguel Alves Ferreira[2]

1 – Institute of High Technologies, Taras Shevchenko National University of Kyiv; 2 – Faculty of Medicina, University of Coimbra, Coimbra, Portugal.

Background: The increasing integration of digital technology into children's daily lives has sparked discussions on its potential cognitive and emotional consequences.

Aim: This narrative review explores the impact of digital device usage on attention regulation, executive functions, and emotional wellbeing in paediatric populations.

Results: While some studies highlight cognitive benefits, such as improved problem-solving and digital literacy, others point to risks, including attention deficits and increased emotional dysregulation. Factors such as screen time duration, content quality, and parental mediation play crucial roles in shaping these effects. The review also examines the moderating influence of socioeconomic status and family environment on children's digital engagement and developmental outcomes. Findings suggest that a balanced approach—promoting digital literacy while setting healthy boundaries—is essential to harness the benefits of technology while mitigating its risks.

Conclusion: Understanding these dynamics can inform paediatric psychological interventions, educational policies, and parental guidance strategies, fostering healthier cognitive and emotional development in the digital age.

## Bridging the Gap: A Digital Platform for Early Pediatric Mental Health Care.

Hila Segal[1,2], Arriel Benis[3], Shirley Saar[1,4], Iris Shachar-Lavie[1,5], Silvana Fennig[1,4]

1 – Schneider Children's Medical Center; 2 – Shalvata Mental Health Center; 3 – Holon Institute of Technology; 4 – Tel Aviv University; 5 – Israel Ruppin Academic Center

Background: The prevalence of mental health disorders among children and adolescents presents a significant public health challenge. Children exposed to mass disasters, such as armed conflicts or natural disasters, are at a particularly high risk of developing mental health problems, necessitating prompt and robust intervention. The acute need for early intervention in these situations is well recognized, as timely support can mitigate long-term negative outcomes. Pediatricians are particularly suited to delivering such interventions due to their role as primary health care providers and their frequent contact with children and families. However, barriers such as limited training and resources often hinder their ability to effectively address these issues.

Objective: This study aimed to describe the rapid development of a digital mental health tool for community pediatricians, created in response to the urgent need for accessible resources following the October 7th terror attack in Israel. The goal was to create a comprehensive resource that addresses a wide range of emotional and behavioral challenges in children and adolescents, with a particular focus on those affected by armed conflict and significant trauma exposure. In addition, the study aimed to evaluate the platform's usability and relevance through feedback from primary users, thereby assessing its potential for implementation in routine pediatric practice.

Methods: Developed through collaboration between pediatricians and mental health professionals at Schneider Children's Medical Center in Israel, the platform consists of 15 structured modules covering key pediatric mental health concerns such as sleep disturbances, anxiety, school refusal, eating behavior changes, and emotional dysregulation. Each module includes clinical guidance, initial intervention strategies, parental psychoeducation, and referral recommendations. The usability and relevance of the platform were evaluated through structured feedback from a focus group of seven primary care pediatricians.

Results: Early evaluations demonstrated high satisfaction among pediatricians in terms of usability (mean 4.57/5), content relevance (4.71/5), and layout suitability (4.66/5). Participants emphasized the importance of concise, actionable content tailored to time-constrained clinical environments. The findings highlight the platform's potential to enhance early mental health intervention, addressing a critical gap in pediatric primary care.

Future Directions: Recognizing the broader need for integrating mental health into routine pediatric care, we are currently in the process of enhancing accessibility and user engagement. Future iterations will focus on interactive features, real-time clinical consultations and updates, and multilingual support, ensuring widespread applicability throughout Israel. Additionally, further research will assess the impact of the platform on pediatric practice and clinical outcomes.

Conclusion: This initiative demonstrates the feasibility of a responsive and targeted digital mental health platform during periods of heightened need, emphasizing the essential role of pediatricians in delivering timely and proactive care, both in routine situations and during crises.

