



# Health and education outcomes of children across Europe with congenital anomalies



## European Conference

Poznan, Poland, April 7–8, 2022

Online Conference

<http://eurolinkcat2022.bok-ump.pl>



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## Contents

Welcome Message .....	2
Honorary Patronage .....	3
Conference Committees.....	4
Scientific Program.....	5
Introduction to EUROLinkCAT .....	8
EUROLinkCAT Working Group .....	9
EUROLinkCAT Presentations.....	10
EUROLinkCAT Presentations: Abstracts.....	12
Professional Posters .....	25
Professional Posters: Abstracts.....	29
Students' Posters.....	45
Students' Posters: Abstracts.....	47
General Posters .....	58
General Posters: Abstracts .....	59
Gallery of Wanessa Bąkowska .....	65
Connecting People and Places.....	67
EUROLinkCAT Working Group: Acronym details .....	71

## Welcome Message

Dear Colleagues and Friends,

On behalf of the International Scientific Committee and of the Organising Committee, we are glad to welcome all participants to the [European Conference “Health and education outcomes of children across Europe with congenital anomalies”](#) organised by the [EUROlinkCAT](#) consortium and Poznan University of Medical Sciences.

The conference was originally going to have both in-person and online participants, however, due to the COVID-19 pandemic we have decided to remove the in-person component. Hosting the conference entirely online means everyone interested in attending can engage with the conference in a safe and secure way.

The conference welcomes healthcare professionals, academic researchers, educators, leaders in healthcare and education, students, parents and carers, and any others who work or are interested in the field of congenital anomalies.

The Conference aims to disseminate [EUROlinkCAT](#) results, discuss them in the context of related research and to agree a set of recommendations for the medical care and education of children with congenital anomalies.

Sessions of the workshop will cover health care and education (1), medications for chronic diseases (2), hospitalisations and surgeries (3), survival (4) and evaluating and enhancing the use of hospital discharge data in the surveillance of congenital anomalies. Panel discussions with authorities in the field will be held, each with summing up and recommendations.

In addition to the European [EUROlinkCAT](#) Conference, two satellite conferences (in Polish) will be organised by parent associations. This reflects a key ethos of the [EUROlinkCAT](#) Project which is to support communication and foster positive relationships between healthcare professionals, researchers and parents – to improve the medical care and education of children with congenital anomalies.

Whilst we will not be able to host you in Poznań for the conference due to the COVID-19 pandemic, we highly recommend you visit Poznań on another occasion. Poznań is the capital of Great Poland, the oldest Polish province from which Polish statehood began to form in the 10th century and the first capital of Poland. Today Poznań is a large academic centre with over 135,000 students, famous for its rich trading traditions, fascinating sights, original cuisine and welcoming atmosphere. Poznań is very much worth knowing and visiting!

Best regards,

On behalf of the [EUROlinkCAT](#) Steering Committee



Professor Joan K Morris



Dr Amanda Neville



Professor Anna Latos-Bielenska

## Honorary Patronage

Tomasz Latos  
Chairman of the Polish Parliamentary Health Committee



WOJEWODA  
WIELKOPOLSKI  
MICHAŁ ZIELIŃSKI

Michał Zieliński  
Voivode of Wielkopolska Region



MARSHAL  
OF THE WIELKOPOLSKA REGION

Marek Woźniak  
Marshal of Wielkopolska Province

## Honorary Scientific Patronage



Prof. Andrzej Tykarski  
Rector of the Poznan University of Medical Sciences

## Conference Committees

### **EUROlinkCAT International Scientific Committee**

#### **Members of the Steering Committee:**

Prof Joan Morris, UK – Scientific Coordinator  
Dr Maria Loane, UK – Data Coordinator  
Dr Ester Garne, Denmark – Clinical Coordinator  
Prof Ingeborg Barišić, Zagreb, Croatia  
Dr James Densem, UK  
Prof Anna Latos-Bielenska, Poland  
Dr Amanda Neville, Italy  
Dr Anna Pierini, Italy  
Prof Judith Rankin, UK  
Dr Hermien de Walle, The Netherlands

#### **Members of the EUROlinkCAT Action Advisory Panel**

Dr Domenica Taruscio, National Centre for Rare Diseases  
Dr Luca Autelitano, Operation SMILE  
Hildrun Sundseth, European Institute of Women's Health  
Renee Jopp, International Federation for Spina Bifida and Hydrocephalus  
Dorica Dan, EURORDIS  
Laust H Mortensen, Statistics Denmark

#### **Senior Project Manager**

Hugh Claridge, UK

### **EUROlinkCAT Organizing Committee**

Chair: Dr Amanda Neville, Italy

Members:

Prof Anna Latos-Bielenska, Poland  
Prof Ingeborg Barišić, Croatia  
Prof Joan Morris, UK

#### **Local Organizing Committee**

Chair: Prof Anna Latos-Bielenska

Members:

Prof Anna Materna-Kiryłuk  
MSc Anna Jamry-Dziurla  
Dr Katarzyna Wiśniewska  
Dr Karolina Matuszewska  
Dr Marzena Wiśniewska  
Dr Anna Wawrocka  
Dr Łukasz Kuszel  
Dr Magdalena Badura-Stronka  
Dr Joanna Walczak-Sztulpa  
Kinga Skotnicka, MD  
Dr Anna Skorczyk-Werner  
Dr Anna Sowińska-Seidler

#### **Student Session Organizing Committee**

Chair: Dr Katarzyna Wołyńska

Members:

Marta Andrzejewska – Chair of the Student Research Group of Medical Genetics  
Ewelina Truskowska  
Wiktoria Zgorecka  
Michał Nowak  
Cynthia Szymańska  
Bartosz Nowak  
Julia Dzierła  
Mateusz Zawileński  
Paweł Głuszak  
Jakub Czarny  
Valeriia Babak  
Agnieszka Mariowska  
Julia Michalak  
Filip Glista  
Ali Kraziński  
Marta Lubarska  
Maks Kołodziej  
Weronika Szymonik  
Weronika Sikora  
Michał Smuszkiewicz

## Scientific Program

All listed times are Central European Summer Time (CEST)

### Thursday 7 April 2022

12:00–14:00	<b>Student poster presentations</b>
14:15–15:45	<b>OPENING SESSION</b>
	<p><b>Chairs:</b> Prof Anna Latos Bielenska, Prof Joan Morris</p> <p><b>Conference Welcome</b> Speaker: Prof Anna Latos Bielenska</p> <p><b>EUROlinkCAT: Why create a linked European cohort of children with congenital anomalies?</b> Speaker: Prof Joan Morris</p> <p><b>EUROCAT: Maximising EUROCAT's potential</b> Speaker: David Tucker</p> <p><b>Multi-stakeholder engagement to support person-centred health outcomes</b> Speaker: Dr Sylvia Roozen</p>
15:45–16:00	<i>Break</i>
16:00–17:50	<p><b>SESSION 1</b> The Voice of Parents and Science: Health care and education of children with congenital anomalies</p>
	<p><b>Chair:</b> Prof Ingeborg Barisic <b>Co-Chair:</b> Dr Amanda Neville</p> <p><b>The voice of the parents</b> Speaker: Dr Kristina Garne Holm</p> <p><b>The information and support needs of parents of children with congenital anomalies: an online survey in 10 European countries</b> Speaker: Dr Elena Marcus</p> <p><b>Some insights into educational achievements in children born with a congenital anomaly</b> Speaker: Prof Judith Rankin</p> <p><b>Panellists' presentations</b> Speakers: Dorica Dan, Dominika Madaj-Solberg, Prof Jolanta Wierzba</p> <p><b>Panel discussion</b></p>
17:50–18:00	<i>Break</i>
18:00–20:00	<p><b>Virtual discussion rooms</b> (for anyone to discuss posters, parents' experiences, foundations and associations)</p>

**Friday 8 April 2022**

08:15–08:35	<b>Winning student poster presentations</b>
08:35–09:00	<b>How do you create a linked European cohort of children with congenital anomalies?</b> Speaker: Prof Joan Morris
09:00–10:45	<b>SESSION 2</b> Medications for chronic diseases in children with and without congenital anomalies
	<b>Chair:</b> Dr Maria Loane <b>Co-Chair:</b> Dr Mads Damkjær  <b>Type 1 diabetes mellitus in children up to ten years of age</b> Speaker: Dr Joanne Given  <b>Anti-asthmatic prescriptions in children with and without congenital anomalies</b> Speaker: Natalie Divin  <b>Prescription of cardiovascular medication to children with congenital heart defects</b> Speaker: Dr Mads Damkjær  <b>Panellists' presentations</b> Speakers: Dr Tania Schink, Prof Anne-Marie Nybo Andersen, Dr Christine Damase-Michel  <b>Panel discussion</b>
10:45–11:15	<i>Break</i>
11:15–13:05	<b>SESSION 3</b> Hospitalisations and surgeries in children with and without congenital anomalies
	<b>Chair:</b> Dr Ester Garne <b>Co-Chair:</b> Dr Mads Damkjær  <b>Length of children's hospital stays</b> Speaker: Dr Stine Kjaer Urhoj  <b>Timing, numbers and mortality of surgical interventions in children with congenital anomalies</b> Speaker: Dr Mads Damkjær  <b>Intensive care and mechanical ventilation in children</b> Speaker: Dr Cecilia Martellucci  <b>Are permanent feeding tubes used by children with congenital anomalies?</b> Speaker: Dr Ester Garne  <b>Panellists' presentations</b> Speakers: Dr Luca Autelitano, Prof Damien Bonnet, Prof Irene Petersen  <b>Panel discussion</b>
13:05–14:05	<i>Lunch break</i>



## Friday 8 April 2022 (continued)

14:05–15:55	<b>SESSION 4</b> Survival of children born with congenital anomalies
	<b>Chair:</b> Prof Judith Rankin <b>Co-Chair:</b> Dr Anna Pierini <b>Temporal and geographical variations in survival of children born with congenital anomalies in Europe</b> Speaker: Dr Michele Santoro <b>Ten-year survival of children born with major congenital anomalies</b> Speaker: Dr Svetlana Glinianaia <b>Survival of children with rare structural congenital anomalies</b> Speaker: Dr Alessio Coi <b>Difficulties in combining data on the survival of children with congenital anomalies</b> Speaker: Matt Pryce <b>Panellists' presentations</b> Speakers: Prof Ruth Gilbert, Prof Paul Romitti, Dr Jennita Reefhuis <b>Panel discussion</b>
15:55–16:25	<i>Break</i>
16:25–18:25	<b>SESSION 5</b> Evaluating and enhancing the use of hospital discharge data in the surveillance of congenital anomalies
	<b>Chair:</b> Dr Hermien de Walle <b>Co-Chair:</b> Prof Joan Morris <b>Accuracy of congenital anomaly coding on live birth children recorded in health care databases</b> Speaker: Dr Marian Bakker <b>Using EUROlinkCAT data to evaluate cause of death from vital statistics</b> Speaker: Dr Anke Rissmann <b>Algorithms for use in health care databases to improve the surveillance of congenital anomalies</b> Speaker: Dr Cecilia Martellucci <b>Lessons learned from the EUROlinkCAT study on the quality of data in health care databases</b> Speaker: Dr Ester Garne <b>Panellists' presentations</b> Speakers: Prof Domenica Taruscio, Prof Sonia Hernández-Díaz, Prof Helen Dolk, Prof Robert Smigiel <b>Panel discussion</b>
18:25–18:45	CONFERENCE CLOSING SESSION

## Introduction to EUROLinkCAT

**EUROLinkCAT** was funded for five years and five months from January 2017 by the European Union's Horizon 2020 research and innovation programme under grant agreement No. 733001 to establish a linked European cohort of children with congenital anomalies. Data were linked from seventeen congenital anomaly registries in 14 countries to electronic databases on mortality, hospital stays and prescriptions up to the age of 10 years. Data from 180,00 liveborn children with a congenital anomaly and 2,000,000 reference children without an anomaly born from 1st Jan 1995 to 31st Dec 2014 have been analysed. Aggregate tables and analytic results from each registry on 100 different congenital anomaly subgroups for children aged <1 year, 1–4 years and 5–9 years are stored in a central results repository (CRR). Research teams perform meta-analyses and summarise the results across all registries.

The following abstracts provide an overview of some of the results arising from **EUROLinkCAT**. Table 1 provides details about the data each registry were able to contribute. If research teams are interested in using these data, please contact the EUROLinkCAT Management Committee.


**Table 1: List of EUROCAT Registries who provided data to the listed EUROLinkCAT studies**

EUROCAT Registry Number	Country	Registry name	Small number suppression	Data Provided					
				Survival	Hospital Stay	Surgery	Prenatal Diagnosis	Prescription	Morbidity Data for Reference Children
3	Denmark	Odense	A	Yes	Yes	Yes	Yes	Yes	Yes
5	France	Paris	No	Yes					
8	Italy	Tuscany	No	Yes	Yes	Yes	Yes	Yes	Yes
13	Netherlands	Northern Netherlands	B	Yes	Yes			Antibiotics only	Yes
18	Italy	Emilia Romagna	No	Yes	Yes	Yes	Yes	Yes	Yes
21	Croatia	Zagreb	No	Yes	Yes				Yes
23	Malta	Malta	No	Yes					
29	Belgium	Antwerp	B	Yes					
33	Germany	Saxony Anhalt	No	Yes					
38	Finland	Finland	No	Yes	Yes	Yes	Yes	Yes	Yes
57	United Kingdom	Wales	C	Yes	Yes	Yes	Yes	Yes	Yes
59	Norway	Norway	No	Yes					
62	Ukraine	OMNI-Net	No	Yes					
68	United Kingdom	PHE/Thames Valley	C	Yes	Yes	Yes	Yes		
70	United Kingdom	PHE/Wessex	C	Yes	Yes	Yes	Yes		
72	United Kingdom	PHE/East Midlands & South Yorkshire	C	Yes	Yes	Yes	Yes		
86	Spain	Valencia Region	No	Yes	Yes	Yes	Yes	Yes	Yes

A: Small number suppression is applied before data is released to researchers, but some EUROLinkCAT personnel can analyse original data

B: Small number suppression is applied

C: Small number suppression must be applied by researchers prior to any publication

 Data not available

## EUROlinkCAT Working Group

All below named members have contributed to the project\*. The names are given in Consortium organisation numerical order:

Acronym, (partner's number)	Partner/Registry	Names of contributors
SGUL, QMUL (1; 23)	UK: St George's University of London; Queen Mary University of London	Joan Morris, Joachim Tan, Abigail Reid, Elizabeth Limb, Gillian Briggs, Hannah Evans, Nicholas Connor, Kristina Garne Holm, Joanna Brigden, Elena Marcus, Hugh Claridge
	UK: CAROBB	Jenny Kurinczuk
	UK: EMSYCAR	Elizabeth Draper
	UK: WANDA	Diana Wellesley
	Malta	Miriam Gatt
	Norway	Kari Klungsøyr
UU (2)	UK: Ulster University	Maria Loane, Joanne Given, Natalie Divin, Katy Karnell, Jaiilos Lubinda, Leke Aminkeng, Joanne Watt
RSD (3)	Denmark: Funen	Ester Garne, Stine Kjaer Urhoj, Jane Clemensen, Christina Neergaard Pedersen, Mads Damkjær
UNEW (4)	UK: Newcastle University	Svetlana Glinianaia, Judith Rankin, Theophile Bigirumurame
UNIFE (5)	Italy: Emilia Romagna	Amanda Neville, Gianni Astolfi, Aurora Puccini, Annarita Armaroli, Elisa Ballardini, Cecilia Martellucci
KDB (6)	Croatia: Zagreb	Ingeborg Barišić, Ljubica Odak
CNR-IFC (7)	Italy: Tuscany	Anna Pierini, Silvia Baldacci, Francesca Gorini, Lorena Mezzasalma, Alessio Coi, Michele Santoro
UMCG (8)	Netherlands: Northern	Hermien de Walle, Renée Lutke, Marian Bakker, Nicole Siemensma-Mühlenberg
PHW NHS, SU (9,22)	UK: Wales	David Tucker, Daniel Thayer, Anna Rawlings, Ieuan Scanlon, Ting Wang, Sue Jordan
INSERM (10)	France: Paris	Babak Khoshnood, Nathalie Lelong, Makan Rahshenas, Nathalie Bertille
FISABIO (11)	Spain: Valencian Region	Clara Caveró Carbonell, Sandra Moreno Marro, Laura García-Villodre, Óscar Zurriaga, Laia Barrachina Bonet, Lucía Páramo-Rodríguez, Juan Rico
PUMS (12)	Poland	Anna Latos-Bieleńska, Anna Jamry-Dziurla, Anna Materna-Kiryłuk
THL (13)	Finland	Mika Gissler, Anna Heino, Sonja Kiuru-Kuhlefelt, Tuuli Puroharju
OMNI NET (14)	Ukraine: OMNI-Net	Wladimir Wertelecki, Lyubov Yevtushok, Lyubov Ostapchuk, Nataliia Zymak-Zakutnia, Oksana Tszih, Serhii Lapchenko, Diana Akhmedzhanova
OVGU (15)	Germany: Saxony-Anhalt	Anke Rissmann, Dorit Goetz, Annika Niemann
INSA (16)	Portugal: South	Carlos Matias Dias, Liliana Antunes, Ausenda Machado, Ana João Santos, Paula Braz
CHURéunion (17)	France: Île de la Réunion	Hanitra Randrianaivo-Ranjatoelina, Benedicte Bertaut Nativel
PIH (18)	Belgium: Antwerp	Vera Nelen, Guy Thys, Carmen Franken, Elly Den Hond, Lucas Genard
BIOEF (19)	Spain: Basque Country	Olatz Mokoroa Carollo
BIOMED (20)	UK: Biomedical Computing Limited	James Densem

\* Partner acronyms are detailed on page 71

## EUROlinkCAT Presentations

PRESENTATION CATEGORY	TITLE	AUTHORS
<b>OPENING SESSION</b>		
EUROlinkCAT	EUROlinkCAT: Why create a linked European cohort of children with congenital anomalies?	Joan Morris on behalf of the EUROlinkCAT Working Group <i>Population Health Research Institute, St George's, University of London, United Kingdom</i>
EUROlinkCAT	Maximising EUROCAT's potential	David Tucker <sup>1,2,3</sup> <i><sup>1</sup>President – EUROCAT Association; <sup>2</sup>Honorary Senior Lecturer – Swansea University; <sup>3</sup>CARIS Manager – Congenital Anomaly Register &amp; Information Service for Wales, Public Health Wales, Singleton Hospital, Wales, UK</i>
EUROlinkCAT	Multi-stakeholder engagement to support person-centred health outcomes	Sylvia Roozen <i>International Federation for Spina Bifida and Hydrocephalus, Brussel, Belgium</i>
<b>SESSION 1</b>		
<b>THE VOICE OF PARENTS AND SCIENCE: HEALTH CARE AND EDUCATION OF CHILDREN WITH CONGENITAL ANOMALIES</b>		
EUROlinkCAT	The voice of the parents	Kristina Garne Holm <sup>1,2</sup> on behalf of the EUROlinkCAT Working Group <i><sup>1</sup>Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark; <sup>2</sup>Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark</i>
EUROlinkCAT	The information and support needs of parents of children with congenital anomalies: an online survey in 10 European countries	Elena Marcus on behalf of the EUROlinkCAT Working Group <i>Population Health Research Institute, St George's, University of London, United Kingdom</i>
EUROlinkCAT	Some insights into educational achievements in children born with a congenital anomaly	Judith Rankin on behalf of the EUROlinkCAT Working Group <i>Population Health Sciences Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom</i>
<b>PRE SESSION 2</b>		
EUROlinkCAT	How do you create a linked European cohort of children with congenital anomalies?	Joan Morris on behalf of the EUROlinkCAT Working Group <i>Population Health Research Institute, St George's, University of London, United Kingdom</i>
<b>SESSION 2</b>		
<b>MEDICATIONS FOR CHRONIC DISEASES IN CHILDREN WITH AND WITHOUT CONGENITAL ANOMALIES</b>		
EUROlinkCAT	Type 1 diabetes mellitus in children up to ten years of age	Joanne Given on behalf of the EUROlinkCAT Working Group <i>Institute of Nursing &amp; Health Research, Ulster University, UK</i>
EUROlinkCAT	Anti-asthmatic prescriptions in children with and without congenital anomalies	Natalie Divin on behalf of the EUROlinkCAT Working Group <i>School of Nursing, Ulster University, UK</i>
EUROlinkCAT	Prescription of cardiovascular medication to children with congenital heart defects	Mads Damkjær <sup>1,2</sup> on behalf of the EUROlinkCAT Working Group <i><sup>1</sup>Department of Paediatrics and Adolescent Medicine, Lillebaelt Hospital, University Hospital of Southern Denmark, Kolding, Denmark; <sup>2</sup>Department of Regional Health Research, University of Southern Denmark</i>