## Diagnosis of Iron Deficiency Anemia in Children Using Conjunctival Photography: A Color Intensity Analysis Approach.

Ozan Emre EYUPOGLU[1]

1 – Istanbul Medipol University

Objective: This study aims to diagnose iron deficiency anemia in prepubescent children by using photographs of their conjunctiva. This method targets diagnosing iron deficiency anemia without the need for blood samples or kits. Early diagnosis aims to prevent problems related to iron deficiency in children and support healthy growth and development processes.

Method: The study included 100 girls and 100 boys aged 3-10 years. High-resolution photographs of the conjunctiva were taken using a smartphone or digital camera. These photographs were transferred to the Image J program, and the intensities of the red (R), green (G), and blue (B) color components were analyzed. The obtained color intensity data were compared with ferritin values to create calibration graphs. From the created calibration graphs, when the mean value of the color intensity of the conjunctival photograph of any child whose anemia status is unknown was placed, the ferritin value and thus the anemia status were determined. Statistical significance between control and healthy groups was given using the Student's t-test. Children with multiple medication use and those with diseases other than iron deficiency anemia were not included in the study.

Results: This method provides a sustainable and inexpensive approach to diagnosing iron deficiency anemia. The color intensity analysis of conjunctival photographs yielded results consistent with hemogram data. The study was successful in diagnosing iron deficiency anemia with an accuracy rate of 82.37%. Thus, early diagnosis of iron deficiency anemia was made possible, and the healthy growth and development processes of children were supported.

## Feasibility and Preliminary Efficacy of Sailing-Based Rehabilitation for Adolescents with Rare Skeletal Disorders: A Single-Center Pilot Study.

Manila Boarini[1], Federico Banchelli[1], Davide Scognamiglio[1], Silvia Fittipaldi[1], Giuseppina M. Farella[1], Daniela Platano[1,2], Giulia Rogati[1], Enrica Di Sipio[3], Giacomo Villa[3], Lisa Berti[1,2], Alberto Leardini[1], Silvana Sartini[1], Annalisa Scopinaro[4], Luca Sangiorgi[1]

1 – IRCCS Istituto Ortopedico Rizzoli; 2 – Università di Bologna; 3 – Euleria srl Società Benefit; 4 – UNIAMO Federazione Italiana Malattie Rare

Background: Rare Skeletal Disorders (RSDs) are characterized by skeletal deformities, chronic pain, and disability, significantly impacting physical and psychological well-being. Individuals with RSDs often experience social isolation, reduced independence, and barriers to accessing coordinated healthcare. Conventional rehabilitation primarily targets motor function in controlled settings but may not fully address psychosocial well-being. Adventure-based interventions incorporating physical activity and group engagement may offer additional benefits. Sailing-based rehabilitation integrates motor training with dynamic environmental adaptation, teamwork, and psychological stimulation. This study assessed the feasibility, safety, and preliminary efficacy of a sailing-based rehabilitation intervention in adolescents with RSDs, integrating objective motion analysis and patient-reported outcomes.

Methods: This single-center, non-randomized, single-arm feasibility study included eight participants aged 12–18 years with RSDs who completed the intervention on two adapted sloops under certified instructors' supervision. Feasibility was assessed through recruitment, retention,

adherence, and satisfaction. Safety was evaluated by recording adverse events. Secondary outcomes included health-related quality of life (HRQoL), psychological well-being (assessed via EQ-5D-5L, PODCI, RSES, YP-CORE, and TSK), and physical function measured using inertial measurement unit (IMU)-based motion analysis. Data were analyzed descriptively, and changes over time were evaluated using the Wilcoxon signed-rank test.

Findings: The intervention demonstrated 100% retention, compliance, and adherence, with only mild adverse effects reported. Post-intervention assessments revealed improvements in HRQoL (VAS, p=0.10), happiness (p=0.06), proprioception (p=0.01), postural stability (p=0.01), gait quality (p=0.04), and upper limb function (p=0.02), though some benefits diminished at three-month follow-up. The structured and immersive nature of sailing, requiring real-time adaptation to wave-induced motion and team-based coordination, contributed to these positive outcomes. The integration of IMU-based motion analysis provided objective quantification of physical improvements, while validated patient-reported outcomes captured psychosocial changes. IMUs enabled precise, remote monitoring of participants' motion performance by tracking kinematic parameters such as joint angles, balance, and movement symmetry in real time. This approach allowed for a comprehensive assessment of physical function outside conventional clinical settings, offering insights into neuromuscular adaptation and motor learning.

Conclusion: This study is the first to systematically explore the feasibility and safety of a sailing-based rehabilitation intervention for adolescents with RSDs. Findings suggest that this intervention is feasible, safe, and potentially effective in promoting both physical and psychological benefits. The structured yet adaptable format of sailing may offer a replicable model for integration into diverse therapeutic settings. By demonstrating that a structured sailing intervention can enhance quality of life, motor function, and psychological well-being in adolescents with RSDs, this study supports the inclusion of holistic, experiential therapies in rehabilitation practice. The use of IMU-based motion analysis underscores the feasibility of remote monitoring, allowing clinicians to track physical improvements objectively and tailor interventions accordingly. Future research should explore scalability, long-term efficacy, and integration into healthcare policies. Further studies, including larger controlled trials with extended follow-up, are needed to confirm these preliminary findings and optimize intervention protocols for broader clinical application.

Funding: Supported by Catalent Inc. via the King Baudouin Foundation United States.

## Artificial Intelligence in Pediatric Health: Linking Toxicology and Disease Research via Web Platforms.

Nicola Gambarcota[1], Fulvio Ciriaco[2], Nicola Amoroso[3], Daniela Trisiciuzzi[3], Maria Vittoria Togo[3], Fabrizio Mastrolorito[3], Antonella Liantonio[3], Paola Imbrici[3], Giuseppe d'Orsi[4], Massimo Carella[5], Orazio Nicolotti[3], Cosimo D. Altomare[3]

1 – IRCCS "Casa Sollievo della Sofferenza"; 2 – Department of Chemistry, University of Bari "Aldo Moro"; 3 – Department of Pharmacy - Drug Sciences, University of Bari "Aldo Moro"; 4 – Neurology Unit, IRCCS Foundation Casa Sollievo della Sofferenza; 5 – Division of Medical Genetics, IRCCS Foundation-Casa Sollievo della Sofferenza

In the quest for innovative tools to advance drug discovery, repurposing in pediatrics, and toxicological endpoint prediction, we have developed three publicly accessible web platforms: PLATO, TISBE, and CIRCE. PLATO (Polypharmacology pLATform for predictiOn) is a ligand-based predictive platform designed for target identification and bioactivity assessment. It serves a dual purpose: narrowing down potential protein drug targets and computationally estimating biological

affinity values. PLATO is particularly effective in reverse screening for drug repurposing, identifying promising candidates for pediatric disease treatment. TISBE (TIRESIA Improved on Structure-Based Explainability) is a cutting-edge tool for predicting developmental toxicity—an essential factor in ensuring maternal and child health. It is highly effective in assessing chemical safety for pediatric populations while ensuring transparent and interpretable predictions through an explainable machine learning approach. CIRCE (Cannabinoid Iterative Revaluation for Classification and Explainability) is a multi-layer machine learning framework designed to predict selective and unselective CB1/CB2 binders. By computing Shapley values, CIRCE identifies the key molecular features influencing predictions and enhances model interpretability. Given the putative critical role of the cannabinoid system in pediatric conditions such as refractory epilepsy or tuberous sclerosis complex, CIRCE facilitates the design of CB1/CB2 binders and aids in repurposing existing drugs for pediatric treatments. Collectively, these platforms represent a significant step forward in pediatric drug research and repurposing, offering powerful computational tools for discovering and validating therapeutic options while ensuring safety and efficacy through explainable AI methodologies. The platforms are accessible at the following links:

PLATO is free available at https://prometheus.farmacia.uniba.it/plato/
TISBE is free available at https://prometheus.farmacia.uniba.it/tisbe/
CIRCE is free available at https://prometheus.farmacia.uniba.it/circe/