SESSION 3 HOSPITALISATIONS AND SURGERIES IN CHILDREN WITH AND WITHOUT CONGENITAL ANOMALIES		
EUROlinkCAT	Hospitalisations and surgeries in children with and without congenital anomalies. Length of children's hospital stays	Stine Kjaer Urhoj <sup>1,2</sup> on behalf of the EUROlinkCAT Working Group <i><sup>1</sup>Department of Paediatrics and Adolescent Medicine, Lillebaelt Hospital, University Hospital of Southern Denmark, Kolding, Denmark; <sup>2</sup>Section of Epidemiology, Department of Public Health, University of Copenhagen, Copenhagen, Denmark</i>
EUROlinkCAT	Timing, numbers and mortality of surgical interventions in children with congenital anomalies	Mads Damkjær <sup>1,2</sup> on behalf of the EUROlinkCAT Working Group <i><sup>1</sup>Department of Paediatrics and Adolescent Medicine, Lillebaelt Hospital, University Hospital of Southern Denmark, Kolding, Denmark; <sup>2</sup>Department of Regional Health Research, University of Southern Denmark</i>
EUROlinkCAT	Intensive care and mechanical ventilation in children	Cecilia Martellucci on behalf of the EUROlinkCAT Working Group <i>IMER Registry (Emilia Romagna Registry of Birth Defects), University of Ferrara, Italy</i>
EUROlinkCAT	Are permanent feeding tubes used by children with congenital anomalies?	Ester Garne on behalf of the EUROlinkCAT Working Group <i>Department of Paediatrics and Adolescent Medicine, Hospital Lillebaelt, Denmark</i>
SESSION 4 SURVIVAL OF CHILDREN BORN WITH CONGENITAL ANOMALIES		
EUROlinkCAT	Temporal and geographical variations in survival of children born with congenital anomalies in Europe	Michele Santoro on behalf of the EUROlinkCAT Working Group <i>Unit of Epidemiology of Rare Diseases and Congenital Anomalies, Institute of Clinical Physiology, National Research Council, Pisa, Italy.</i>
EUROlinkCAT	Ten-year survival of children born with major congenital anomalies: a linked cohort EUROlinkCAT study	Svetlana Glinianaia on behalf of the EUROlinkCAT Working Group <i>Population Health Sciences Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom</i>
EUROlinkCAT	Survival of children with rare structural congenital anomalies	Alessio Coi on behalf of the EUROlinkCAT Working Group <i>Unit of Epidemiology of Rare Diseases and Congenital Anomalies, Institute of Clinical Physiology, National Research Council, Pisa, Italy</i>
EUROlinkCAT	Difficulties in combining data on the survival of children with congenital anomalies	Matthew Pryce on behalf of the EUROlinkCAT Working Group <i>Department of Medical Statistics, London School of Hygiene &amp; Tropical Medicine, London, England</i>
SESSION 5 EVALUATING AND ENHANCING THE USE OF HOSPITAL DISCHARGE DATA IN THE SURVEILLANCE OF CONGENITAL ANOMALIES		
EUROlinkCAT	Accuracy of congenital anomaly coding on live birth children recorded in health care databases	Marian K Bakker on behalf of the EUROlinkCAT Working Group <i>University of Groningen, University Medical Center Groningen, Department of Genetics, Netherlands</i>
EUROlinkCAT	Using EUROlinkCAT data to evaluate cause of death from vital statistics	Anke Rissmann on behalf of the EUROlinkCAT Working Group <i>Malformation Monitoring Centre Saxony-Anhalt, Medical Faculty, Otto-von-Guericke University, Magdeburg, Germany</i>
EUROlinkCAT	Algorithms for use in health care databases to improve the surveillance of congenital anomalies	Cecilia Martellucci on behalf of the EUROlinkCAT Working Group <i>IMER Registry, University Hospital of Ferrara, Italy</i>
EUROlinkCAT	Lessons learned from the EUROlinkCAT study on the quality of data in health care databases	Ester Garne on behalf of the EUROlinkCAT Working Group <i>Department of Paediatrics and Adolescent Medicine, Lillebaelt Hospital, University Hospital of Southern Denmark, Kolding, Denmark</i>

### EUROlinkCAT: Why create a linked European cohort of children with congenital anomalies?

Joan Morris on behalf of the EUROlinkCAT Working Group

Population Health Research Institute, St George's, University of London, United Kingdom

Around 1 in 25 babies are born with a major congenital anomaly (CA) in Europe. These children experience more ill health and have lower survival rates than children without CAs. The aim of the EUROlinkCAT project was to quantify the survival, health and educational needs of children with CA up to the age of 10 years, and investigate differences across Europe.

The survival of children with CAs has often been compared across countries by relying on information from death certificates. However, death certificates state the direct or primary cause of death which may be infection, seizures or other causes and may not mention the CA or the CA may not be accurately coded. It has been recommended that the best way to accurately study survival in children with rare CAs is to link these data to mortality databases. Hence, the first stage of EUROlinkCAT was to link the births reported in 21 population-based EUROCAT CA registries to regional and national data on deaths in children and then pool these data in meta-analyses. This enabled not only survival, but also the accuracy of death certificates, to be evaluated across Europe.

Advances in fetal, neonatal and paediatric care have improved the outcomes for children with many CAs, but at the cost of spending a considerable amount of time in hospital and often undergoing several surgeries. There is a lack of information on the length of hospital stays for children with specific CAs and the surgeries they undergo during and after their first year of life. The second stage of EUROlinkCAT was to link the births in 17 EUROCAT registries to national/regional health care databases and to include a population-based sample of children without CAs for comparison purposes.

A systematic review of neurocognitive outcomes following general anaesthesia and surgery in children concluded that exposure to general anaesthesia in young children affected their development in some neurocognitive domains. However, apart from for the more common genetic syndromes, the school performance of children with CAs and their additional educational needs have not been quantified. The third stage of EUROlinkCAT was to link the births reported in nine EUROCAT registries to national educational databases and again to include a population-based sample of children without CAs to evaluate how well children with different CAs achieve in school and what additional needs they may have.

Many populations worldwide are not covered by CA registries and rely on electronic health care data for their surveillance of CAs. The final stage in the EUROlinkCAT project was to develop recommendations to enable the maximum information from electronic health care data to be extracted for surveillance and research purposes and to quantify the limitations of these data.

### Maximising EUROCAT's potential

David Tucker<sup>1,2,3</sup>

(1) President – EUROCAT Association; (2) Honorary Senior Lecturer – Swansea University; (3) CARIS Manager – Congenital Anomaly Register & Information Service for Wales, Public Health Wales, Singleton Hospital, Wales, UK

#### Introduction

It is my privilege to write a few words about European Surveillance of Congenital Anomalies (EUROCAT), as the President of the EUROCAT Association.

#### Background

EUROCAT is a network of population-based congenital anomaly registries spread across Europe. The work began in 1979 and was seen as a way that EU member states could co-operate together in Public Health. The network has flourished and continues to grow. There are now 39 active registers in 21 countries, monitoring over 1.7 million births per year.

#### The Value of Registries

Registries are expensive to run, however they are cost efficient when compared to other data gathering exercises for special audits etc. Accuracy and timeliness are always perennial issues with any datasets and whilst not complacent, EUROCAT at both the local and central level strives to ensure our data is as good as it can be.

#### EUROCAT guides

The EUROCAT guide to registration (currently Guide 1.4) seeks to ensure that all registries have a common dataset, with well-defined variables. This means data are comparable and can be easily aggregated; an advantage that few in other fields of research have.

#### Prevalence & Surveillance

The advantages of being able to combine data in a consistent way are many:

- Prevalence data can be estimated for a range of conditions that are generally too rare at a local level.
- Temporal trends can be seen, not just at a local or national level but at a European level too. This highlights the effects that environmental factors and the wider determinants of health play in the develop-

ment of congenital anomalies. Whilst these factors are still largely not understood in terms of aetiological pathways, temporal trends and clusters point to their reality.

- The impact of antenatal screening can be seen both in earlier diagnosis for some conditions but also on the termination rate and its knock on effect on the live birth rate.

### Research

With data stretching back over 40 years, EUROCAT is a treasure trove for any researcher. Developments in using linkage techniques in projects such as EUROmediCAT, and more recently with EUROLinkCAT, demonstrate ways in which EUROCAT's data can be used to their full potential. Many of the papers from EUROLinkCAT are ground-breaking and will be standard references for years to come.

### Challenges

In a fast changing environment, registries must change and adapt too in order to remain relevant. Already in recent years even before the COVID-19 pandemic, there have been big changes in work practises; the way data are collected at the local level etc. As electronic healthcare becomes more established, this opens up fresh opportunities for registries to capture data both faster and more accurately. So, let us embrace the future and the potential it offers for further and better research in the field of congenital anomalies and rare diseases.

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## Multi-stakeholder engagement to support person-centred health outcomes

Sylvia Roozen

International Federation for Spina Bifida and Hydrocephalus, Brussel, Belgium

### Introduction

Neural tube defects are common forms of congenital anomalies affecting people around the world. Persons with disabilities face a number of individual, environmental and societal barriers, especially with respect to healthcare. The consequences of inadequate access to multidisciplinary care has a wider impact on the lives of individuals with disabilities and their families. Examples of pain, loss of mobility, recovery from surgical procedures or management of comorbidities are also a threat to independent living of persons with disabilities (Article 19 of the United Nations Convention on the Rights of Persons with Disabilities – UNCRPD). One of the key elements to improve health is to involve persons with disabilities in their own health.

Health is an enabler of inclusion. It requires the engagement of multi-stakeholders to foster inclusion and independence for both parents and individuals with disa-

bilities. Multidisciplinary care must take a personalised approach and examples of services coproduced with service users and clinical teams. However, the development of such services remains inconsistent as national guidelines are lacking. Too often, these services exist only for children with disabilities, with little to no integrated multidisciplinary services available for the transition from childhood to adulthood, for adults and those ageing.

Multi-stakeholder engagement to support person-centered health outcomes is more than medical services. It is therefore important to pay close attention to related issues such as stigma, mental health, and family support or after care in those services. The benefits to healthcare professionals and systems are also numerous, with improved communications and efficiencies.

### Conclusion

The right to the enjoyment of the highest attainable standard of health without discrimination on the basis of disability is enshrined in article 25 of the UNCRPD. Continued commitments are needed to generate lasting and meaningful change for persons with disabilities. As a state party to the Convention, the International Federation for Spina Bifida and Hydrocephalus and EUROLinkCAT in close collaboration with healthcare professionals, academic researchers, educators, leaders in healthcare and education, students, parents and carers, and any others who work or are interested in the field of congenital anomalies can really inspire to respect and implement these principles through effective collaborations and actions to really make a difference in terms of prevention, early detection, and optimizing management and integrated care.

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## SESSION 1

### The voice of the parents

*Kristina Garne Holm<sup>1,2</sup> on behalf of the EUROLinkCAT Working Group*

(1) Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark; (2) Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

### Introduction

Survival of children with congenital anomalies has improved, so up-to-date knowledge about childhood morbidity is required in order to counsel parents. With increasing survival, more families are caring for infants and children with complex care needs and thereby face many everyday challenges. More knowledge on parental experiences are therefore needed. Further, to increase parental involvement and support their engagement in EUROLinkCAT research, a close collaboration between researchers and parents is essential.

## Aim

The aim of the study was to investigate parental experiences of having a child with a heart defect requiring surgery, cleft lip, spina bifida or Down syndrome, and to identify their research priorities.

## Methods

The study had a qualitative approach. In total, seven interviews with 12 parents and eight focus groups with 58 parents and two caregivers were carried out in four European countries. Data were analysed using systematic text condensation.

## Results

We identified that parents request more positive information with a focus on quality of life and what the children can achieve rather than solely focusing on the negative aspects and limitations of the congenital anomaly. Some parents also highlighted discrepancies between the family's need for support and the lack of support received from the local authority. Finally, it was challenging for the parents to address specific research priorities.

## Conclusion

The parents had great concerns about their children's quality of life and cognitive and physical achievements and were caught between seeking the best possibilities for their child and the limited resources that the public system can provide. Future research should focus on the potential of children with a congenital anomaly and dissemination of research must be with a positive aspect of opportunities for the children.

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## The information and support needs of parents of children with congenital anomalies: an online survey in 10 European countries

*Elena Marcus on behalf of the EUROLinkCAT Working Group*

Population Health Research Institute, St George's, University of London, United Kingdom

## Introduction

Parents of children with congenital anomalies (CAs) can experience significant psychosocial impacts, including concern about their child's health and additional caring duties. Providing adequate information and support may help reduce such impacts. This study surveyed parents about their information and support needs, and also about their healthcare experiences during the COVID-19 pandemic, which has brought new challenges.

## Method

A cross-sectional survey was developed in nine languages. Parents and carers of children (0–10 years) with four different anomalies (spina bifida, congenital heart defect requiring surgery, cleft lip, and/or Down syndrome) were recruited online via relevant organisations in 10 Europe-

an countries from March–July 2021: Belgium, Croatia, Denmark, Germany, Italy, Netherlands, Poland, Portugal, Spain, and the United Kingdom. Descriptive analyses with multivariate logistic regressions were conducted, controlling for the child's CA type, parental country of residence, age, and education level.

## Results

1,070 participants were recruited. Most were mothers (92%) and aged 31–40 years (71%). Participants lived in Poland (n=476), the UK (n=120), Germany (n=97), the Netherlands/Belgium (n=74), Croatia (n=68), Italy (n=59), other European countries (n=92), and not specified/non-European countries (n=84). Participants were most likely to rate support groups (63%), patient organisations (60%), specialist doctors/nurses (58%), and social media (57%) as “very helpful” information sources. “Very trustworthy” ratings remained high for specialist doctors/nurses (61%), however, they declined for support groups (47%), patient organisations (48%), and social media (35%). Nearly half of participants (49%) reported that they would have liked professional psychological support around the time of their child's diagnosis, whereas only 15% of participants reported receiving any. With regards to healthcare experiences during the pandemic, the UK (67%) and Poland (65%) had the highest proportion of parents reporting “cancelled or postponed” procedures, compared with only about 20% in Germany and the Netherlands/Belgium. The UK and Poland also had the highest proportion of parents reporting “cancelled or postponed” surgeries, 33% and 35% respectively. This compared to only 8% in Germany.

## Conclusion

Our findings suggest that whilst informal sources of information (e.g. support groups) are of value to parents, they are not deemed as trustworthy as specialist medical sources. A large proportion of parents did not receive the psychological support they needed when their child was diagnosed. Regional differences in disruptions to healthcare appointments due to COVID-19 indicate that improvements should be strived for in some regions.

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## Some insights into educational achievements in children born with a congenital anomaly

*Judith Rankin on behalf of the EUROLinkCAT Working Group*

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## Introduction

Children born with a congenital anomaly have lower academic achievement compared to their peers, but there is insufficient evidence for specific isolated congenital anomalies.



## Objectives

To investigate educational outcomes and special education needs (SEN) of school-aged children born with specific isolated congenital anomalies.

## Materials and Methods

We conducted a survey among the 21 population-based European congenital anomaly registries participating in the multi-centre linked cohort study (EUROlinkCAT) to identify the data available on education in European countries. We then linked data on school age children with congenital anomalies with individual-level education data for the registries that obtained access to education data in their regions. Due to the heterogeneity of the available education data in the participating registries, no standardisation of education data was performed and different measures indicating educational achievements at ages 11 and 16 in the four English and the Welsh registries, and at age 16 (the end of compulsory school) in the Finnish registry. Data on special education needs (SEN) were analysed in the five UK registries and in the Funen (Denmark) registry.

## Results

Due to barriers to obtaining ethics and governance approvals and access to education data, only seven registries were able to access different types of education data. Provisional results in Wales showed that children with congenital anomalies were less likely to achieve the expected level in the main school subjects (English/Welsh and Maths) compared to the reference children. However, the majority did still achieve the expected academic level at ages 11 and 16 years, but this varied by specific anomaly.

In Finland, although grade point averages for all subjects at the end of compulsory school (age 16 years) were relatively high, a lower proportion of children with congenital anomalies applied to continue further education compared to reference children.

Provisional results from the English, Welsh and Danish registries showed that children with specific anomalies had higher SEN rates up to age 11 years than reference children.

## Conclusion

Provisional results showed that the majority of children with congenital anomalies achieved the expected academic level at the ages we examined. However, children with congenital anomalies were more likely to underperform academically compared to children without congenital anomalies and had a higher need for special education services which varied by congenital anomaly subgroup.

## EUROlinkCAT: How do you create a linked European cohort of children with congenital anomalies?

*Joan Morris on behalf of the EUROlinkCAT Working Group*

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## Introduction

EUROCAT is a European network of population-based registries for the epidemiological surveillance of congenital anomalies (CA). EUROlinkCAT supported 22 EUROCAT registries in 14 countries to link their data on births with CAs to mortality, hospital discharge, prescription and educational databases. Four registries did not manage to participate due to delays in obtaining the necessary permissions and issues relating to COVID-19.

## Materials and Methods

Sixteen registries linked information on survival up to the age of 10 years in 96% of children recorded in the anomaly registries, born between 1995 and 2014, creating a dataset of 180,000 live births with 9,000 deaths occurring from 1st Jan 1995 to 31st Dec 2015.

Eleven registries linked information on hospital stays and surgeries for 89% of children with a CA and seven obtained data on 95% of children without a CA born during the same time-period and from the same population area covered by their registry to form a reference population. Data from 99,000 EUROCAT children and 2,000,000 reference children were analysed.

Six registries linked information on prescriptions for 95% of children with a CA and children without a CA up to the age of 10 years. Data from 60,000 EUROCAT children and 1,700,000 reference children were analysed.

Each registry transformed their case data into a Common Data Model (CDM) format. Identical STATA syntax scripts were run by all registries to analyse their data. Analyses were performed on 100 different CA subgroups for children <1 year, 1–4 years and 5–9 years. Some analyses included risk factors such as gestational age, birth weight and year of birth. The resulting aggregate tables and analysis results were submitted to a Central Results Repository (CRR). EUROlinkCAT research teams were sent the relevant data to enable them to perform meta-analyses and summarise the results across all registries.

Six registries from four countries obtained data on educational achievements and/or educational needs at age 11 for 86% of children with a CA and 93% of reference children. Data from 38,000 EUROCAT children and 790,000 reference children were analysed. A common data model was not applied, and meta-analyses were not performed due to the heterogeneity of the education measures available.

## Ethics

The CA registries all have permission for routine surveillance and transmission of anonymised data to the EURO-CAT central database. Each registry obtained additional ethics and other permissions required for their participation in EUROLinkCAT, and Ulster University obtained permission to store data in a Central Results Repository.

## Dissemination

Findings from EUROLinkCAT will provide evidence-based information to parents, health professionals and public health authorities on the health of children with CAs. The CDM and associated documentation, including linkage and standardisation procedures, will be publicly available thus facilitating future local, national and EU-level analyses using health care databases. Data from the CRR will be available for valid research purposes on application to EUROLinkCAT.

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## SESSION 2

### Type 1 diabetes mellitus in children up to ten years of age

*Joanne Given on behalf of the EUROLinkCAT Working Group*

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#### Introduction

Children and young adults with Down syndrome have an increased risk of type 1 diabetes. However, there is less information on the risks of type 1 diabetes associated with other congenital anomalies (CAs). Indeed, there is conflicting evidence on risks associated with diabetes for children with congenital heart defects (CHD). The risk of type 1 diabetes among children with CAs has not previously been examined in a large multi-centre sample using standardised methodology.

#### Objective

To evaluate prescription rates of insulin/insulin analogues as an indicator of type 1 diabetes in children 0 to 9 years of age with and without CAs, and to explore associations with specific risk factors.

#### Materials and Methods

A EUROLinkCAT data linkage cohort study, involving six population-based registries from the European Surveillance of Congenital Anomalies (EUROCAT) network in five countries. Children with major CAs (60,662) and children without CAs (1,722,912), the reference group, born 2000–2014 were linked to prescription databases for 2000–2015. Prescriptions recorded in the regional/national prescription databases using the WHO Anatomical Therapeutic Chemical (ATC) classification codes starting with A10A were used to classify a child as being exposed to insulin/insulin analogues. A child must also have had at least two prescriptions in a single year to

be classified as exposed. Risk factors included were birth cohort, premature birth (<37 weeks compared with ≥37 weeks) and sex.

#### Results

In children with CAs, 0.04 per 100 child-years (95% CI 0.01–0.07) had >1 prescription for insulin/insulin analogues recorded between 0–3 years of age compared with 0.03 per 100 child-years (95% CI 0.01–0.06) in reference children. The prevalence of insulin prescriptions increased ten-fold by age 8 to 9 years (children with CAs 0.40 per 100 child-years, 95% CI 0.22–0.63; reference children 0.31 per 100 child-years, 95% CI 0.10–0.63). Children with any chromosomal anomaly (Risk Ratio (RR) 2.37, 95% CI 1.91–2.96), and particularly Down syndrome (RR 3.44, 95% CI 2.70–4.37), had a significantly increased risk of receiving prescriptions for insulin. Children with CHD were less likely to receive insulin prescriptions (RR 0.97, 95% CI 0.84–1.12). Children born in 2000–2004 had a similar risk of receiving >1 prescription for insulin/insulin analogues aged 0–3 years as those born in 2005–2009. Reference children born at <37 weeks gestational age were more likely to receive >1 prescription for insulin compared with those born ≥37 weeks gestation (RR 1.28, 95% CI 1.20–1.36). Male children were more likely to receive prescriptions for insulin/insulin analogues.

#### Conclusions

While type 1 diabetes is rare in children <10 years, children with chromosomal anomalies had an increased risk of receiving insulin/insulin analogue prescriptions compared with reference children, while children with CHD and other non-chromosomal anomalies were not at increased risk.

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### Anti-asthmatic prescriptions in children with and without congenital anomalies

*Natalie Divin on behalf of the EUROLinkCAT Working Group*

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#### Introduction

Asthma is the most common chronic disease in childhood. Rates of parent-reported asthma and wheeze in children vary globally and within Europe, yet little is known about rates of asthma and wheezing in children with congenital anomalies. Previous research involving children with congenital anomalies indicates higher asthma rates than in studies of children without congenital anomalies, but these studies are generally based on single-centre cross-sectional methodology with small sample sizes.

#### Objectives

This study explored the prevalence and risk of receiving anti-asthmatic prescriptions in children with and without

congenital anomalies using six regional European databases.

### Materials and Methods

This was a EUROLINKCAT data linkage cohort study using data from those born between 2000–2014 up to ten years of age. Data from both children with and without congenital anomalies (used as the reference population) were linked to prescription databases. Anatomical Therapeutic Chemical classification codes beginning with R03 were used to identify whether a child had been prescribed >1 anti-asthmatic in a year. The prevalence and relative risk of being prescribed >1 anti-asthmatic were explored by age group, European region, class of anti-asthmatic (beta-2 agonists and inhaled corticosteroids), and congenital anomaly.

### Results

Data were analysed from 60,662 children with congenital anomalies and 1,722,912 reference children. Children with congenital anomalies had a higher prevalence of >1 anti-asthmatic prescription and a significantly higher risk of being prescribed anti-asthmatics (RR=1.41, 95% CI 1.35–1.48) compared to reference children. The increased risk was consistent across all age groups. Children with congenital anomalies were more likely to be prescribed beta-2 agonists (RR=1.71, 95% CI 1.60–1.83) and inhaled corticosteroids (RR=1.74, 95% CI 1.61–1.87) compared to reference children. Children with oesophageal atresia, diaphragmatic hernia, genetic syndromes and chromosomal anomalies had over twice the risk of being prescribed anti-asthmatics compared to reference children. Regional differences in prevalence and risk of having prescriptions for anti-asthmatics were identified.

### Conclusion

Children below the age of ten years with congenital anomalies had higher prevalence and risk of receiving anti-asthmatic prescriptions than reference children. These increases remained consistent across each age group and across all European regions explored. Our findings are beneficial to clinicians in identifying congenital anomalies associated with a higher risk of asthma.

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## Prescription of cardiovascular medication to children with congenital heart defects

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### Introduction

Advances in surgical management strategies have substantially reduced fatality from congenital heart defects (CHD). Decreased infant mortality might be expected,

consequently to result in greater morbidity in older children due to complications later in childhood and adolescence.

### Objective

This study aims to evaluate the use of cardiovascular medication (CVM) as an indicator of disease burden in children born with CHD in the first 10 years of life.

### Materials and methods

Six population-based registries from the European Surveillance of Congenital Anomalies (EUROCAT) network participated. Data from live born children with major congenital anomalies (CA) born from 2000–2014 were linked to prescription databases. Four groups of children were analysed: CA, CHD, severe CHD (sCHD) and Ventricular Septal Defect (VSD) without sCHD. Live born children without CA were included as reference group. We obtained data on 61,038 children born with a CA, including 19,678 with CHD, 3,392 with sCHD, 12,728 children with VSD without sCHD, and 1,725,496 reference children.

### Results

Children born with sCHD were the most likely to receive a CVM prescription (42.9%, 95% CI, 26.3–58.5) in the first year of life compared to 13.3% (6.7–22.0) of children with any CHD, 5.9% (3.7–8.7) of children with any CA and 0.1% (0.0–0.1) of reference children. Medication was less likely to be prescribed after the first year of life for sCHD; 18.8% (14.8–23.1) for children 1–4 years and 15.8% (12.0–20.1) 5–9 years. Children with sCHD were most likely to receive a diuretic (36.4%, 18.6–54.5), an antihypertensive (6.9%, 3.7–11.3) or a beta-blocker (5.5%, 2.9–9.2).

### Conclusion

Almost half of all children with sCHD were prescribed CVM in their first year of life. For all four groups of children with anomalies, the proportion of children with a CVM prescription decreased with age.

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## SESSION 3

## Hospitalisations and surgeries in children with and without congenital anomalies. Length of children's hospital stays

Stine Kjaer Urhoj<sup>1,2</sup> on behalf of the EUROLINKCAT Working Group

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### Introduction

Little information is published about the length of hospital stays for children with congenital anomalies, which

is important for making parents aware of their child's healthcare needs and potential impact on family life.

### Objectives

To evaluate the percentage of children hospitalised and the length of stay in hospital for children with and without congenital anomalies.

### Materials and methods

The study is a European population-based record-linkage study in 11 regions in eight countries. The study includes children with congenital anomalies (EUROCAT children) and children without congenital anomalies (reference children) living in the same regions. The children were born between 1995 and 2014 and were followed to their tenth birthday or 31/12/2015.

European meta-analysis of percentage hospitalised, median length of stay in hospital per year and percentage with extended stays ( $\geq 10$  days) for children  $< 1$  year and children 1–4 years by anomaly subgroup were performed.

### Results

The study included 99,414 EUROCAT children and 2,021,772 reference children. A larger percentage of the EUROCAT children were hospitalised during the first years (85%) than among the reference children (30%). After one year, fewer children were hospitalised in both groups, but still the percentage was larger among the EUROCAT children (55%) than among the reference children (25%). The median length of the hospitalisations was 2–3 times longer for EUROCAT children in both age groups and the percentage of children with extended stays ( $\geq 10$  days) were also much higher among the EUROCAT children (25% in the first year) than among the reference children (1% in the first year). The percentage hospitalised and the median length of stay varied greatly between the congenital anomaly subgroups.

### Conclusion

Children with congenital anomalies were more often hospitalised and their median length of stay was longer than children without congenital anomalies. Therefore, parents of children with congenital anomalies should be adequately supported, not only by health care professionals, but also by relevant authorities and by the health and social policies.

## Timing, numbers and mortality of surgical interventions in children with congenital anomalies

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### Introduction

Surgical intervention for congenital heart defects (CHD) has undergone a dramatic evolution in the past 70 years. From the 1990s onwards, pressure has moved towards perfection of results to further reduce mortality to  $< 2\%$ . To achieve this goal, a multifaceted strategy is employed, which encompasses enhanced prenatal detection through screening, postnatal screening by pulse oximetry, advanced imaging combined, and reduced use of blood products during surgical procedures to mention a few. As part of this multifaceted approach, there has been a trend towards earlier surgical interventions in CHD.

### Objective

To compare timing and number of surgical interventions for various types of congenital heart defects (CHD) across Europe.

### Materials and methods

Six population-based registries from the European Surveillance of Congenital Anomalies (EUROCAT) network participated. Data from live born children with major congenital anomalies born from 2000–2014 were linked to hospital records and survival databases. We examined timing of cardiac surgery, number of cardiac surgeries and 5-year mortality. Twelve groups of children were analysed: CHD, severe CHD (sCHD), ventricular septal defect (VSD), atrial septal defect (ASD), transposition of great vessels (TGA), atrioventricular septal defect (AVSD), Tetralogy of Fallot (TOF), hypoplastic left heart syndrome (HLHS), pulmonary valve stenosis (PS), pulmonary valve atresia (PA), coarctation of the aorta (CoA), patent arterial duct (PDA) and total anomalous pulmonary vein return (TAPVR).

### Results

For all children born with a CHD, the mean age at first cardiac surgical intervention was 12.1 (Interquartile range (IQR); 1.6–34.0) weeks, for those with sCHD it was 5.0 (IQR; 0.7–21.8) weeks. Timing of surgical intervention varied greatly between different CHDs, from 0.8 (IQR; 0.1–2.2) weeks for TGA to 62.6 (IQR; 23.7–126.3) weeks for ASD. Children with CHD underwent cardiac surgery on average 2.1 (IQR; 1.1–3.6) times and those with sCHD 2.4 (IQR; 1.7–4.2) in their first 10 years of life. Those with most cardiac surgical interventions in the first 10 years of life were in children with PA who underwent cardiac interventions 4.1 (IQR; 2.4–6.8) times and those

with fewest were children with PDA (1.1 (IQR; 1.0–1.1) times). The 5-year survival for all children born with CHD was 95% (IQR; 94–97), for specific severe anomalies it ranged from 90% (IQR; 97–93) for TGA to 52% (IQR; 45–60) for children with HLHS.

### Conclusion

On average, children born with CHD undergo cardiac surgery 2.1 times, with timing varying greatly between defects. Those with most cardiac surgical interventions are children with PA. While prognosis overall is good, some anomalies such as HLHS still have a poor prognosis with a 5-year survival rate of 52%.

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## Intensive care and mechanical ventilation in children

*Cecilia Martellucci on behalf of the EUROLINKCAT Working Group*

IMER Registry (Emilia Romagna Registry of Birth Defects), University of Ferrara, Italy

### Introduction

Congenital anomalies (CAs) are a major cause of childhood morbidity and long-term disability. Data on the patterns of healthcare utilisation of children with CAs can be useful to monitor the costs of hospitalisation and to explore the possible differences in management across different settings.

### Objectives

To assess the use of Intensive Care Units (ICU) and of mechanical ventilation to support respiration in children with CAs, compared to reference children without CAs, across multiple EUROCAT registries.

### Materials and Methods

Cases for the study were all children with a major CA as defined in EUROCAT and born between 1995–2014. Data were included from nine population-based CA registries which are members of EUROCAT, which used both registry and health care databases to link the cases to hospitalisations with either ICU admissions or ventilation. Reference children were all or a selection of children without CAs born during the same period and in the same geographical area as the cases. The proportions of children needing ICU and ventilation were calculated by age group and registry, then meta-analyses were performed to obtain an estimate of these proportions for each anomaly, pooled across all registries.

### Results

Out of 31,806 children <1 year of age with CAs from eight registries, 4475 were admitted to ICU: this was a mean proportion of 12.6% (95% CI 9.3–16.5%), ranging from 6.4% (95% CI 4.4–9.3) in Wessex, UK, to 25.6% (95% CI 24.3–27.0) in Tuscany, Italy, compared to a mean of 1.9% (95% CI 1.3–2.8) among reference children. During the

first year of life, ventilation was needed by 3956 children with CA out of 52,645 children which was 7.8% (95% CI 5.2–11.1) (nine registries). As for ICU, percentages varied greatly across registries, ranging from 2.5% (95% CI 2.2–2.8) in Finland to 14.3% (95% CI 13.3–15.4) in Tuscany, Italy. Proportions were lower in the 1–4 years age group, although still statistically significantly higher in EURO-CAT children than in reference children: 2.2% and 0.2% respectively for ICU and 1.3% and 0.1% for ventilation. Results for specific CAs will be presented.

### Conclusion

Children with CAs use six to 24 times as much ICU and ventilation as children without CAs, especially when below one year of age. Variations were substantial across the different CAs, according to the severity of the condition, but also across different registries. This may reflect misclassifications, but also under- or over-registration of hospitalisation episodes, and warrants closer investigations of these variations.

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## Are permanent feeding tubes used by children with congenital anomalies?

*Ester Garne on behalf of the EUROLINKCAT Working Group*

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### Introduction

The main indications for a permanent feeding tube (gastrostomy) are severe neurological disorders and congenital anomalies with severe feeding problems.

### Objectives

To report the frequency of surgery for permanent feeding tubes in children with congenital anomalies up to the age of 5 years compared to all children without congenital anomalies living in the same geographical areas.

### Material and Methods

Data from nine EUROLINKCAT registries in six countries comparing the presence of surgery codes for permanent feeding tubes for children with major congenital anomalies compared to the children without congenital anomalies living in the same geographical areas.

### Results

The study included 91,504 EUROCAT children and 1,960,272 reference children. Overall, 1,200 (1.3%, 95% CI 1.2–1.6) of the EUROCAT children and 374 (0.016%, 95% CI 0.009–0.026) of the reference children had a surgery code for a permanent feeding tube within the first 5 years of life. There were geographical differences across Europe with higher rates in Northern Europe compared to Southern Europe. For some specific anomalies and genetic syndromes, the proportion of children having a surgery code for a permanent feeding tube was over 15%.

## Conclusion

The majority of surgeries for permanent feeding tubes within the first 5 years of life occur in children with congenital anomalies and for some specific anomalies the proportion of children having a permanent feeding tube is high. There is a geographical variation in Europe in surgery for a permanent feeding tube in children less than 5 years.

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## SESSION 4

### Temporal and geographical variations in survival of children born with congenital anomalies in Europe

*Michele Santoro on behalf of the EUROlinkCAT Working Group*

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#### Introduction

Congenital anomalies (CAs) are a major cause of perinatal, neonatal and infant mortality. Despite reported improvements in long-term survival, CAs have an important role when interpreting the regional differences in neonatal, infant and child mortality across the European countries.

#### Objectives

The aim of this study was to investigate temporal changes and geographical variation in survival of children with major CAs in different European areas. The study also describes some methodological issues in studying survival of children with CAs across different countries and in a long temporal span.

#### Materials and Methods

Seventeen CA registries in 12 different European countries participated to this population-based linkage cohort study. The registries were members of EUROCAT, the European network for the surveillance of CAs, and linked their data on live births with CAs to mortality databases. Using a central analysis script, registries fitted Cox's proportional hazards models comparing mortality at 1 year (infant mortality) and 1–9 years of age for children born during 2005–2014 with those born during 1995–2004. The hazard ratios (HR) from each registry were combined centrally using a random-effects model. Furthermore, registries estimated Kaplan-Meier survival at 28 days and 5 years of age, and the 5-year survival conditional on having survived to 28 days.

#### Results

Data on 115,219 children born with a major CA were successfully linked to mortality records. The overall risk of death by 1 year of age for children born with any major CA in 2005–2014 significantly decreased compared to

1995–2004 (HR 0.68; 95%CI: 0.53–0.89), as well as for deaths from 1–9 years of age (HR 0.75; 95%CI: 0.62–0.91). Also considering only live births with isolated severe congenital heart defects a significant decrease in the risk of infant death was observed (HR 0.59; 95%CI: 0.46–0.74). Survival at 5 years of age ranged between registries from 97.6% to 87.0%. The lowest survival was observed for the registries of OMNI-Net (Ukraine) (87.0%; 95%CI: 86.1–87.9) and Malta (90.6%; 95%CI: 88.7–92.1). The 5-year conditional survival on having survived to 28 days largely increased compared to the unconditional survival.

#### Conclusion

Survival improved in the most recent period (2005–2014) and a high variability in estimated survival across the registries was observed. The linkage of CA data from population-based registries to mortality records from national/vital statistics is an efficient and powerful method of analysing the survival of children born with CAs. The proportion of terminations of pregnancy for fetal anomaly, the criteria of exclusion/inclusion of less severe CAs, the source of mortality data, and the linkage methods, are important factors to consider in the design of future studies and in the interpretation of the results on survival of children with CAs.

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### Ten-year survival of children born with major congenital anomalies: a linked cohort EUROlinkCAT study

*Svetlana Glinianaia on behalf of the EUROlinkCAT Working Group*

Population Health Sciences Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom

#### Introduction

Congenital anomalies are a major cause of perinatal and infant mortality and their contribution to child mortality is increasing globally. There is paucity of population-based research on survival beyond infancy for specific congenital anomaly subgroups.

#### Objectives

To investigate the survival of live born children up to 10 years of age with a major congenital anomaly.

#### Materials and Methods

This multi-centre retrospective linkage cohort study (EUROlinkCAT) linked data on births during 2005–2014 from 13 population-based European congenital anomaly registries with national/vital statistics or mortality records in nine Western European countries. Pooled Kaplan-Meier survival estimates at specific age points up to 10 years of age were calculated for 77,054 children born alive with a major isolated structural congenital anomaly and for 4,011 children with Down syndrome.

## Results

The highest mortality of children with isolated structural congenital anomalies was within the first year of life: one year survival of 97.3% (95% confidence interval [CI]: 96.6–98.1%) and 10-year survival of 96.9% (95% CI: 96.0–97.7%). The 10-year survival exceeded 90% for the majority of congenital anomaly subgroups (27 of 32), with considerable variations between specific congenital anomalies. Thus, it varied from 51.6% (95% CI: 44.9–59.4%) for hypoplastic left heart to 99.8% (95% CI: 99.6–100.0%) for cleft lip with or without cleft palate. Survival of children with a specific isolated anomaly was higher than in all children with the same anomaly when those with associated anomalies were included. For children with Down syndrome, the 10-year survival was significantly higher for those without associated cardiac or digestive system anomalies (97.6%; 95% CI: 96.5–98.7%) compared to children with Down syndrome associated with a cardiac anomaly (92.3%; 95% CI: 89.4–95.3%), digestive system anomaly (92.8%; 95% CI: 87.7–98.2%) or both (88.6%; 95% CI: 83.2–94.3%).

## Conclusion

Ten-year survival of children born with congenital anomalies in Western Europe during 2005–2014 was relatively high, but with considerable variations between congenital anomalies of different severity. Reliable information on long-term survival of children born with specific congenital anomalies is of major importance for parents whose child is affected by a congenital anomaly and for the health professionals involved in their care.

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## Survival of children with rare structural congenital anomalies

*Alessio Coi on behalf of the EUROLINKCAT Working Group*

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## Introduction

Congenital anomalies (CA) are the leading cause of perinatal, neonatal and infant mortality in developed countries. Large long-term follow-up studies investigating survival beyond the first year of life in children with rare CAs are costly and time-consuming. Furthermore, due to the rarity of some CAs, sufficiently large standardised cohorts are difficult to obtain and the only way to accurately study survival in children with these CAs is to pool data across several registries and link cases to mortality databases.

## Objectives

This study aimed to investigate the survival up to 10 years of age of children born with a rare structural CA in the period 1995–2014, pooling data from thirteen EUROC

(European network for the epidemiological surveillance of CAs) registries.

## Materials and Methods

This study focused on the survival of children with 31 different rare structural CAs (defined within EUROLINKCAT as CAs with a live birth prevalence lower than 1 per 10,000). Live births from the European population-based CA registries were linked to mortality records. Survival for 12,685 live births was estimated at 1 week, 4 weeks and 1, 5 and 10 years of age within each registry and combined across Europe using random effects meta-analyses. Similarly, 10-year survival estimates conditional on having survived at 4 weeks calculated for each registry were combined in a random-effects meta-analysis. Differences between registries were evaluated for the eight rare CAs which had at least 500 live births at risk.

## Results

Amongst the investigated CAs, prune belly sequence and anophthalmos were the rarest investigated CAs with only 48 and 103 live births, respectively. Arhinencephaly/holoprosencephaly had the lowest survival at all age points (58.1%, 95% Confidence Interval (CI): 44.3–6.2% at 1 week; 47.4%, CI: 36.4–61.6% at 1 year; 35.6%, CI: 22.2–56.9% at 10 years). At 10 years of age, survival was below 80% for 17 CAs, which included all the investigated severe rare congenital heart defects. In general, children with rare CAs of the digestive system had the highest survival (>95% at 1 week, >84% at 10 years). Most deaths occurred within the first four weeks of life resulting in a 10-year survival conditional on surviving 4 weeks of over 95% for 17 out of 31 rare CAs. A moderate variability in survival between participating registries was observed for the eight selected rare CAs.

## Conclusion

This multi-centre population-based European study provided a sufficiently large, standardised cohort to produce reliable survival estimates of children with rare structural CAs up to 10 years of age. Having consistent information on long-term survival of children born with specific CAs is of major importance for the health professionals involved in counselling parents, especially when facing a prenatal diagnosis of a rare CA.

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## Difficulties in combining data on the survival of children with congenital anomalies.

*Matthew Pryce on behalf of the EUROLINKCAT Working Group*

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When investigating the survival of children with congenital anomalies, the information a single country can provide is limited due to the scarcity of each anomaly. To

overcome this, one option is to combine the survival information from countries across Europe to produce summary survival curves. Due to data sharing restrictions this must be done in a two-step process, by first estimating the survival within each country and then pooling this information across all countries. Current methods available to do this are generally focused on pooling large sample sizes and can result in biased estimates when applied to small sample sizes. In this presentation we discuss how to improve these techniques in the small sample size setting as is present when reviewing congenital anomalies.

When looking to combine aggregated survival curves, the most suitable current method is a distribution-free meta-analytic approach. This method combines transformed conditional survival probabilities rather than the raw survival probabilities, allowing for favourable properties such as a monotonic decreasing curve to be produced. The downfall of this approach is that within the transformation a correction term is used. In large sample sizes, this has little to no impact, however, in small sample size settings or high survival settings this can introduce large biases. We explored three variations of this correction and assessed their performance over a range of sample size survival settings using simulation studies. In addition, we reviewed analytic methods which can help deal with the additional biases that are encountered when survival rates approach 1 and sample sizes are very small.

The simulations highlighted how standard correction of 0.25 will considerably underestimate the combined survival curve when the cohort level conditional survival rates are close to 1, especially in very small sample sizes. Improvements were found by altering the correction to a reciprocal correction (1 over the country level sample size), which reduced the bias in extreme cases, while still providing relatively accurate estimates as conditional survival rates decreased. In addition, we showed how both collapsing time points, to prevent no outcome time intervals, and applying sample size restriction when using the reciprocal correction proved beneficial to improving estimate bias.

In conclusion, we presented how the current best methods can be adapted and used to combine survival data from small cohorts with high survival, allowing for more reliable information to be obtained on the survival of children with congenital anomalies.

## Accuracy of congenital anomaly coding on live birth children recorded in health care databases

*Marian K Bakker on behalf of the EUROLinkCAT Working Group*

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### Introduction

Electronic health care databases (EHCDs) are increasingly being used to investigate the epidemiology of congenital anomalies (CAs), often due to the absence of a CA register. However, because EHCDs are not designed for research or surveillance, their data on CAs may be inaccurate and incomplete.

### Objectives

To evaluate the accuracy and the quality of the coding of CAs in hospital databases, compared to EUROLinkCAT data which was assumed to be the gold standard, and to ascertain which CAs can be accurately identified using hospital databases.

### Materials and methods

Eleven EUROCAT registries linked their CA data to regional or national hospital databases. Inclusion criteria for this study were: all live births born between 2010–2014, recorded in the EUROCAT registries and linked to hospital data and all children identified in the hospital databases with a CA code registered in the first year of life. We focused on 17 specific anomaly groups. For each child, we compared the diagnosis codes in the hospital database to the codes in EUROLinkCAT and calculated sensitivity for the specific anomaly groups. Positive predictive value was calculated using data from six registries with access to hospital data of the full reference population. For a specified CA, the exact sensitivity is the proportion of EUROLinkCAT children correctly identified in the hospital data with exactly the same CA code as they have in EUROLinkCAT. For a specified CA, the exact PPV is the proportion of children in hospital data correctly identified in EUROLinkCAT with exactly the same CA code as they have in the hospital data.

### Results

Most registries linked more than 85% of their cases to hospital data. The proportion of linked EUROLinkCAT cases with a CA code recorded in the hospital data in the first year of life varied from 49% in Zagreb to 96% in Valencian Region. In most registries sensitivity was high (>80%) for cleft lip with or without cleft palate, Down syndrome and Hirschsprung's disease. Low sensitivity (<50%) was frequently observed for clubfoot and congenital hydronephrosis. PPV was high (>80%) for gastroschisis and Down syndrome and low (<50%) for ASD.



## Conclusion

The comparisons between CA coding in hospital databases and the coding in EUROlinkCAT highlighted differences between the hospital databases, often due to differences in the healthcare systems. Information is lacking in hospital databases on terminations of pregnancy, children with CAs that do not require hospitalisations and children with CAs that are treated in specialist centers outside the region of coverage. In the absence of a CA register, hospital data may be used to monitor certain CAs with a high sensitivity and low TOPFA rate, but additional data sources should be used to capture information on CAs with a low sensitivity.

## Using EUROlinkCAT data to evaluate cause of death from vital statistics

*Anke Rissmann on behalf of the EUROlinkCAT Working Group*

Malformation Monitoring Centre Saxony-Anhalt, Medical Faculty, Otto-von-Guericke University, Magdeburg, Germany

### Introduction

Congenital anomalies (CAs) are a major cause of infant and childhood mortality. Data on underlying cause of death on death certificates are frequently analysed to monitor improvements in primary and secondary prevention over time.

### Objectives

To evaluate the accuracy of reporting of CAs on death certificates according to age at death and specific anomaly.

### Materials and Methods

All live born children with a major CA born between 1st January 1995 and 31st December 2014, recorded in 13 population-based CA registries who are members of EUROCAT, were linked to mortality records up to the child's 10th birthday or to 31st December 2015, whichever was earlier. The underlying cause of death and other additional causes were examined to determine if a CA was listed and this was compared to the known CA that the child had to evaluate accuracy of reporting.

### Results

A total of 5,487 deaths in infants and children were reported. Overall, 69% (95%CI: 63–76%) of deaths in infants with a major CA had a CA recorded as the underlying cause of death. However, this varied significantly according to registry. Only 49% (95%CI: 56–41%) of deaths from age 1 to 9 in children with a major CA had a CA recorded as the underlying cause of death. Fatal anomalies were more likely to have a CA recorded and were more likely to have an appropriate CA code reported, but the proportions were low. For example, severe congenital heart disease only had an appropriate code provided 40% (95%CI: 55–26%) of the time.

## Conclusion

The inclusion of codes for CAs on European death certificates is incomplete and the accuracy is low. Estimates of the proportions of deaths due to CAs will be about 30% underestimated in the first year of life and between 20% and 50% for children (ages 1 to 9). Currently, the data recorded are too inaccurate on their own to be used to evaluate mortality for specific anomalies.

## Algorithms for use in health care databases to improve the surveillance of congenital anomalies

*Cecilia Martellucci on behalf of the EUROlinkCAT Working Group*

IMER Registry, University Hospital of Ferrara, Italy

### Introduction

Congenital anomaly (CA) registries often depend on individual case identification by clinicians or by searching clinical records. Recently, health care databases (HCD) are seen as a data source for identifying cases. The possibility for registries to ascertain cases by searching for CA codes in HCD is becoming more widespread.

**Objectives** To develop an algorithm to reduce the limitations of HCD by using filters and evaluation criteria applicable to all selected CAs with the ultimate aim of classifying the individual patients into three categories:

- Validated cases whose data will be included automatically into the CA registry
- Excluded cases whose data will not be included into the CA registry
- Cases to be evaluated through further consultation of medical records to ascertain the presence/absence of CA.

### Materials and Methods

A single HCD database can be used for the algorithm or several data sources (eg. Hospital discharge records, Surgical Procedures datasets, birth and death certificates) can be merged. In all the sources used, each patient (child) is uniquely identified by the patient code (primary key).

The algorithm searches for possible cases by running five modules in sequence:

1. Search for diagnosis to be excluded or evaluated
2. Validation of the diagnosis
3. Analysis of the case
4. Case classification
5. Analysis output

The algorithm logic follows EUROCAT Guide 1.4 <https://eu-rd-platform.jrc.ec.europa.eu/eurocat/data-collection/guidelines-for-data-registration#inline-nav-2>.

## Results

The algorithm developed minimizes the number of cases to be evaluated, without increasing the probability of error in the validated cases (false positives) and in those excluded (false negatives).

The probability of error and the reliability of the classification depends on the quality of the information, the effectiveness of the filters and the criteria applied. The results from the algorithm should be considered as probabilistic evaluations.

## Conclusion

The proposed algorithm allows surveillance of all or specific congenital anomalies exclusively through healthcare databases, and the use of electronic health records may ensure a sufficiently complete coverage of geographical areas. Care should be taken to ensure all pregnancy outcomes are captured not only births in order to have accurate surveillance. The algorithm is freely available to any registry to implement.

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## Lessons learned from the EUROLINKCAT study on the quality of data in health care databases

*Ester Garne on behalf of the EUROLINKCAT Working Group*

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## Introduction

The aim of EUROLINKCAT was to compare the health of children with congenital anomalies to that of children without congenital anomalies living in the same regions. To achieve this, researchers in EUROLINKCAT have spent over five years successfully linking and analysing data from regional and national health care databases in Europe.

## Objectives

This presentation will discuss some of the challenges of such data linkage and the problems overcome in this type of research.

Difficulties encountered: Health care databases are all unique, are not designed specifically for research purposes and their use in research causes problems from permissions to access the data, to the quality of the data in them and finally permissions to publish results from them. In addition, problems with registrations of hospital stays and surgeries taking place within the first days after birth were found in many registries.

Problems Overcome: Establishing a common data model so that all required variables had the same name and formatting in each database was extremely time consuming and required close collaboration with people with a detailed knowledge of their Health Care Databases. However, once completed it enabled each analysis program to run simply and quickly on every database. This ensured standardisation of data and analytic methods as well as simplifying the subsequent pooling of data across registries. Having data from many registries for children born from 1995–2014 meant that, despite excluding years with less accurate data using pre-set data quality criteria, sufficient data were available for analysis. Several registries needed to apply stringent data suppression criteria before data could be extracted from their data safe havens and additional analysis programs were written to do this automatically.

## Conclusion

EUROLINKCAT has demonstrated that linking data on children with congenital anomalies from population based EUROCAT registries to Health Care Databases allows valuable information on longterm mortality and morbidity outcomes and the burden of disease during childhood for these children to be obtained. The methodology developed, including the Common Data Models, are freely available and will be a useful resource for future research.

## Professional Posters

POSTER NUMBER	POSTER CATEGORY	TITLE	AUTHORS
PROF 1.	Professional	Cardiovascular abnormalities as one of the main signs of Williams syndrome	Galagan V. <sup>1</sup> , Zhovnir V. <sup>2</sup> , Tsyhankova M. <sup>1</sup> , Kurakova V. <sup>1</sup> , Mykhailova D. <sup>1</sup> , Cherevasho V. <sup>1</sup> , Olifir O. <sup>1</sup> , Zhurakhovska O. <sup>1</sup> <i><sup>1</sup>National Children's Specialized Hospital "OKHMATDYT" of Ministry of Health of Ukraine, Specialized Center of Medical Genetics, Kyiv, Ukraine; <sup>2</sup>National Children's Specialized Hospital "OKHMATDYT" of Ministry of Health of Ukraine</i>
PROF 2.	Professional	Non-syndromic forms of congenital heart defects in children: frequency, structure, prenatal diagnosis	Dudierina Y. <sup>1</sup> , Govseev D. <sup>1</sup> , Galagan V. <sup>2</sup> , Kurkevych A. <sup>3</sup> , Datsko O. <sup>1</sup> , Olifir O. <sup>2</sup> <i><sup>1</sup>Communal non-commercial enterprise "Kyiv city maternity hospital №5", Kyiv, Ukraine; <sup>2</sup>National Children's Specialized Hospital "Okhmatdyt", The Center of Medical Genetics; <sup>3</sup>Government Agency" Scientific Practical Medical Centre of Pediatric Cardiology and Cardiac Surgery"</i>
PROF 3.	Professional	The impact of the COVID-19 pandemic on cleft care	Rossetti G. <sup>1</sup> , Battista V.M.A. <sup>1</sup> , Meazzini M.C. <sup>1</sup> , Autelitano L. <sup>1</sup> <i><sup>1</sup>Cleft lip and palate regional center, Operation Smile, S.Paolo Hospital, Milano</i>
PROF 4.	Professional	The impact of Covid 19 pandemic on Cleft Patients travelling to the Milan Cleft Centre	Battista V.M.A. <sup>1</sup> , Rossetti G. <sup>1</sup> , Meazzini M.C. <sup>1</sup> , Autelitano L. <sup>1</sup> <i><sup>1</sup>San Paolo Hospital Milan, Italy, Maxillofacial Department, Cleft Unit, Operation Smile</i>
PROF 5.	Professional	The essence of neuro-speech therapy care in working with a newborn with Down syndrome and their parents	Niemyska P.
PROF 6.	Professional	Folic acid supplementation in the Congenital Anomalies population-based registry in a Spanish Region	Barrachina-Bonet L. <sup>1</sup> , García-Villodre L. <sup>1</sup> , Arribas-Díaz B. <sup>1</sup> , Ruiz-Palacio A. <sup>1</sup> , Páramo-Rodríguez L. <sup>1</sup> , Guardiola-Villarrog S. <sup>1,2</sup> , Zurriaga O. <sup>1,2</sup> , Caverro-Carbonell C. <sup>1</sup> <i><sup>1</sup>Rare Diseases Joint Research Unit, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region – Valencia University (FISABIO-UVEG), Valencia, Spain; <sup>2</sup>Public Health Regional Health Administration, Generalitat Valenciana, Valencia, Spain</i>
PROF 7.	Professional	Congenital Anomalies and assisted conception in the population-based Registry from the Valencian Region (Spain)	García-Villodre L. <sup>1</sup> , Barrachina-Bonet L. <sup>1</sup> , Ruiz-Palacio A. <sup>1</sup> , Arribas-Díaz B. <sup>1</sup> , Páramo-Rodríguez L. <sup>1</sup> , Guardiola-Villarrog S. <sup>1,2</sup> , Zurriaga O. <sup>1,2</sup> , Caverro-Carbonell C. <sup>1</sup> <i><sup>1</sup>Rare Diseases Joint Research Unit, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region – Valencia University (FISABIO-UVEG), Valencia, Spain; <sup>2</sup>Public Health Regional Health administration, Generalitat Valenciana, Valencia, Spain</i>
PROF 8.	Professional	Osteogenesis Imperfecta, in less than one-year olds, in the Valencian Region (Spain)	Arribas-Díaz B. <sup>1</sup> , García-Villodre L. <sup>1</sup> , Ruiz-Palacio A. <sup>1</sup> , Barrachina-Bonet L. <sup>1</sup> , Páramo-Rodríguez L. <sup>1</sup> , Rico J. <sup>1</sup> , Guardiola-Villarrog S. <sup>1,2</sup> , Zurriaga O. <sup>1,2</sup> , Caverro-Carbonell C. <sup>1</sup> <i><sup>1</sup>Rare Diseases Joint Research Unit, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region – Valencia University (FISABIO-UVEG), Valencia, Spain; <sup>2</sup>Public Health Regional Health Administration, Generalitat Valenciana, Valencia, Spain</i>
PROF 9.	Professional	Oesophageal Atresia in the Valencian Region (Spain): prevalence and sociodemographic study	Ruiz-Palacio A. <sup>1</sup> , Agurto-Ramirez A. <sup>1</sup> , García-Villodre L. <sup>1</sup> , Arribas-Díaz B. <sup>1</sup> , Barrachina-Bonet L. <sup>1</sup> , Páramo-Rodríguez L. <sup>1</sup> , Rico J. <sup>1</sup> , Guardiola-Villarrog S. <sup>1,2</sup> , Zurriaga O. <sup>1,2</sup> , Caverro-Carbonell C. <sup>1</sup> <i><sup>1</sup>Rare Diseases Joint Research Unit, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region – Valencia University (FISABIO-UVEG), Valencia, Spain; <sup>2</sup>Public Health Regional Health administration, Generalitat Valenciana, Valencia, Spain</i>

PROF 10.	Professional	Variability of genetic defect in Polish patients with aniridia	Wawrocka A. <sup>1</sup> , Kuchalska K. <sup>2</sup> , Krawczyński M.R. <sup>1,3</sup> <i><sup>1</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poland; <sup>2</sup>Student Scientific Society of Medical Genetics, Department of Medical Genetics, Poznan University of Medical Sciences, Poland; <sup>3</sup>Centers for Medical Genetics GENESIS, Poznań, Poland</i>
PROF 11.	Professional	Cytogenetic tests in newborns hospitalised in a multidisciplinary reference hospital: indications and results – the experience of our center	Wicher D. <sup>1</sup> , Kowalczyk M. <sup>1</sup> , Skórka A. <sup>1,2</sup> , Markowska K. <sup>1</sup> , Urbańska K. <sup>1</sup> , Zduńczyk K. <sup>1</sup> , Chrzanowska K. <sup>1</sup> , Pleskaczyńska A. <sup>3</sup> , Wójcicka-Kowalczyk K. <sup>3</sup> , Gradowska K. <sup>3</sup> , Czech-Kowalska J. <sup>3</sup> , Młynek M. <sup>1</sup> <i><sup>1</sup>Department of Medical Genetics, Children's Memorial Health Institute, Warsaw, Poland; <sup>2</sup>Department of Pediatrics, The Medical University of Warsaw, Warsaw, Poland; <sup>3</sup>Department of Neonatology and Neonatal Intensive Care, Children's Memorial Health Institute, Warsaw, Poland</i>
PROF 12.	Professional	Multidisciplinary medical care in patients with cranioectodermal dysplasia	Walczak-Sztulpa J., Latos-Bieleńska A. <i>Department of Medical Genetics, Poznan University of Medical Sciences, Poland</i>
PROF 13.	Professional	Different types of aberrations at 7q21.2-q21.3 locus in patients affected with isolated or syndromic form of split-hand/foot malformation – genotype-phenotype correlation	Sowińska-Seidler A. <sup>1</sup> , Socha M. <sup>1</sup> , Materna-Kiryłuk A. <sup>1,2</sup> , Jamsheer A. <sup>1,2</sup> <i><sup>1</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poland; <sup>2</sup>Centers for Medical Genetics GENESIS, Poznan, Poland</i>
PROF 14.	Professional	Targeted next-generation sequencing in the diagnosis of craniosynostoses	Bukowska-Olech E. <sup>1</sup> , Adamek Z. <sup>2,6</sup> , Dominiak P. <sup>2,6</sup> , Glista F. <sup>2,6</sup> , Larysz D. <sup>3</sup> , Koczyk G. <sup>5,6</sup> , Popiel D. <sup>5</sup> , Materna-Kiryłuk A. <sup>1,5</sup> , Jamsheer A. <sup>1,5</sup> <i><sup>1</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poznan, Poland; <sup>2</sup>Medical student, Poznan University of Medical Sciences, Poznan, Poland; <sup>3</sup>Department of Head and Neck Surgery for Children and Adolescents, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland; <sup>4</sup>Centers for Medical Genetics GENESIS, Poznan, Poland; <sup>5</sup>Biometry and Bioinformatics Team, Institute of Plant Genetics, Polish Academy of Sciences, Poznan, Poland; <sup>6</sup>These authors have contributed equally to this work</i>
PROF 15.	Professional	Rapid whole-exome sequencing as a diagnostic tool in a neonatal/pediatric intensive care unit	Biela M. <sup>1</sup> , Śmigiel R. <sup>1</sup> , Rydzanicz M. <sup>2</sup> , Płoski R. <sup>2</sup> <i><sup>1</sup>Department of Familial and Pediatric Nursing, Wrocław Medical University, Wrocław, Poland; <sup>2</sup>Department of Medical Genetics, Medical University of Warsaw, Poland</i>
PROF 16.	Professional	The results of multiple hereditary exostoses' molecular screening	Szymczak A. <sup>1</sup> , Bukowska-Olech E. <sup>2</sup> , Piechota M. <sup>3</sup> , Jamsheer A. <sup>2,3</sup> <i><sup>1</sup>Medical student, Poznan University of Medical Sciences, Poland; <sup>2</sup>Centers for Medical Genetics GENESIS, Poznan, Poland; <sup>3</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poland; <sup>4</sup>These two authors contributed equally to this work</i>
PROF 17.	Professional	The evaluation of given parameters of sight organ, especially morfological changes of cornea in Williams syndrome patients	Musiorska M. <sup>1</sup> , Trapkowski A. <sup>2</sup> <i><sup>1</sup>Świat Oka, Warszawa, Poland; <sup>2</sup>NZOZ OKO, Gdynia, Poland</i>

PROF 18.	Professional	Medical imaging of anatomical changes in Mayer-Rokitansky-Kuster-Hauser syndrome	Podkowa P. <sup>1</sup> , Tuczyńska N. <sup>1</sup> , Białek M. <sup>1</sup> , Kucharska M. <sup>1</sup> , Skoczylas M.M. <sup>2</sup> , de Sousa N.M. <sup>3</sup> , Rudnicki J. <sup>4</sup> , Poncyłjusz W. <sup>2</sup> <i><sup>1</sup>Student Scientific Circle on Diagnostic Imaging of Rare Diseases, Department of Diagnostic Imaging and Interventional Radiology, Pomeranian Medical University in Szczecin; <sup>2</sup>Hospital Dr José Maria Grande, Unidade Local de Saúde do Norte Alentejano (ULSNA), Portalegre (Portugal); <sup>3</sup>Department of Diagnostic Imaging and Interventional Radiology, Pomeranian Medical University in Szczecin; <sup>4</sup>Department of Humanities in Medicine, Pomeranian Medical University in Szczecin</i>
PROF 19.	Professional	Polish Registry of Congenital Malformations as a rare disease registry and a partner for the Polish Registry of Rare Diseases	Latos-Bieleńska A. <sup>1</sup> , Wiśniewska K. <sup>2</sup> , Materna-Kiryłuk A. <sup>1</sup> , Jamry-Dziurla A. <sup>1</sup> , Jamsheer A. <sup>1,3</sup> , Wiśniewska M. <sup>1,3</sup> , Badura-Stronka M. <sup>1,3</sup> , Glazar R. <sup>1</sup> , Matuszewska K. <sup>3</sup> , Wolnik-Brzozowska D. <sup>3</sup> , Śmigiel R. <sup>4</sup> , Wierzbza J. <sup>5</sup> , Haus O. <sup>6</sup> , Chrzanowska K. <sup>7</sup> , Obersztyn E. <sup>8</sup> , Ślęzak R. <sup>9</sup> , Posmyk R. <sup>10</sup> , Wojciechowska K. <sup>11</sup> , Jaszczuk I. <sup>12</sup> , Krawczyński M. <sup>1,3</sup> <i><sup>1</sup>Chair and Department of Medical Genetics, Poznan University of Medical Sciences, Poznan, Poland; <sup>2</sup>Epidemiology Unit, Department of Preventive Medicine Poznan, University of Medical Sciences, Poznan, Poland; <sup>3</sup>Centers for Medical Genetics GENESIS, Poznan, Poland; <sup>4</sup>Department of Paediatrics, Division of Propaedeutic of Paediatrics and Rare Disorders, Medical University, Wrocław, Poland; <sup>5</sup>Department of Internal and Pediatric Nursing, Medical University of Gdansk, Poland; <sup>6</sup>Department of Clinical Genetics, Faculty of Medicine, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń, Poland; <sup>7</sup>Department of Medical Genetics, The Children's Memorial Health Institute, Warsaw, Poland; <sup>8</sup>Department of Medical Genetics, Institute of Mother and Child, Warsaw, Poland; <sup>9</sup>Department of Genetics, Wrocław Medical University, Wrocław, Poland; <sup>10</sup>Department of Clinical Genetics, Medical University of Białystok, Białystok, Poland; <sup>11</sup>Laboratory of Genetic Diagnostic, Medical University of Lublin, Lublin, Poland; <sup>12</sup>Department of Paediatric Haematology, Oncology and Transplantology, Children Clinical Hospital, II Dept. of Paediatrics, Medical University, Lublin, Poland</i>
PROF 20.	Professional	Prenatal diagnosis and genetic counselling of Fraser syndrome: a case report	Olifir O. <sup>1,3</sup> , Gryshuk Y. <sup>1</sup> , Denysova O. <sup>1</sup> , Galagan V. <sup>2</sup> , Tsyhankova M. <sup>2</sup> <i><sup>1</sup>National Children's Specialized Hospital "OKHMATDYT" of Ministry of Health of Ukraine, Specialized Center of Medical Genetics, Division of Prenatal Diagnostic Kyiv, Ukraine; <sup>2</sup>National Children's Specialized Hospital "OKHMATDYT" of Ministry of Health of Ukraine, Specialized Center of Medical Genetics, Clinical Diagnostics Division Kyiv, Ukraine; <sup>3</sup>Shupyk National Healthcare University of Ukraine</i>
PROF 21.	Professional	Coexistence of de novo complex chromosomal rearrangement between chromosomes 3, 5 and 9 and interstitial deletion of chromosome 4 in a patient with congenital anomalies – case report	Repczyńska A. <sup>1</sup> , Łazarczyk E. <sup>1</sup> , Jułga K. <sup>1</sup> , Sowińska-Seidler A. <sup>3</sup> , Jamsheer A. <sup>2,3</sup> , Latos-Bieleńska A. <sup>2,3</sup> , Haus O. <sup>1</sup> <i><sup>1</sup>Department of Clinical Genetics, Faculty of Medicine, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland; <sup>2</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poznan, Poland; <sup>3</sup>Center of Medical Genetics, Genesis SA, Poznan, Poland</i>
PROF 22.	Professional	Risk factors for microcephaly with congenital CNS malformations based on Polish Registry of Congenital Malformations (PRCM) data	Jaroszewska-Swiątek B. <sup>1</sup> , Wisniewska K. <sup>2</sup> , Więckowska B. <sup>3</sup> , Pawłowicz M. <sup>4</sup> , Materna-Kiryłuk A. <sup>5</sup> <i><sup>1</sup>University of Warmia&amp;Mazury, Regional Specialized Children's Hospital in Olsztyn, Poland; <sup>2</sup>Epidemiology Unit, Department of Preventive Medicine Poznan, Poznan University of Medical Sciences, Poznan, Poland; <sup>3</sup>Department of Computer Science and Statistics, Poznan University of Medical Sciences, Poland; <sup>4</sup>Department of Pediatric Neurogenetics and Rare Diseases, University of Warmia&amp;Mazury, Regional Specialized Children's Hospital in Olsztyn, Poland; <sup>5</sup>Chair and Department of Medical Genetics, Poznan University of Medical Sciences, Poland</i>

PROF 23.	Professional	Caregiver reported barriers in utilization of medical and rehabilitation services for children with congenital and developmental disorders resident in rural areas in Maharashtra, India	Radhakrishnan B., Kar A. <i>Birth Defects and Childhood Disability Research Centre, Pune, India</i>
PROF 24.	Professional	Neonatal and infant mortality associated with spina bifida: a systematic review	Ho P.S.Y. <sup>1</sup> , Quigley M. <sup>1</sup> , Tatwavedi D. <sup>2</sup> , Britto C. <sup>3</sup> , Kurinczuk J. <sup>1</sup> <i><sup>1</sup>National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford; <sup>2</sup>Radcliffe Department of Medicine, University of Oxford; <sup>3</sup>Oxford Vaccine Group, University of Oxford</i>

**PROF 1.****Cardiovascular abnormalities as one of the main signs of Williams syndrome**

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**Introduction**

Williams syndrome (WS) affects approximately one in 10 000 people and is caused by the deletion of genes on chromosome 7q11.23. The deletion includes 26–28 genes and is almost always de novo; however, familial cases have been reported. WS is characterised by dysmorphic facies (100%), cardiovascular disease (80%), intellectual disability (75%), a characteristic cognitive profile (90%), and idiopathic hypercalcemia (15% to 45%). The most common cardiovascular abnormalities are supravalvular aortic stenosis (SVAS) and/or stenosis of the main or branch pulmonary arteries. Other structural cardiac abnormalities include ventricular septal defect (VSD), mitral valve prolapse and aortic insufficiency.

**Objectives, materials and methods**

Genetic counselling was conducted in the Specialized Center of Medical Genetics at the National Children's Specialized Hospital „OKHMATDYT” of the Ministry of Health of Ukraine (SCMG) in Kyiv (Ukraine). In the period 2018–2020, consultations were made for 35 children with WS. The cytogenetic examination included G-banding karyotyping according to the standard method of chromosomes differential staining. The FISH using locus-specific DNA-probes was applied to verify the microdeletion. The standard cytogenetic preparations were examined using the Nikon E400 microscope and FISH – with the Nikon E600 fluorescence microscope (Japan).

**Results**

The sex distribution was 14 girls and 21 boys. The average birth weight was 2750 g, average length 49 cm. The mean age of confirmation of the diagnosis coincided with the initial consultation with a geneticist and was 3 years 1 month. All children were diagnosed with typical facial features – a broad forehead, a stellate iris pattern, periorbital fullness, short nose, flat bridge of the nose, full cheeks, long philtrum, a small delicate chin, wide mouth. Cardiovascular abnormalities were present in 80% of cases. Supravalvular aortic stenosis was found in 43% of cases, peripheral pulmonary artery stenosis in 29%, supravalvular pulmonary stenosis in 34%, long-segment stenosis of the thoracic aorta in 9% and VSD in 3%.

Of these, a combination of  $\geq 2$  cardiac abnormalities occurred in 34% of cases. Intellectual disability of varying degrees was present in 85% of cases. Additional signs and symptoms of WS were muscular hypotonia (48%) hearing impairment (6%), inguinal hernia (14%) and joint laxity (10%).

**Conclusions**

Various organs and systems are affected in WS. The medical management of children with WS requires a multidisciplinary team. Cardiovascular abnormalities are present in a large majority of patients. The most common heart abnormalities are supravalvular aortic stenosis, peripheral pulmonary artery stenosis and supravalvular pulmonary stenosis.

**PROF 2.****Non-syndromic forms of congenital heart defects in children: frequency, structure, prenatal diagnosis**

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**Introduction**

Congenital heart defects (CHDs) are the most common pathology in childhood, accounting for up to 20% of all stillbirths and 30% of neonatal deaths. Despite significant progress in understanding the mechanisms involved in heart formation, the causes remain unclear in most cases and require the study of epidemiological characteristics and the interaction of genetic and environmental factors. Timely prenatal diagnosis of cardiovascular defects remains relevant today.

**Objectives**

The aim of the work was to determine the frequency of isolated forms of CHDs among live births, analysis of data on the type of CHDs and the results of prenatal diagnosis.

**Materials and methods**

The work was performed for the period 2018–2020. A multidisciplinary team of obstetricians – gynaecologists, cardiologists, specialists in ultrasound diagnostics and genetics took part in the study. An isolated heart defect was confirmed by echocardiographic examination in 743 neonates born in Kyiv. Clinical, instrumental and laboratory methods were used to verify this diagnosis

and to exclude syndromic forms of CHDs. Ultrasound of the heart was performed on a Philips expert device – EPIQ 7; cytogenetic examination of newborns – on blood lymphocytes by standard methods (G-method of differential staining of chromosomes) and FISH method using locus-specific DNA probes – Vysis Di George Region Probe- LSY TUPLE1 Spectrum Orange / LSI ARSA Spectrum Green and others, to exclude chromosomal pathology, including microdeletion syndromes. If a syndromic form of CHD was suspected, a geneticist was consulted.

### Results

The frequency of isolated forms of CHDs (per 1,000 live births) in the city of Kyiv for the period 2018–2020 was 9.2, 9.6, 7.6, respectively, which is consistent with the data of other clinics. The share of isolated CHDs among all congenital anomalies in newborns in the city of Kyiv was 33.8% in 2018, 34.8% in 2019, 26.4% in 2020. The structure of non-syndromic forms of CHDs in newborns was: ventricular septal defect (VSD) – 41.3%, transposition of great arteries (TGA) – 10.2%, coarctation of the aorta (CoA) – 7.8%, atrium septum defect (ASD) – 4.2%. The proportion of severe isolated CHDs among all heart defects was 28.7%.

The analysis of obstetric history data of prenatally diagnosed isolated CHDs showed that in 50% of cases a heart defect was diagnosed for the first time by an outpatient ultrasound doctor, and then referred to a specialised cardiologic centre. The gestational age at which the CHD was confirmed corresponded to 22–23 + 5.04 gestational weeks.

### Conclusions

Given the frequency of isolated CHDs among live births, and their significant proportion among all anomalies, each pregnant woman should undergo an ultrasound examination in a specialised cardiology facility and in the case of diagnosed CHD, genetic counselling to exclude syndromic forms of pathology.

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### PROF 3.

## The impact of the COVID-19 pandemic on cleft care

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### Introduction

The COVID-19 pandemic has had multiple effects on the provision of health care, including the suspension of elective and nonessential surgeries and delay in essential surgeries.

### Objectives

The objective of this study was to investigate the early effect of the COVID-19 pandemic on case volume, surgical timing and operational aspects of cleft surgical procedures.

### Materials and Methods

A retrospective comparative study of cleft surgical care in 2019 (the pre-pandemic cohort) and 2020 (the COVID-19 cohort) was conducted. All patients who underwent cleft surgical procedures were included in the analysis. Procedures were divided into two groups. Group 1 primary procedures: cleft lip repair, cleft lip and soft palate repair, cleft lip soft and hard palate repair (all in one), palate repair, gingivoperiostoplasty and hard palate repair. Group 2 secondary procedures: bone graft, rhinoplasty, velopharyngeal insufficiency surgery, orthognathic surgery, lip scar revision. Variables investigated in this study included: surgical volume, protocol changes, delay time, duration of hospitalisation.

### Results

The number of patients who underwent primary procedures was stable in 2019 and 2020 (75 and 70 respectively). However, the number of patients who underwent secondary procedures significantly decreased in 2020 (37 patients) if compared to 2019 (67 patients).

The mean age at primary surgery in pre-pandemic and pandemic cohorts didn't change. The mean age at cleft lip repair with or without palate repair was 6 months, at palate repair 8 months, at gingivoperiostoplasty and hard palate repair 24 months. No delay on primary surgery was registered in the pandemic cohort.

The analysis of the duration of hospitalisation showed that after correction of cleft palate with or without cleft lip duration did not change, as adequate sucking takes an average of 4 days after surgery to become normal. A reduction in hospitalisation time after correction of cleft lip, without cleft palate during the pandemic period was found (3 days instead of 5 days). This is due to the use of resorbable sutures during the period of the pandemic. No change was found after gingivoperiostoplasty and hard palate repair (3 days in each cohort).

### Conclusions

The COVID-19 pandemic caused delays of cleft lip and/or palate related procedures; however, only secondary surgeries were significantly affected. This study emphasises the importance of prioritising primary surgery and adapting to the health emergency protocol to ensure a safer treatment plan for the patient.

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#### PROF 4.

### The impact of Covid 19 pandemic on Cleft Patients travelling to the Milan Cleft Centre

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#### Introduction

The Covid-19 was first described in Europe in the Northern area of Italy, at the end of February 2020. The impact on the Italian Public Health System and consequently on patients had multiple aspects, one of those was that travel around the country was restricted.

#### Objectives

The aim of this study was to compare cleft patients travelling to the Milan Cleft Centre in 2019 and in 2020 to understand the impact of the Pandemic on the access to care of cleft patients who chose the Milan Cleft Centre.

#### Material and Methods

A retrospective comparative study was carried out. We recruited patients who underwent surgery in Milan Cleft Centre in 2019 (pre-pandemic cohort) and 2020 (Covid 19 Cohort).

We divided the patients into two groups according to the type of surgery:

- 1) Primary Surgery
- 2) Secondary surgery

We collected the place of origin of the patients and divided it into four areas based on the distance from Milan:

- 1) Province of Milan
- 2) North of Italy
- 3) Centre of Italy
- 4) South of Italy, islands and foreign Countries

We divided the years into four periods according to the lockdown in 2020:

- 1) Jan–Feb
- 2) Mar–May (lockdown)
- 3) June–Sept
- 4) Oct–Dec (lockdown)

#### Results

Primary Cases:

The number of patients was stable in 2019 and 2020 (75 and 70 respectively)

Travelling around the country was almost stable and, in some periods, and was increased in the Covid 19 Cohort (2020) compared to the pre-pandemic Cohort (2019).

Secondary Cases:

The number of patients decreased in 2020 (37 patients) compared to 2019 (67 patients) and the travelling around the country was stable in the two cohorts.

#### Conclusions

The Covid-19 Pandemic didn't impact the number of surgical treatments of primary cases but affected secondary surgery. The pandemic had no impact on the access to care for cleft patients who chose to move around the country for health reasons.

#### PROF 5.

### The essence of neuro-speech therapy care in working with a newborn with Down syndrome and their parents

Niemyska P.

#### Introduction

We live in a time when perinatal and postnatal care is an area that is visibly moving forward, caring more and more for the wellbeing of parents and their newborn babies.

In terms of caring for the parents of newborns with Down syndrome, there are attempts to meet their real needs – a sense of security, psychological care and instructions on how to take care of their disabled child during the first days and weeks of life.

The first weeks and months in the life of a child with Down syndrome are doubly important. Firstly, it is the time when parents become familiar with their child, his disability and their new life situation. Secondly, it is a time that largely influences the further functioning of the child with Down syndrome.

However, much remains to be done. For example, in the field of early stimulation of the newborn with Down syndrome, not all parents are informed in the hospital about the process of caring for their child, which is also a stimulus for development. From my conversations with parents of children with Down syndrome, it appears that they did not receive in the hospital full instructions and necessary guidance that go beyond the area of primary paediatric care, and are equally important in the case of children with Down syndrome.

One area that is underresearched is activities in the field of neurologopedic care – that is examining the functions of the oral system of a newborn, examining the way the newborn consumes food, identifying possible causes of feeding difficulties reported by parents, giving parents instructions on how to work with the child at home in order to give them the opportunity to gain new experiences and skills.

What would such an early parent education (while still in the postpartum hospital) do for parents of a newborn with Down syndrome? How could it minimise the risk of feeding difficulties? How could it improve the work of the muscles of the mouth, lips and tongue, which

are often in abnormal tension? Early parent education could facilitate the involvement of parents in their role and have a positive impact on building relationship with the child, which may be difficult for parents in the initial period due to their baby's disability. And finally, it would have a positive effect on the functions of the oral system – which translates later into the ability to speak, one of the main difficulties of people with Down syndrome.

It is our social responsibility to educate parents on how they can work in the first weeks of their child's life with Down syndrome.

My postulates are based on observation of the environment of people with Down syndrome and their families, on cooperation and interviews with parents, on the knowledge resulting from specialised training, public reports on problems of families of children with Down syndrome and the available literature on the topic.

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#### PROF 6.

### Folic acid supplementation in the Congenital Anomalies population-based registry in a Spanish Region

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#### Introduction

The Congenital Anomalies (CA) population-based registry of Valencian Region (RPACCV) has identified 11353 cases, live births (LB) and stillbirths (SB), between 2007 and 2019 with at least one major CA, diagnosed prenatally or up to 1 year old. Folic Acid supplementation (FAS) in pregnancy is also registered.

#### Objectives

To identify differences in sociodemographic and clinical characteristics as well as in CA presentation, in cases from RPACCV according to prenatal FAS.

#### Materials and Methods

A cross-sectional study was performed using the RPACCV to identify exposure to FAS (yes/no) in pregnancies of LB and SB with CA between 2007 and 2019. Pregnancies with unknown exposure were excluded. Percentages and their 95% confidence intervals (95%CI) of sociodemographic and clinical characteristics of the cases were determined and compared according to pregnancy exposure to FAS. Frequency and 95%CI of the different CA groups were identified by exposure.

#### Results

FAS' information was available in 27.9% of cases (n=3165), 47.7% exposed to FAS, 52.3% unexposed to FAS. Differences were found in the following sociodemographic variables (shown as % in exposed cases /% in unexposed): weight <2500 grams and gestational age <36 week at birth (21.0%/30.0%); LB who died before the first year of life (2.6%/9.3%); prenatal diagnosis (32.0%/21.0%); mother older than 35 years (39.4%/29.6%); medicines taken during pregnancy (94.8%/30.2%). Although the association between the exposure to FAS and the number of anomalies per case was not found (proportion ratio, PR=1.0) to be significant, statistically significant differences were found in some CA groups. The proportion of cases (shown as % in exposed cases /% in unexposed) have been higher in exposed to FAS for these groups: Eye (4.4%/1.6%), specifically in congenital cataract; Urinary (16.8%/10.1%), related to congenital hydro-nephrosis; and Limb (13.5%/8.0%), found in club foot and polydactyly. Contrary, in unexposed to FAS: Heart defects (36.9%/52.7%); Digestive (6.4%/10.3%), found in oesophageal atresia; and Abdominal wall defects (0.7%/1.9%), have shown a higher proportion.

#### Conclusions

In Spain, FAS doesn't require a prescription and, as its use is customary in pregnancy, it doesn't seem to be considered as significant drug exposure in pregnancy. Although several studies have identified that FAS prevent some CA, the fact that in only 28% of pregnant women there is information about FAS, highlights the difficulties of its registration in the clinical documentation. However, with the available information, it was identified that children of unexposed pregnant women presented CA from groups with a higher impact on morbidity and mortality.

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#### PROF 7.

### Congenital Anomalies and assisted conception in the population-based Registry from the Valencian Region (Spain)

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#### Introduction

The Congenital Anomalies (CA) population-based Registry of Valencian Region (RPAC-CV) has identified 5690 cases including live births (LB) and stillbirths (SB) during

the 2013–2019 period, confirmed by clinical documentation. The Spanish Fertility Society (SEF) has identified a CA prevalence of 258.2 per 10000 LB from the assisted conception, with a 95% confidence interval (CI) of 251.4–265.0 during 2013–2019.

### Objective

To identify differences in sociodemographic and clinical characteristics between cases with CA according to the type of conception: natural (N) or assisted (A). To determine the CA prevalence in LB in the RPAC-CV.

### Methods

RPAC-CV cases (LB+SB) from 2013 until 2019 were classified as N or A conception, and their sociodemographic and clinical characteristics were compared. Terminations of pregnancy due to CA and cases with no information about the type of conception were excluded. The prevalence per 10000 LB with 95%CI in the RPAC-CV between 2013 and 2019 was calculated.

### Results

Information on conception was available in 58.8% of cases (84.4% N, 15.1% A). Statistically significant differences were found in the following variables (values are shown in %N/%A): multiple pregnancies (6.8%/42.5%); birth before the 37th gestational week (26.5%/50.2%); birth weight less than 2500 grams (26.3%/49.2%); mother older than 30 years (68.1%/94.2%); cases whose mothers were born in Spain (70.6%/85.7%); no folic acid supplementation during pregnancy (1.2%/0.4%); medication during the first trimester (45.1%/55.2%). No association was found between the type of conception and the number of anomalies per case, proportion ratio (PR= 0.9). Furthermore, no differences were found in the proportion of cases per CA group, neither in the proportion of SB nor in the survival of LB during the first year of life. The prevalence of CA per 10000 LB in the RPAC-CV was 196.5 (95%CI: 191.4–201.5).

### Conclusions

The CA prevalence in the RPAC-CV was significantly lower compared to SEF's which has identified assisted conception cases at the national level for the same period. This could be partially due to the fact that SEF includes minor CA and RPAC-CV does not, although differences were overly high. Even so, by analysing natural versus assisted conception, significant differences in case characteristics have been identified in CA. The collection of information on conception in clinical documentation will increase data quality on assisted conception and make available interesting information for the development of health policies and research.

## PROF 8.

### Osteogenesis Imperfecta, in less than one-year olds, in the Valencian Region (Spain)

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### Introduction

Osteogenesis Imperfecta (OI), also known as brittle bone disease, is a rare genetic disorder characterised by low bone mass and bone fragility caused by a congenital defect in collagen production.

### Objective

To describe the characteristics and distribution of OI, diagnosed in less than one-year-olds, born between 2007–2019 in the Valencian Region and to identify its prevalence.

### Methods

Live births (LB), stillbirths(SB) and termination of pregnancy due to fetal anomalies (TOPFA) between 2007 and 2019 diagnosed with OI (code Q78.0 of the International Classification Diseases 10th with British Paediatric Association extension) were selected from the Congenital Anomalies population-based Registry of Valencian Region (RPAC-CV). The prevalence of 10000 births with 95% confidence intervals (95%CI) was calculated for the period and by year, and a descriptive analysis of sociodemographic and clinical variables was performed.

### Results

Fourteen cases were identified, 71.4% were LB, 21.4% TOPFA and 7.1% SB. 10.0% of the live births died during the first year of life. 57.1% were female, 21.4% were male and 21.4% were of unknown sex. 92.9% were simple? pregnancies and 64.3% were diagnosed prenatally. 28.6% had been confirmed by genetic tests, however, 64.3% of the cases had unknown genetic test information. 28.6% had a positive family history for OI. The most common age group of pregnant mothers was 25–29 years old (35.7%), although 42.9% of pregnant women were older than 30 years. The overall prevalence of OI between 2007–2019 in the Valencian Region was 0.2/10000 births (95%CI:0.1–0.4), with 2008 being the year with the highest prevalence (0.5/10000 births). No cases were identified in 2009, 2010, 2012, 2018, or 2019. The prevalence in LB was 0.17/10000 births (95%CI:0.06–0.27), 0.05/10000 births (95%CI:–0.01–0.11) in TOPFA and 0.02/10000 births (95%CI:–0.02–0.05) in SB.

## Conclusions

Although no significant differences were found, the most common age group of pregnant women identified in the Valencian Region is in line with the mean age of mothers obtained in the National Network of Congenital Anomalies of Argentina that was 27.1 years (years 2009–2016) and in the Utah Birth Defect Network that was 26 years (years 1999–2008). However, lower prenatal detection rates were found in the Valencian Region than in those networks. The overall prevalence obtained in the RPAC-CV was lower than the prevalence obtained in all European Network (EUROCAT) Registries over 2007–2019, 0.6/10000 births (CI95%: 0.5–0.6). The difference could be related to the low prevalence of TOPFA in the Valencian Region compared to that of EUROCAT (0.27/10000 births), mainly due to the lack of specific information on diagnoses in TOPFA cases.

### PROF 9.

#### Oesophageal Atresia in the Valencian Region (Spain): prevalence and sociodemographic study

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#### Introduction

Oesophageal atresia (OA) encompasses a group of congenital anomalies (CA) with an interruption in the continuity of the oesophagus, with or without persistent communication with the trachea.

#### Objective

To determine the prevalence of OA and to describe the characteristics and distribution of OA diagnosed in less than one-year-olds, born between 2007 and 2019 in the Valencian Region.

#### Methods

Live births (LB), stillbirths (SB) and termination of pregnancy due to fetal anomalies (TOPFA) between 2007 and 2019, diagnosed with OA with or without tracheo-oesophageal fistula (International Classification Diseases 10th with British Paediatric Association extension codes Q39.0–Q39.1), were selected from the Congenital Anomalies population-based Registry of Valencian Region (RPAC-CV). Prevalence of OA per 10000 births with 95% confidence intervals (95%CI) was calculated, and a distribution study was performed by analysing socio-demographic and clinical variables.

## Results

One hundred and forty-six OA cases were identified in the RPAC-CV, born between 2007 and 2019. The overall prevalence was 2.4/10000 births (95%CI: 2.0–2.8), 2016 was the year with the highest prevalence (3.8/10000 births) and 2014 the year with the lowest (1.6/10000 births) prevalence. Prevalence by type of pregnancy was 2.3/10000 (95%CI: 2.0–2.7) in LB and 0.03/10000 (95%CI: –0.01–0.08) in both SBs and TOPFAs. Diagnosis of OA cases occurred mostly at birth; however, 37.7% of cases were diagnosed prenatally. 13.0% of pregnancies were conceived by assisted conception. Polyhydramnios and gestational diabetes were more frequently observed as gestation-related diseases. 71.2% of the cases were associated with another CA, mainly with a congenital heart defect (CHD), and 15.8% were associated with syndromes. 86.3% of cases required surgery during the first year of life.

## Conclusions

Significant variations in the annual prevalence of OA in the Valencian Region have been detected during the study period. The overall prevalence of OA obtained in the Valencian Region was similar to that of the European Network (EUROCAT) for the same period (2.3/10000 births). However, EUROCAT identified a higher prevalence in SB (0.06/10000 births) and TOPFA (0.13/10000 births), than the Valencian Region. In accordance with several studies, an association between OA cases and CHD has been identified.

### PROF 10.

#### Variability of genetic defect in Polish patients with aniridia

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#### Introduction

Aniridia (MIM:106210) is usually an autosomal dominant, rare congenital ocular disorder that occurs with an incidence of approximately 1 in 40,000–100,000 live births worldwide. In addition to complete or partial iris hypoplasia presenting in early infancy, other clinical manifestations found in aniridia patients include foveal hypoplasia resulting in reduced visual acuity, nystagmus, cataract, keratopathy and glaucoma. Aniridia can occur either as an isolated malformation or as a part of a syndrome, such as WAGR syndrome or Gillespie syndrome.

Pathogenic variants in the PAX6 gene are associated with aniridia in most patients. However, in up to 30% of individuals, the anomaly results from 11p13 chromosomal

rearrangements, either including the entire PAX6 gene or affecting only the 3' regulatory enhancers, or encompassing PAX6, and other neighbouring genes like WT1 (WAGR syndrome). In connection to the great variability of the genetic mechanisms involved in aniridia, molecular analysis of the patients is performed by combining: Sanger sequencing, MLPA analysis, and array genomic hybridization (aCGH). Although the intragenic PAX6 gene mutations are more common than microdeletions, in newborns affected with aniridia the analysis toward deletions is recommended first, due to the clinical importance of early WAGR syndrome identification.

### Objectives

The aim of the study was to determine the underlying genetic defect of the disease in 22 Polish patients with aniridia.

### Materials and Methods

Twenty-two unrelated patients with a clinical diagnosis of aniridia were screened for the presence of microdeletions in the 11p13 region by means of MLPA analysis. In two patients, aCGH was performed. Furthermore, all coding and flanking intronic regions of PAX6 were Sanger sequenced in all probands. In one patient, WGS (Whole Genome Sequencing) analysis was also conducted.

### Results

PAX6 sequence analysis showed eight different point variants in 10 patients with aniridia. In six patients, heterozygous deletions of the downstream flanking region of the PAX6 gene were detected. In one case, the deletion included the WT1 gene, which confirmed the diagnosis of WAGR syndrome. In the last patient, we reported a novel homozygous deletion located in the 11p13 region, which does not include the PAX6 gene or any known PAX6 enhancers.

### Conclusion

The results show the diversity of the molecular basis of aniridia. It varies from point mutations to different size deletions in the 11p13 region. Furthermore, for the first time, we report the case of a patient presented with isolated aniridia carrying a homozygous microdeletion downstream of the PAX6 gene.

The molecular diagnosis of aniridia is crucial to determine the risk of Wilms' tumour, as well as for estimation of aniridia risk recurrence (in sporadic and familial cases) and reliable genetic counselling of families. Furthermore, it will allow gene-specific therapy in the future.

## PROF 11.

### Cytogenetic tests in newborns hospitalised in a multidisciplinary reference hospital: indications and results – the experience of our center

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### Introduction

Birth defects affect 2–4% of newborns and they are often detected prenatally or in the first weeks/months of life. Known causes of congenital anomalies include single gene defects, chromosomal disorders, multifactorial diseases, infections and environmental teratogens.

### Objective

A retrospective analysis of indications and results of cytogenetic diagnostics at the Department of Neonatology and Neonatal Intensive Care (NNICD) with the aim to detect a rate of chromosome abnormalities in patients with congenital anomalies

### Materials and Methods

The data on cytogenetic tests [GTG-banded karyotype, FISH (CytoCell), array CGH (Agilent Technologies 60K and 180K)] ordered by clinicians from NNICD in the period from January 2019 to December 2021 were collected. The number of tests, indications and results of identification of chromosomal abnormalities among children with congenital anomalies were analysed.

### Results

During the study period, cytogenetic tests: karyotype (n=55), FISH (n=8) and array CGH (n=69) were ordered in 123 patients. The most common indications for cytogenetic tests were: multiple congenital anomalies (n=22), brain defects (n=18), heart defects and/or deletion 22q11.2 suspicion (n=18) sex differentiation disorders/ambiguous genitalia (n=14), trisomies (n=14) and dysmorphic features (n=10).

Chromosomal aberrations were found in 36/123 (29%) patients. Abnormal results were obtained in 20/55 karyotypes (36%), in 2/8 FISH (25%) and in 14/69 aCGH (20%). Trisomy 21 was confirmed in 11 patients (in 1 due to Robertsonian translocation), trisomy 18 in two, and trisomy 13 in one patient. Monosomy X was found in two patients (one in mosaic form: 45,X/46,XY). Complex, unbalanced chromosomal aberration as a result of translocation was detected in 4 patients. Detected microdeletions and microduplications concerned regions: 3p25.2;

5p13.2; 9p24.1p22.2; 9p24.3; 15q11.2 (Prader-Willi syndrome); 15q24.1q24.3; 16p11.2; 21q22.2q21.3; 22q11.2; Xp11.3p11.23; Xp21.1p11.4 and Xp22.31.

## Conclusion

Multiple and isolated congenital anomalies, as well as minor anomalies/dysmorphic features, are common indications for cytogenetic testing in newborns. If a trisomy or known microdeletion syndrome are suspected, the karyotype and/or FISH analysis are sufficient. In other cases, array CGH is a more effective technique, and it is used more and more in clinical practice.

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## PROF 12.

### Multidisciplinary medical care in patients with cranioectodermal dysplasia

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## Introduction

Cranioectodermal dysplasia (CED), is a clinically and genetically heterogeneous disorder characterised by skeletal, craniofacial, and ectodermal abnormalities. CED belongs to a group of disorders known as ciliopathies and is associated with defective cilia function and structure. Cilia are present in most of the human cell types. Ciliopathies are multiorgan disorders usually affecting the kidney, liver, skeleton, heart, and eye. Clinical features include dolichocephaly, craniosynostosis, facial dysmorphism, narrow thorax, limb shortening and brachydactyly. Renal and liver insufficiency have also been associated with this syndrome. To date, six genes have been linked to CED (WDR35, IFT122, IFT140, IFT144, IFT52, and IFT43).

## Objectives

To report on clinical and molecular examination of patients with cranioectodermal dysplasia.

## Materials and Methods

14 CED patients from 11 independent families. Genetic analysis performed in affected individuals revealed the presence of variants in the WDR35 (10 patients), IFT140 (2 patients) and IFT122 (2 patients) genes.

## Results

CED is a multiorgan disorder. Due to the complex phenotype affected individuals require multidisciplinary medical care. These include:

Surgeon. Surgical correction in patients with inguinal/umbilical hernias and polydactyly of hands and feet.

Neurosurgeon. Head computed tomography (CT) examination in patients with dolichocephaly is needed to diagnose craniosynostosis. Surgery to correct premature suture(s) synostosis is usually performed in the first year of life.

Nephrologist. Renal disease is a common feature in CED-affected individuals, therefore those patients should be under regular kidney function monitoring. This includes renal ultrasound examination, serum creatinine and blood urea concentration, urinalysis to identify polyuria, osmolality testing of morning urine. Blood pressure should also be monitored.

Hepatologist. Liver ultrasound examination, transaminases, and synthetic liver function tests.

Ophthalmologist. Standard ophthalmologic evaluation including electroretinography (ERG) and funduscopy should be performed at the age of 4 years to detect early signs of retinal degeneration.

Pulmonologist. Standard treatment for patients with recurrent respiratory infections.

Cardiologist. Cardiac examination including an echocardiogram (ECG).

Dentist and orthodontist. Standard treatment for dental anomalies.

Neurologist and physiotherapist. Appropriate physical and speech therapy are needed for patients with developmental delay.

Additional notes: in patients with end-stage renal disease (ESRD) and end-stage of liver disease (ESLD) and organ replacement therapy is recommended. In CED individuals with growth deficiency, a human growth hormone (HGH) therapy may be considered.

## Conclusion

Our long-standing clinical observation of patients with cranioectodermal dysplasia showed that multidisciplinary medical care improves the quality of life of individuals affected by this ultra-rare syndrome.

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## PROF 13.

### Different types of aberrations at 7q21.2-q21.3 locus in patients affected with isolated or syndromic form of split-hand/foot malformation – genotype-phenotype correlation

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## Introduction

Split-hand/foot malformation (SHFM) refers to the group of congenital limb malformations characterised by the absence or hypoplasia of the central rays of the autopods. Eight loci are associated with this clinically and genetically heterogeneous disorder. SHFM type 1 (SHFM1) maps to 7q21.2-q21.3 and occurs in an isolated form, or associated with other abnormalities as a part of a multiple congenital anomaly syndrome. In most cases, SHFM1

results from deletions encompassing the DLX5/DLX6 genes or their regulatory elements.

### Objectives

The main objective of the study is to perform the genotype-phenotype correlation in a group of five newly reported and two previously published index cases of Polish origin, affected with SHFM1 that resulted from 7q21.2-q21.3 rearrangements.

### Materials and methods

Chromosome analysis including conventional GTG banding and array-based comparative genomic hybridization (aCGH) were applied to identify the causative aberrations in affected patients. The precise breakpoints of CNVs (copy number variants) were established by a series of qPCRs and Sanger sequencing. Additionally, the whole genome sequencing (WGS) approach was applied to precisely establish the breakpoints of balanced translocations.

### Results

Balanced translocations: t(7;12)(q21.3;q21.3) and t(7;10)(q21.3;q22.2), identified by GTG banding, were detected in the most severely affected patient diagnosed with EEC and developmental delay, and in a patient with bilateral ectrodactyly of the hands and feet and hearing loss, respectively. The latter aberration was also present in the daughter of the index patient, affected with a minimal manifestation of the disorder, characterised by slight shortening of the 2nd and 3rd toe of both feet. WGS confirmed reciprocal translocation in both familial cases and revealed complex rearrangements in the sporadic severely affected case. The aberration included several breakpoints on both chromosomes along with an inverted segment derived from chromosome 7. The established breakpoints in all three cases will be confirmed by Sanger sequencing. Two other sporadic patients affected with isolated ectrodactyly of the feet carried microdeletions spanning less than 200 kb encompassing the limb-specific enhancers within DYNC111. Also, a 4.5 Mb deletion of the 7q21.2-q21.3 region was identified in a sporadic patient diagnosed with EEC syndrome.

### Conclusions

We present the spectrum of abnormalities in SHFM1 cases that depends on the aberration breakpoints, patterns of local interactions, deletion size and its gene/regulatory elements content.

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## PROF 14.

### Targeted next-generation sequencing in the diagnosis of craniosynostoses

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### Introduction

Craniosynostoses (CS) encompass a group of distinct, clinically variable phenotypes. Since the first dysmorphological description of the disease by Wheaton in the late 19th century, researchers have been extensively investigating the molecular background of CS. The first causative gene for this condition was identified by Jabs et al. in 1993, who described a pathogenic variant with in MSX2 in a family affected by autosomal dominant CS. In the next four years, a few novel genes – FGFR1, FGFR2, FGFR3, TWIST1 – have been linked to premature fusion of the cranial sutures. Recently, the development of high-throughput next-generation sequencing (NGS)-based strategies allowed for unravelling of the molecular basis of the condition at an unprecedented scale.

### Objectives

Our study aimed to analyse the molecular background of various CS phenotypes.

### Material and methods

We have examined gDNA isolated from 87 patients affected with CS. We have applied the custom SureSelect (Agilent Technologies) gene panel comprising 61 genes, and 11 SNVs associated with craniofacial malformations. Variants identified by TorrentSuite were further analysed using a custom pipeline, whereas the final pathogenicity of detected alterations was analysed in line with the American College of Medical Genetics (ACMG) classification. Finally, confirmation and segregation studies were performed applying PCR followed by Sanger sequencing.

### Results

Targeted NGS of a custom gene panel allowed us to establish the molecular diagnosis in 14 sporadic patients (15 variants). We have found 15 following heterozygous variants, from which 9 were not reported in HGMD – c.578\_581del p.Thr193Argfs\*137 in the ALX3 gene (variant of unknown significance, VUS), c.491A>G p.Asp164Gly in the EFTUD2 gene, c.394C>T p.Arg132\* in the ERF gene (linked to Craniosynostosis 4), c.868T>G p.Trp290Gly (HGMD no.: CM1313533), c.1025G>A p.Cy-

s342Tyr (HGMD no.: CM940779), c.1694A>G p.Glu565Gly (HGMD no.: CM020141) in the FGFR2 gene (HGMD no.: CM020141), and c.2066C>T p.Thr689Met in the FGFR3 gene, c.356T>C p.Leu119Pro, c.679del p.Met-227Cysfs\*18, c.932C>G p.Ser311\*, c.2015\_2016ins p.Arg672Serfs\*2 in the TCF12 gene (linked to Craniosynostosis 3), c.1172C>A p.Ser391\*, c.1210T>C p.Ser404Pro (VUS) in the ZIC1 gene (linked to Craniosynostosis 6) and two alterations in compound heterozygosity – c.308C>T p.Pro103Leu (HGMD no.: CM033805), and c.3062G>A p.Arg1021Gln (HGMD no.: CM033810) located within the RECQL4 gene (linked to Rothmund-Thomson, Baller-Gerold, and RAPADILINO syndromes).

## Conclusions

We have shown the clinical utility of applied custom gene panel in CS diagnosis. The approach presented here allowed us to achieve high quality NGS data and confirmed molecular diagnosis in 16% of cases, reaching the diagnostic yield similar to some of the published research reports.

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## PROF 15.

### Rapid whole-exome sequencing as a diagnostic tool in a neonatal/pediatric intensive care unit

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## Introduction

Genetic disorders are the leading cause of infant morbidity and mortality. Due to a large number of genetic diseases, molecular and phenotype heterogeneity and often severe course, these diseases remain undiagnosed. In infants with a suspected acute monogenic disease, rapid whole-exome sequencing (rapid-WES) can be successfully performed.

## Material and methods

Rapid-WES (singletons) was performed in 57 unrelated infants with a severe and/or progressing disease with the suspicion of genetic origin hospitalised in an Intensive Care Unit (ICU), which met the inclusion criteria. Blood samples were also collected from the parents. The results from the rapid-WES were available after 5–14 days.

## Results

A conclusive genetic diagnosis was obtained in 34 children, corresponding to an overall diagnostic yield of 59.6%. For 25 patients, rapid-WES was used as a first-tier test. Twenty-four patients were diagnosed with inborn errors of metabolism, of which 50% had mitochondrial

diseases. In four patients, the disease was caused by variants in genes that so far have not been associated with human disease (NFASC, NARS1 and DCAF5) or by ultrarare mutations (TRMT10C). The death rate was 61.4% (35/57) – the main reason for this high rate was the severity of the clinical condition in our cohort.

## Conclusion

Rapid-WES proved to be an effective diagnostic tool for critically ill infants in ICUs suspected of having a genetic disorder. It also should be considered as a first-tier test after precise clinical description. The quickly obtained diagnosis impacts the patient's medical management, and families can receive genetic counselling.

## PROF 16.

### The results of multiple hereditary exostoses' molecular screening

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## Introduction

Hereditary multiple exostoses (HMEs) is a rare orphan disease with unknown prevalence due to asymptomatic individuals that remain undiagnosed. The disease is characterised by multiple benign cartilage-capped bony outgrowths, termed exostoses or osteochondromas, that locate most commonly in the juxta-epiphyseal portions of long bones. Affected individuals usually complain of persistent pain caused by the pressure on neighbouring tissues, disturbance of blood circulation, or rarely by spinal cord compression. However, the most severe complication of this condition is malignant transformation into chondrosarcoma, occurring in up to 3.9% of HMEs patients. HMEs result mainly from heterozygous loss-of-function alterations in the EXT1 or EXT2 genes. Importantly, results from various populations studies have shown that pathogenic variant are usually located within the EXT1 gene.

## Objectives

Our study aimed to analyse the EXT1 gene in 89 patients, who presented phenotype indicative for HMEs.

## Material and methods

The gDNA of 89 probands was subject to targeted PCR followed by Sanger sequencing of the EXT1 gene.

## Results

We detected 27 pathogenic variants located in the EXT1 gene – three intronic, one nonsense, one missense, one in-frame, and 21 frameshift mutations.



## Conclusions

We have shown that 30% of all diagnosed patients harboured pathogenic variants in the EXT1 gene. In the next step of our study, we plan to screen EXT2 gene and genes linked to HMEs' overlapping syndromes such as metachondromatosis (PTPN11 gene), Ollier disease and Maffucci syndrome (IDH1, IDH2; PTH1R genes), fibrodysplasia ossificans progressiva (ACVR1 gene), occipital horn syndrome (ATP7A gene) or Gardner syndrome (APC gene) applying targeted next-generation sequencing of custom gene panel.

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### PROF 17.

## The evaluation of given parameters of sight organ, especially morfological changes of cornea in Williams syndrome patients

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## Introduction

Williams-Beuren syndrome is caused by a microdeletion of a portion of chromosome 7. It is a rare genetic disorder, occurring once in every 6 400 to 20 000 live births. The range of abnormalities depends on the size of the deletion. However, basic structural defects are the same and are caused by the loss of the ELN gene, which encodes a protein called elastin. Elastin deficiency causes structural changes in the walls of arterial vessels of the whole body and other non-vessel structures. Apart from collagen, elastin is the main protein in elastic tissue, originating from the mesodermal germ layer. It has numerous functions. Elastin is an integral part of the eyeball wall, ensuring its shape by balancing out the influence of centripetal and centrifugal forces. The latest research has shown the presence of elastin in other parts of the eye such as lamina cribrosa, cornea and around the trabecular meshwork of Schlemm's canal. The vast majority of people with this disorder are patients of interventional cardiology. Most are also ophthalmological patients due to frequently occurring sight defects and strabismus.

## Material and methods

This publication was inspired by ophthalmological test results done on the author's first cases of patients with Williams syndrome.

## Results

Over seventy people with microdeletion were tested and have shown previously undescribed results. Significant statistical difference of the thickness of the central cornea of people with Williams syndrome (OD 502,986 micrometer;  $p < 0,001$ ; OS 503,729 micrometer;  $p < 0,001$ )

compared to the control group (OD 570,500; OS 571,757) was found. This symptom was connected with a change in the structure of blood vessels in the fundus of the eye. For the purpose of the test, a subjective scale of tortuosity of blood vessels was created, where "zero" is no tortuosity, "one" is slight tortuosity and "two" is intensified tortuosity. The whole study was done by one person which excludes subjective differences in evaluation.

## Results

We found significant statistical differences in the cornea thickness in patients with different tortuosity of the blood vessels. This relation was slightly different for the right eye and left eye, but in both eyes it was statistically significant.

## Conclusion

Pachymetry examination, also known as measuring the thickness of the central cornea, is a non-invasive, cheap and fast test. Hence it can be used as a screening test to diagnose the condition of blood vessels in patients with Williams syndrome.

### PROF 18.

## Medical imaging of anatomical changes in Mayer-Rokitansky-Kuster-Hauser syndrome

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Mayer-Rokitansky-Küster-Hauser syndrome (MRKH syndrome, OMIM % 277000) is an illness, in which there is a failure of development of Müllerian duct, which results in a congenital malformation. Lack of the uterus and the vaginal upper part hypoplasia is specific for this syndrome. This is possible to distinguish several types of MRKH syndrome, including typical MRKH, atypical MRKH and MURCS syndrome. The main symptom is primary amenorrhoea. Examination of patients using ultrasonography and magnetic resonance imaging is the basis of diagnosis as can visualize changes characteristic for MRKH syndrome with the possibility to define types of this syndrome.

The frequency of this illness has an estimated rate of 1 in 4000–5000 of general population women. MRKH syndrome is second most common cause of primary amenorrhoea. Although the syndrome is probably highly un-

derestimated – it is present since birth, but mainly not identified since adolescence. Lack of menstruation is the first reason to begin diagnostics. Also fertility problems may urge to see a doctor.

Accurate diagnosis is made by exclusion of other causes of amenorrhea, because MRKH syndrome is quite rare. When it turns out that none of suspected causes are causing lack of menstruation, it comes to specialized imaging techniques. Transabdominal ultrasonography is an examination of the first choice. It can be supplemented by MRI. Also karyotyping can be performed, but women with MRKH have a standard 46 XY karyotype.

MRKH syndrome is associated with other malformations, when syndrome is suspected or even diagnosed, a holistic examination has to be undertaken to look for other malformations. That means at least a transabdominal ultrasonography and spinal radiography have to be done. Ovarian function is preserved, thus levels of FSH, LH and 17B-oestradiol are within the scope of the norm.

Treatment is based on both psychological support and surgery. Surgery includes creating a neovagina which enables sexual intercourse. Females with MRKH do not have developed uterus, that's why they are unable to have children. Specific comorbidities should be treated in their own way, for example those with unilateral renal agenesis have higher urinary tract infections.

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## PROF 19.

### Polish Registry of Congenital Malformations as a rare disease registry and a partner for the Polish Registry of Rare Diseases

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## Introduction

Approx. 20–25% of rare diseases are associated with congenital anomalies (CA). For this group of rare diseases, CA registers can also be registers of rare diseases. The Polish Registry of Congenital Malformations (PRCM) performs this function in Poland. PRCM is a population-based registry established in 1997 and a member of EUROCAT since 2001. In 2015, PRCM introduced changes significant for its role as a rare disease registry: obligation to report to PRCM, the extension of the reporting age to 18 years, the use of ORPHA codes. It is also important that PRCM covers the entire territory of Poland (since 2008). In 2016, close cooperation with 20 paediatric genetic clinics in Poland was developed, and detailed information on genetic syndromes was received. Since 2018, PRCM has been supplemented with data from the National Health Fund (hospitalisation of children with CA).

This 25 years of PRCM experience was used in the preparation of the Plan for Rare Diseases, and PRCM experts elaborated the PRRD. As part of the Rare Diseases Plan, cooperation between PRCM and PRRD is planned based on the mutual transfer of data on syndromes with the assigned ORPHA code.

## Objectives

To assess PRCM as a source of data on rare diseases associated with CA.

## Materials and Methods

Identification in the PRCM database of children born in Poland in 2015–2021 with rare congenital anomalies and with the assigned ORPHA code. We also included Down syndrome, which is not a rare disease in Poland but is listed in Orphanet. In many countries, it occurs with a prevalence of less than 1/2000 live births, so it meets the criteria for a rare disease. Moreover, people with Down syndrome have similar problems as people with rare syndromes and are in need of coordinated medical care. For these reasons, Down syndrome is also treated as a rare disease in Poland.

## Results

5,145 children born in 2015–2021 with rare congenital anomalies were identified in the PRWWR database. In 2015–2021, 3,378 children with chromosomal anomalies were reported to PRCM, including 2,514 children with Down syndrome, 223 children with Edwards syndrome, 91 children with Patau syndrome, and 19 children with Wolf-Hirschhorn syndrome. Moreover, 567 children were diagnosed with microdeletion and/or microduplication syndrome, including Di George's s. (128 children), Williams s. (31 children), 22q11.2 microduplications (14 chil-

dren). Other specific syndromes that occurred in 1,423 children reported to PRCM in 2015–2021 were: NF (134), TS (100), achondroplasia (79), FAS (74), OI (57), PWS (43), BWS (47), Noonan s. (27), Crouzon s. (18), SLOS (10), CdL (10). In almost all cases clinical diagnosis has been confirmed by genetic tests.

## Conclusion

Due to a large number of cases of rare syndromes collected in the database, PRCM is a partner register for the PRRD under the Polish Plan for Rare Diseases.

### PROF 20.

## Prenatal diagnosis and genetic counselling of Fraser syndrome: a case report

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## Introduction

Fraser syndrome is a rare autosomal recessive genetic disorder presenting: cryptophthalmos, cutaneous syndactyly, malformations of the larynx and agenesis or dysgenesis of the kidneys; Diagnostic algorithm and medical genetic expertise are required to make a diagnosis.

## Case report

A 37-year-old was supervised in our Prenatal Diagnostics Department during 10 years. The woman had two earlier miscarriages. For the period of supervision she had 6 pregnancies and 3 deliveries.

She gave first birth to a male with a birthweight of 2560 g. at 39 weeks of gestation. The baby died in the first hour of life. Postmortem autopsy: absence of the left parietal bone with a left cranial hernia, right cryptophthalmos, left anophthalmia, nasal atresia, laryngeal stenosis, polycystic right kidney, agenesis of the left kidney, syndactyly 2–5 toes and hands, hypotrophy. Karyotype 46, XY. Fraser syndrome was considered clinically.

The fourth pregnancy was planned and supervised by specialists in prenatal diagnostics and medical geneticists. Obstetric ultrasound in the 18th week revealed laryngeal atresia, renal agenesis, ascites and oligohydramnios. The option of invasive prenatal diagnosis and termination of pregnancy was refused by parents. The pregnancy ended with a delivery of male infant with a birthweight of 2300 g at 39 weeks of gestation. The baby died 2 hours after birth due to multiple congenital anomalies. Postmortem autopsy: bilateral cryptorchid-

ism, partially bifid nose, syndactyly 2–5 fingers and toes, laryngeal atresia, renal agenesis.

The fifth pregnancy ended with the delivery of a healthy baby.

The sixth pregnancy was detected within 6 weeks. At follow-up, fetal ultrasonography signs of the missed abortion within 10 weeks are established. Ultrasound of the fetus revealed large nuchal translucency.

## Discussion

Prenatal diagnosis of Fraser syndrome is possible as early as 16–18 weeks of pregnancy and is accomplished by fetal ultrasound. The main criteria for diagnosing Fraser syndrome are oligohydramnios, renal agenesis, evidence of high airway obstruction, syndactyly and craniofacial abnormalities such as cryptophthalmos and deformed ears and nose.

The With positive family history recurrence rate among siblings is 25% and every next pregnancy must be evaluated by a medical geneticist and specialist in prenatal diagnostics. Genetic testing of mutations in FRAS1, FREM2 and GRIP1 genes can be performed for confirmation of diagnosis.

Depending on the severity of inborn defects, Fraser Syndrome can be lethal before or shortly after birth (due to bilateral renal agenesis or severely malformed larynx and trachea).; Less affected cases can survive and need surgical treatment.

## Conclusion

Fraser syndrome can be diagnosed antenatally with ultrasonography and postnatally thorough clinical examination. This emphasizes the importance of adequate antenatal follow-up of pregnant women.

### PROF 21.

## Coexistence of de novo complex chromosomal rearrangement between chromosomes 3, 5 and 9 and interstitial deletion of chromosome 4 in a patient with congenital anomalies – case report

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## Introduction

The majority of constitutional chromosomal abnormalities are usually simple rearrangements involving less than three breaks in one or two chromosomes. Constitutional

complex chromosomal rearrangements (CCRs) usually involve at least two chromosomes and three breakpoints with varied outcomes. CCRs may involve distal segments causing reciprocal translocations, or interstitial segments leading to insertion, inversion, deletion, duplication, or a combination of both distal and interstitial segments. At least two aberrations such as inversions and translocations may coexist on the same chromosome.

Congenital anomalies are structural defects of an organism developed during the prenatal period and present at birth. They can be generated by unbalanced chromosomal rearrangements that disrupt loci of many developmentally important genes, which results in specific and complex phenotypes. The confirmation of a chromosomal anomaly requires GTG-banded chromosomal analysis in association with supplementary analyses, such as FISH, MLPA, or array-CGH.

### Objectives

Cytogenetic, FISH and array-CGH study of patient with congenital anomalies.

### Materials and Methods

4 months old boy and his parents underwent medical interview and clinical examination in Genetic Outpatient Clinic. The boy presented with psychomotor retardation, as well as congenital anomalies and dysmorphic features; micrognathia, large head, tall and broad forehead, deep-set eyes, down slanting and short palpebral fissures, epicanthal folds, broad hands and feet.

Peripheral blood lymphocytes were cultured in RPMI growth medium. Metaphase chromosomes were harvested, and slides were made for analysis. GTG banding was used for staining. Chromosomal analysis was performed using CytoVision software. Aberrations were classified, and karyotypes described according to the International System for Human Cytogenomic Nomenclature (ISCN 2020).

FISH was performed using whole chromosome painting probes for chromosomes 3, 5 and 9.

Array comparative genomic hybridization was performed using aCGH platform in an 135k format (NimbleGen CGX-12).

### Results

GTG technique showed a 46,XY,t(3;5;9)(p13;q13;q22) karyotype in the patient and normal karyotypes in both parents. With FISH we confirmed the presence of complex chromosomal rearrangement involving chromosomes 3, 5 and 9. To complete the cytogenetic diagnosis, we applied an array-CGH that revealed a 1.98 Mb interstitial deletion of the 4p15.31-p15.2 region (according to GRCh37 genomic coordinates on chromosome 4: 23423761–25400360). aCGH results in parents were normal.

### Conclusions

We present here a complex chromosomal anomaly identified using cytogenetic and molecular cytogenetic methods. We suppose that the boy phenotype could be influenced by the 4p interstitial deletion, however of uncertain clinical significance. Thus, to exclude DNA mutations as a possible cause of abnormal phenotype, the Whole Exome Sequencing (WES) should be performed.

### PROF 22.

#### Risk factors for microcephaly with congenital CNS malformations based on Polish Registry of Congenital Malformations (PRCM) data

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### Introduction

A number of genetic causes of microcephaly with co-occurring central nervous system (CNS) defects have been identified. Much less is known about the non-genetic risk factors for the concomitance of these defects.

### Objective

The aim of this study is to identify non-genetic risk factors for the occurrence of microcephaly with concurrent CNS malformations in the Polish population.

### Material and Methods

The analysis involved a group of 139 children with microcephaly and morphological CNS malformations reported to PRCM and 519 control births reported from the same region and time period without any evidence of birth malformations. The following risk factors were examined by logistic regression as potential risk factors for microcephaly and CNS malformations: fetal age, birthweight, sex; mother's age, father's age, parental education, mother's place of residence, parents' relationship, and factors related to maternal history and mother's health during pregnancy: type of pregnancy (single, twin), order of pregnancy (1, 2, ≥ 3), complications of pregnancy, infections during pregnancy (upper respiratory tract infections, urinary tract infections and genital tract infections), mother's chronic diseases, and use of drugs (tocolytics, progesterone, antibiotics, non-steroidal anti-inflammatory drugs and antiepileptic drugs) and stimulant substances (cigarettes). Exposures in all three

trimesters were taken into account due to the different possible timing of the development of microcephaly during pregnancy. In the multivariate model used in this study to determine the risk of microcephaly in mothers using non-steroidal anti-inflammatory drugs during pregnancy, upper respiratory tract infection was included as an additional corrective variable.

## Results

The fetal factors that were associated with the occurrence of microcephaly in both univariate and multivariate models were fetal age below 37 weeks' gestation and low birthweight  $\leq 2499$ . The factors that increased the risk of microcephaly with associated congenital CNS abnormalities compared to controls were polyhydramnios, smoking during pregnancy, maternal history of upper respiratory tract infection during pregnancy and use of non-steroidal anti-inflammatory drugs. Lack of detailed information on the doses and duration of treatment with non-steroidal anti-inflammatory drugs means that the relationship calls for the countercheck in a larger group of cases.

## Conclusion

A relationship was found between preterm birth and low birthweight, as well as polyhydramnios and the risk of microcephaly with associated CNS abnormalities. Moreover, risk factors such as smoking during pregnancy, use of non-steroidal anti-inflammatory drugs and maternal history of upper respiratory tract infection during pregnancy were identified.

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### PROF 23.

#### Caregiver reported barriers in utilization of medical and rehabilitation services for children with congenital and developmental disorders resident in rural areas in Maharashtra, India

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## Introduction

A public, community-based child screening and early intervention service (RBSK) provides free of cost surgeries, medical care and rehabilitation services for children with congenital malformations and developmental disabilities. Children are referred from rural settings to District hospitals where the services are located. Despite initial uptake, compliance is low, especially among those requiring rehabilitation therapies.

## Objective

To identify barriers in accessing medical care and rehabilitation services for children with congenital and developmental disorders as reported by caregivers from rural areas

## Methods

Data on caregivers who had dropped out from the treatment/therapy was available from an earlier study conducted in three districts in Maharashtra, the second most populous Indian state. In order to obtain a comprehensive picture of the barriers to care, six case studies (cerebral palsy (3), one case each of congenital hearing impairment, speech delay and orofacial cleft) were conducted, using in-depth interview of caregivers.

## Results

Caregiver related barriers included both child-related and individual factors. Child-related barriers were difficulty in transporting a child with a disability, high cost of transportation, financial considerations in terms of loss of wages, lack of awareness and comprehension about rehabilitation therapies, and lack of understanding about the duration of rehabilitation sessions. Individual factors included physical exhaustion due to caregiving, prioritization of sibling's needs, denial in accepting the disability, and lack of empowerment to negotiate surgery for the child. Health service related factors included difficulties in following the referral routes to surgery, location of services, lack of disability accessible healthcare facilities, long waiting hours, inconsistency in visits by specialists, and the inability to effectively communicate to caregivers.

## Conclusion

The study identified health service and caregiver related factors that impede compliance to medical advice and continuation of rehabilitation therapies and are well known in the literature.

## Implication for practice

Existing barriers can be addressed by having information brochures or an information for caregivers, by placing rehabilitation services within communities, making health care spaces more accessible, and training human resources in sensitive communication.

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### PROF 24.

#### Neonatal and infant mortality associated with spina bifida: a systematic review

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## Objectives

Neural tube defects (NTD) contribute to infant mortality globally. A systematic review was conducted to analyse: (1) spina bifida neonatal and infant mortality rates over time, and (2) clinical and socio-demographic factors as-

sociated with mortality in the first year after birth in infants affected by spina bifida.

#### **Data sources**

PubMed, Embase, Ovid, Web of Science, CINAHL, Scopus and the Cochrane Library were searched from 1st January, 1990 to 31st August, 2020 to review evidence.

#### **Study selection**

Population-based studies that provided data for spina bifida infant mortality and case fatality according to clinical and socio-demographical characteristics were included. Studies were excluded if they were conducted solely in tertiary centres.

#### **Data extraction and synthesis**

Independent reviewers extracted data and assessed their quality using Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guideline. Pooled mortality estimates were calculated using random-effects (+/- fixed effects) models metaanalyses. Heterogeneity between studies was assessed using the Cochrane Q test and I<sup>2</sup> statistics. Meta-regression was performed to ex-

amine the impact of year of birth cohort on spina bifida infant mortality. Results Twenty studies met the full inclusion criteria with a total study population of over 30 million liveborn infants and approximately 12,000 spina bifida-affected infants. Significant declines in spina bifida associated infant and neonatal mortality rates 2 (e.g. 4.76% decrease in IMR per 100, 000 live births per year) and case fatality (e.g. 2.70% decrease in infant case fatality per year) were consistently observed over time. Pre-term birth (RR: 4.45; 95% CI: 2.30–8.60) and low birth-weight (RR: 4.77; 95% CI: 2.67–8.55) are the strongest risk factors associated with increased spina bifida infant case fatality.

#### **Significance**

Significant declines in spina bifida associated infant/neonatal mortality and case fatality were consistently observed, advances in treatment and mandatory folic acid food fortification both likely play an important role. Particular attention is warranted from clinicians caring for preterm and low birthweight babies affected by spina bifida.

## Students' Posters

POSTER NUMBER	POSTER CATEGORY	TITLE	AUTHORS
STUD 1.	Student Presentation	Awareness About Folic Acid Uses And Effects Among Medical Students In Ukraine	Mazan A., Savkiv D. <i>Department of Children's Diseases and Paediatric Surgery I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine</i>
STUD 2.	Student Presentation	Awareness about folic acid and its effects among pregnant women in Western Ukraine	Jasinska J., Koval A.-M. <i>Department of Children's Diseases and Pediatric Surgery, Ukraine</i>
STUD 3.	Student Presentation	Noonan syndrome in a female infant – a case report	Kluz N. <sup>1</sup> , Biedroń N. <sup>1</sup> , Kowalczyk E. <sup>1</sup> , Koziej S. <sup>1</sup> , Kwiatkowska A. <sup>1</sup> , Rekowska A. <sup>1</sup> , Rocka A. <sup>1</sup> , Tarkowska A. <sup>2</sup> <i><sup>1</sup>Uniwersytet Medyczny w Lublinie Studenckie Koło Naukowe przy Klinice Patologii Noworodków i Niemowląt; <sup>2</sup>Klinika Patologii Noworodków i Niemowląt I Katedry Pediatrii, Poland</i>
STUD 4.	Student Presentation	Craniosynostosis as an additional feature of chromatinopathies	Adamek Z. <sup>1</sup> , Larysz D. <sup>2</sup> , Jamsheer A. <sup>3,4</sup> , Bukowska-Olech E. <sup>3,4</sup> <i><sup>1</sup>Medical student, Poznan University of Medical Sciences, Poznan, Poland; <sup>2</sup>Department of Head and Neck Surgery for Children and Adolescents, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland; <sup>3</sup>Department of Medical Genetics, Poznan University of Medical Sciences, Poznan, Poland; <sup>4</sup>These two authors contributed equally to this work</i>
STUD 5.	Student Presentation	Women's knowledge on congenital malformations and care for children with disabilities: A qualitative study from Pune district, India	Medhekar A., Dhamdhare D., Kar A. <i>Birth Defects and Childhood Disability Research Centre, Pune, India</i>
STUD 6.	Student Presentation	Congenital disability in children under five years of age in India and access to health and welfare services	Chutke A. <sup>1</sup> , Kar A. <sup>1,2</sup> <i><sup>1</sup>Interdisciplinary School of Health Sciences, Savitribai Phule Pune University, Pune, Maharashtra, India; <sup>2</sup>Birth Defects and Childhood Disability Research Centre, Pune, Maharashtra, India</i>
STUD 7.	Student Presentation	Porencephaly type I in children presenting pathogenic mutations in the COL4A1 gene	Skulimowski B. <sup>1</sup> , Janiszewska M. <sup>1</sup> , Winczewska-Wiktor A. <sup>2</sup> , Steinborn B. <sup>2</sup> , Badura-Stronka M. <sup>1,3</sup> , Monies D. <sup>4,5,6</sup> <i><sup>1</sup>Chair and Department of Medical Genetics, University of Medical Sciences, Poznan, Poland; <sup>2</sup>Chair and Department of Developmental Neurology, University of Medical Sciences, Poznan, Poland; <sup>3</sup>Centers of Medical Genetics Genesis, Poznan, Poland; <sup>4</sup>Department of Genetics, King Faisal Specialist Hospital and Research Centre, Saudi Arabia; <sup>5</sup>Saudi Human Genome Program, King Abdul-Aziz City for Science and Technology, Saudi Arabia; <sup>6</sup>Saudi Diagnostic Laboratories, King Faisal Specialist Hospital and Research Centre, Saudi Arabia</i>
STUD 8.	Student Presentation	Clinical aspects of facial dysostoses	Adamek Z. <sup>1</sup> , Materna-Kiryłuk A. <sup>2</sup> , Jamsheer A. <sup>2,3</sup> , Bukowska-Olech E. <sup>2,3</sup> <i><sup>1</sup>Medical student, University of Medical Sciences, Poznan, Poland; <sup>2</sup>Department of Medical Genetics, University of Medical Sciences, Poznan, Poland; <sup>3</sup>These two authors contributed equally to this work</i>
STUD 9.	Student Presentation	Novel pathogenic variants and clinical features of syndromes associated with the GLI3 gene	Glista F. <sup>1</sup> , Szymczak A. <sup>1</sup> , Jamsheer A. <sup>2,3</sup> , Bukowska-Olech E. <sup>2,3</sup> <i><sup>1</sup>Medical student, University of Medical Sciences, Poznan, Poland; <sup>2</sup>Department of Medical Genetics, University of Medical Sciences, Poznan, Poland; <sup>3</sup>These two authors contributed equally to this work</i>
STUD 10.	Student Presentation	EUROlinkCAT study on survival and morbidity among European children with Klinefelter syndrome	Rud Andersen A.-L. <i>EUROlinkCAT study group</i>

STUD 11.	Student Presentation	Social limitations related to the COVID-19 epidemic and the work structure of associations of patients with rare diseases and their families – the pilot study	Pol M. <sup>1</sup> , Milska-Musa K.A. <sup>1</sup> , Lipska-Ziętkiewicz B.S. <sup>2,3</sup> <i><sup>1</sup>Department of Quality of Life Research, Faculty of Health Sciences with the Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Poland; <sup>2</sup>Rare Diseases Centre, Medical University of Gdansk, Poland; <sup>3</sup>Clinical Genetics Unit, Department of Biology and Medical Genetics, Medical University of Gdansk, Poland</i>
STUD 12.	Student Presentation	The current state of genetic care for children with congenital anomalies in Wielkopolska province – data from the Polish Registry of Congenital Malformations (PRCM)	Andrzejewska A. <sup>1</sup> , Nowak B. <sup>1</sup> , Czarny J. <sup>1</sup> , Dzierła J. <sup>1</sup> , Zawileński M. <sup>1</sup> , Wiśniewska K. <sup>2</sup> , Glazar R. <sup>3</sup> , Wiśniewska M. <sup>4</sup> , Walkowiak A. <sup>3</sup> , Latos-Bieleńska A. <sup>4</sup> <i><sup>1</sup>Student Research Group of Medical Genetics, Chair and Department of Medical Genetics, University of Medical Sciences, Poznan, Poland; <sup>2</sup>Epidemiology Unit, Department of Preventive Medicine, University of Medical Sciences, Poznan, Poland; <sup>3</sup>Medical Genetics Center Genesis, Poznan, Poland; <sup>4</sup>Chair and Department of Medical Genetics, University of Medical Sciences, Poznan, Poland</i>
STUD 13.	Student Poster	Treatment challenges of severe congenital hydrocephalus in India	Budihal B. <i>Third-year medical student, BGS Global Institute of Medical Sciences, Bangalore, India</i>
STUD 14.	Student Poster	Cardiac arrhythmias after the closure of Secundum Atrial Septal defect (ASD II)	Mantiuk P. <sup>1</sup> , Nikitiuk B.E. <sup>1</sup> , Bowtruczuk A. <sup>1</sup> , Bossowski A. <sup>1</sup> , Bieganowska K. <sup>2</sup> , Miszczak-Knecht M. <sup>2</sup> <i><sup>1</sup>Department of Pediatrics, Endocrinology, Diabetology with Cardiology Division, Medical University of Bialystok, Poland; <sup>2</sup>Department of Cardiology in The Children's Memorial Health Institute in Warsaw, Poland</i>
STUD 15.	Student Poster	Identification of the molecular background of hypophosphatemic rickets in polish patients	Smuszkiewicz M. <sup>1</sup> , Sowińska-Seidler A. <sup>1*</sup> , Jamsheer A. <sup>1,2*</sup> <i><sup>1</sup>Department of Medical Genetics, University of Medical Sciences, Poznan, Poland; <sup>2</sup>Centers for Medical Genetics Genesis, Poznan, Poland *Sowińska-Seidler A. and Jamsheer A. are both senior authors</i>
STUD 16.	Student Poster	An unusual case of 18 trisomy in the usual world – follow-up of a 4-year-old boy with Edwards Syndrome	Bałyga P. <sup>1</sup> , Berk K. <sup>1,2</sup> <i><sup>1</sup>Medical University of Bialystok, Faculty of Medicine with the Division of Dentistry and Division of Medical Education in English; <sup>2</sup>University Oncology Center Medical University of Bialystok Clinical Hospital, Department of Clinical Genetics, Poland</i>
STUD 17.	Student Poster	Analysis of phenotype of patients with a rare disease – CHARGE syndrome	Wolańska E., Śmigiel R. <i>Chairs of Nursing and Obstetrics, Department of Family and Pediatric Nursing, Medical University, Wrocław, Poland</i>



### STUDENTS' SESSION (STUD 1.–STUD 12.)

#### STUD 1.

### Awareness about folic acid uses and effects among medical students in Ukraine

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#### Introduction

Spina bifida is a congenital defect, which can be prevented using folic acid.

#### Objectives

The aim of our study was to evaluate the level of awareness of folic acid, its uses and effects, as well as overall knowledge of neural tube defects among medical students in Ukraine.

#### Materials and methods

A cross-sectional survey was administered to 114 fourth- and fifth-year students at TNMU's Faculty of Medicine. The questionnaire contained questions about folic acid, its dietary sources, effects and periconceptional use, as well as spina bifida and its manifestations.

#### Results

Overall, 96.5% of students knew that folic acid was a vitamin and 95.6% were aware of at least one natural product with high folate levels. However, awareness of its quantities in different food sources was insufficient. Of those surveyed, 86.8% knew that folic acid deficiency during pregnancy can be the cause of congenital malformations. Knowledge regarding supplementation before and during pregnancy with manufactured folic acid was low (67.5% and 53.5% respectively). Only 10% of female medical students consumed folic acid regularly.

#### Conclusions

Despite the high level of general knowledge about folic acid and its effects among medical students in Ukraine, awareness of the need for periconceptional administration of folic acid was poor. Additionally, very few respondents regularly took folic acid.

#### STUD 2.

### Awareness about folic acid and its effects among pregnant women in Western Ukraine

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#### Introduction

Neural tube defects are among the most common non-chromosomal birth defects in children. The risk of spina bifida can be reduced by consuming folic acid during the pre-conception period and in the first trimester of pregnancy. According to recommendations introduced in 1992, all women of childbearing age should take 400 µg of folic acid daily. Additionally, many countries have mandatory state policies specifying food fortification with folic acid.

#### Objectives

Spina bifida incidence in Ukraine remains relatively high. At the same time, there is no official information campaign or policy for mandatory folic acid food fortification. The aim of the study was to evaluate awareness amongst pregnant women of folic acid and its benefits.

#### Materials and methods

From June 2021 to August 2021, 80 pregnant women aged between 18 and 41, who visited an outpatient department of a local clinic, completed a self-administered questionnaire. In addition to assessing the respondents' knowledge of folic acid and its use, we also collected their demographic data.

#### Results

Approximately 41.3 % of women were aware of the role of folic acid in preventing neural tube defects. Their main sources of information were gynecologists (26.3 %) and radio/TV (10.0 %). Although 75.0 % of the pregnancies were planned, only 26.3 % of the respondents stated that they had taken folic acid supplements in the pre-conception period when preparing for the planned pregnancy ( $p < 0.05$ ). Approximately 77.5 % of the surveyed women took folic acid supplements during pregnancy ( $p < 0.05$ ). However, the mean time of starting folic acid supplementation was 8–9 weeks of gestation. None of the participants followed the recommended 400 µg daily dose of folic acid. Women educated to a higher level were more likely to take folic acid before (16 out 21) and during (64.5 %) pregnancy. A similar trend was observed when comparing women in different income level groups: those in the middle-income bracket were more likely to take folic acid in the pre-conception period (15 out 21) and during pregnancy (62.9 %).

## Conclusion

Although the surveyed group had an average level of knowledge of folic acid and its benefits, the practical application of this knowledge was low. None of the respondents took folic acid supplements on a daily basis. Periconceptional consumption of folic acid was also insufficient. These findings suggest that drafting and implementing a state-wide policy addressing folic acid food fortification remains a pressing issue of public health in Ukraine.

### STUD 3.

## Noonan syndrome in a female infant – a case report

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### Introduction

Noonan syndrome (NS) is a genetically determined disease with a heterogeneous phenotype and multisystem manifestations. The pathogenesis of this disorder is associated with mutations in the RAS/MAPK signaling pathway involved in cell proliferation and differentiation. Clinical signs of NS include typical facial dysmorphic features, congenital heart defect (often pulmonary valve stenosis), delayed development, short stature, urinary tract malformations, and hemorrhagic diathesis. According to the literature, NS is a relatively common autosomal dominant disorder, with an incidence estimated at 1/1000 to 1/2500. However, many cases remain unrecognized or diagnosed with significant delays. Turner syndrome, that presents very similarly clinically, but unlike NS, affects only females should be considered principally in a differential diagnosis.

### Objectives

The purpose of this study is to present a clinical case of a child diagnosed with NS.

### Materials and methods

A female infant born from first pregnancy at 35 weeks of gestation, with a body weight of 2250g, Apgar 6/8/8. After birth she was treated for respiratory failure, circulatory failure, congenital pneumonia, NEC, sepsis, and anemia. A physical examination revealed features of prematurity, dysmorphic features such as low set ears, flaccid chest, widely spaced nipples. There was an audible midsystolic murmur over the heart, 3/6 on the Levine scale, the loudest in the pulmonary artery field and between the shoulder blades. Laboratory tests revealed anemia. Echocardiographic examination revealed valvular pulmonary stenosis with gradient increase from 44 to

48 mmHg max. A head ultrasound showed features of IVH of I degree. Slight dilatation of the pelvicalyceal system in the left kidney was observed. Given the totality of the clinical picture and the dysmorphic features presented, a screen for genes associated with Noonan syndrome and RASopathies was performed.

### Results

The result showed a mutation in the *PTPN11* gene, confirming the clinical diagnosis of NS.

### Conclusion

Early diagnosis of NS results in increased vigilance and prompt diagnosis for likely associated diseases and the most common complications. This strategy allows the patient to be offered the right treatment at the right time. A patient with NS should receive multidisciplinary care, including the care of a cardiologist, endocrinologist, nephrologist, ophthalmologist, audiologist, hematologist, orthopedist, or others as needed.

### STUD 4.

## Craniosynostosis as an additional feature of chromatinopathies

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### Introduction

Craniosynostosis affects approximately 1 in 2500 births and burdens public health due to the requirement of extensive surgical treatment in the first year of life and multi-level specialist medical care in the subsequent postnatal periods.

Chromatinopathies are disorders caused by a disruption in the chromatin structure aroused during epigenetic processes. Among others there are Mendelian disorders such as Coffin-Siris syndrome type 2, Wiedemann-Steiner syndrome, Kabuki syndrome type 1, and Sotos syndrome type 1; all characterized by intellectual disability, skeletal anomalies, and immune deficiencies.

### Objectives

Our study aimed to reveal the genetic background of craniosynostosis in patients in whom karyotyping, targeted PCR followed by Sanger sequencing, custom gene panel next-generation sequencing, and chromosomal microarray analysis were negative.

### Materials and methods

Genomic DNA samples were subjected to whole-exome sequencing. The coding and flanking intronic regions

were enriched using a custom-designed in-solution exome enrichment (TWIST bioscience, San Francisco, USA) and sequenced using the Illumina NovaSeq system (Illumina, San Diego, USA).

### Results

Six patients harbored pathogenic variants in genes involved in epigenetic processes such as *ARID1A* (linked to Coffin-Siris type 2 syndrome), *KMT2A* (linked to Wiedemann-Steiner syndrome), *KMT2D* gene (linked to Kabuki type 1 syndrome), and *NSD1* gene (linked to Sotos type 1 syndrome).

### Conclusions

We have shown a relatively high co-occurrence of craniostenosis and chromatinopathies. However, this relation has not been broadly described in medical literature and needs further investigation. Our finding might be necessary because individuals affected with chromatinopathies require additional medical treatment such as immune system or oncology status evaluation.

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## STUD 5.

### Women's knowledge on congenital malformations and care for children with disabilities: A qualitative study from Pune district, India

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#### Background

Congenital anomaly birth prevalence in India is estimated to range between 184.48 to 230.51 per 10,000 live births, accounting for 472,177 to 530,208 affected pregnancies annually. Maternal health services in India do not provide awareness messages about congenital malformations or care for children with disabilities.

#### Objective

To understand knowledge of the causes and prevention of congenital malformations among women, and awareness of medical care, rehabilitation and welfare services for children with congenital disabilities.

#### Methodology

Qualitative descriptive design. Twenty-four rural and urban women from the Pune district were included using a purposive sampling strategy. Due to Covid-19 related travel restrictions and social distancing regulations, data was collected through six focus groups, with four women in each group. Data was collected for rural women through face-to-face interviews and through online focus group discussions. Data collection was guided by a pilot-tested topic guide. Qualitative content analysis, both a priori and inductive coding was used. Themes

were evolved from the codes, which were then analyzed with respect to the research questions.

### Results

There local language term for congenital malformations. Sixty-one different descriptions of congenital malformations, which included descriptions of different malformations, pregnancy complications like miscarriage, fetal demise, and examples of children with congenital and acquired disabilities. Lay beliefs predominated understanding of causation. There was no mention of pre-conception care, folic acid supplementation or rubella immunization. Termination of pregnancy for conditions considered to be untreatable (like intellectual disability) was advocated by most women. Knowledge of applicable legal rights for pregnancy termination in case of prenatal detection of a malformation was limited. Stigmatizing attitudes were responsible for children with disabilities being considered a burden, for maternal blaming and for stigma and isolation of families. The benefits of treatment and special schooling were questioned, as most participants believed that these were unlikely to bring about improvement. Knowledge on rehabilitation was limited.

### Conclusion

Knowledge of congenital malformations was limited as there was no structured source of knowledge. Knowledge of care for children with disabilities was fragmentary and based on hearsay.

### Implications for practice

There is an immediate need for the implementation of awareness services to enhance knowledge regarding these conditions, preconceptions and antenatal opportunities for reducing risks, and available medical services for women. Parents should have access to information on treatment and rehabilitation and access to social services. There is a need for disability sensitization messages for communities to ensure inclusion of children with congenital disabilities.

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## STUD 6.

### Congenital disability in children under five years of age in India and access to health and welfare services

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#### Introduction

Child health strategies in low-and-middle income countries and even in India focus on reducing mortality and preventing morbidity. Children with congenital disor-

ders remain under-prioritized. There is limited data on the quality of life of children with congenital disorders in India.

### Objectives

The objective of this study was to determine the number of children with congenital disabilities in the 0–59 months age group in India, and to describe their access to health care and welfare services.

### Methods

Data for an estimated 79,845,372 children under five years of age was extracted from the 76th round of the National Sample Survey on Disability. The survey uses a medical categorization of disability. This results in a likelihood of the data underestimating the actual occurrence. The time of onset of disability was used to categorize children with congenital (reported to be present since birth) or acquired (not reported since birth) disability. Prevalence rates were calculated for disability per 10,000 children under five years of age. Socio-demographic characteristics, number of years lived with disability, and access to care were calculated using Statistical Package for Social Sciences (SPSS version 28).

### Results

In 2018, congenital causes were responsible for 84% of disabilities among children under five years of age (363,700 out of 434,400 children with disabilities; congenital disability rate 46 per 10,000, as compared to acquired disability rate of 9 per 10,000). Compared to those with acquired impairment, children with congenital disability were more severely disabled; a higher number (95%) had no perception of light, profound (84%), or severe hearing impairment (67%), and (95%) were unable to speak. Person years lived with a congenital disability amounted to 10.5 million years. Dependency on activities of daily living was higher for children with congenital disability (78% versus 68%). Very few school-going children between 3 and 4 years old with congenital disability attended preschool intervention programs (3% versus 9%) or were ever enrolled in mainstream schooling (12% versus 16%). Only 2% were ever enrolled at a special school. Among those enrolled in mainstream schooling, very few attended the school (11% versus 14%) at the time of the survey. Nearly half of these children were unable to attend school due to disability (46% versus 67%). Access to healthcare and assistive devices was similar for both groups of children (approximately 40% and 8% respectively).

### Conclusions

Even though the data underestimate the actual numbers, the study identifies a significant number of children with congenital disability in the 0–59 month age group and their limited access to health care and educational services.

### Implications for practice

The study suggests the need for measurement, services, and research studies to determine the number and health and the educational status of survivors with congenital disorders.

## STUD 7.

### Porencephaly type I in children presenting pathogenic mutations in the COL4A1 gene

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### Introduction

Pathogenic mutations in the *COL4A1* gene cause impairment of the synthesis of the collagen IV alpha 1 chains. As a consequence of increased fragility of cerebral artery walls, prenatal intracranial hemorrhages may occur, resulting in severe porencephaly (known as porencephaly type 1) and intracranial calcifications, mimicking prenatal infection, perinatal injury, or schizencephaly. Other known phenotypes related to the *COL4A1* gene impairment include HANAC syndrome (hereditary angiopathy with neuropathy, aneurysms, and muscle cramps) and Axenfeld-Rieger anomaly with leukoencephalopathy and stroke.

### Patients and methods

In this report, we describe two children, 3 and 7 years old, affected with porencephaly type I. The boy was born with schizencephaly, Dandy-Walker malformation, periventricular calcifications, congenital cataract, and posterior urethral valve. He had profound psychomotor delay and epilepsy.

The girl suffered epileptic attacks when she was 25 months old. A neurological examination found she had left-sided spastic paresis. Magnetic resonance imaging of the brain showed agenesis of the right thalamus and basal ganglia of the right hemisphere, and schizencephaly.

Both children have been referred to genetic counselling for further diagnosis. We have identified pathogenic variants in the *COL4A1* gene with the use of NGS-based techniques in both probands. The result of genetic testing combined with clinical data allowed us to diagnose porencephaly I in both cases.

## Conclusions

In differential diagnoses of a child with structural brain malformations, including schizencephaly, fluid-filled cavities, or diffuse cerebral calcifications, a diagnosis of porencephaly type I with the COL4A1 gene mutations should be taken into account. Next-generation sequencing is a method of choice to confirm the diagnosis.

### STUD 8.

## Clinical aspects of facial dysostoses

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### Introduction

Facial dysostoses (FDs) are a group of rare and heterogeneous diseases that result from defects of I and II pharyngeal arches' development. Consequently, various malformations of the viscerocranium may occur such as hypoplasia of the maxilla, mandible, zygomatic arches, various anomalies of the external and middle ear, and other facial defects including coloboma of the lower eyelid with partial to total absence of eyelashes or down-slanting palpebral fissures. FDs have been divided into two main groups based on additional limb involvement – mandibulofacial dysostoses (MFDs), and acrofacial dysostoses (AFDs).

Children affected with FDs require specialist care from early childhood, not only due to many surgical operations but also supervision of a neonatologist and an anesthesiologist if breathing insufficiency occurs or an ophthalmologist in case of eye anomalies. Moreover, they also require plastic surgery, and long-term psychological support.

### Objectives

Our study aimed at analyzing multi-level specialistic care required by patients affected with various forms of FDs.

### Material and methods

We examined 14 families with variable clinical symptoms of FDs. The patients were affected with such syndromes as Treacher Collins syndrome, Nager syndrome, acrofacial dysostosis Guion-Almeida type or Miller syndrome diagnosed either dysmorphologically and/or through molecular testing.

### Results

We have summarized the required clinical treatment. We have also listed support groups and qualified medical centers where patients and their families can seek medical care.

## Conclusions

FDs are disorders that can be easily recognized based on dysmorphic features. Disorders from the FDs spectrum should be always suspected when abnormalities of I and II pharyngeal arches occur. Patients affected by an FD require long-term specialized medical care followed by psychological support.

### STUD 9.

## Novel pathogenic variants and clinical features of syndromes associated with the GLI3 gene

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### Introduction

Deleterious variants in the *GLI3* gene result in various phenotypes, depending on their location. Pathogenic variants located within the first and last third of the *GLI3* are responsible for Greig cephalopolysyndactyly (GCPS) (MIM: 146510). whereas variants located in the middle third of *GLI3* are a cause of Pallister-Hall syndrome (PHS) (MIM: 175700).

The clinical features of GCPS comprise craniofacial abnormalities such as craniosynostosis (scaphocephaly), hypertelorism and prominent forehead. Preaxial polydactyly type IV may also occur as an additional phenotype. Interestingly, a few studies have linked pathogenic variants in the *GLI3* gene with the acrocallosal syndrome (ACLS) (MIM: 200990), which is distinguished from GCPS by brain malformations, such as the agenesis of corpus callosum.

PHS phenotype spectrum is variable and may include hypothalamic hamartoma, impairment of pituitary gland, visceral malformations, and postaxial polydactyly (type A or B).

### Aim of the study

We aimed to reveal the molecular background of clinical features observed in a group of patients who presented symptoms suggestive of GCPS or PHS.

### Materials and methods

We examined ten families. Only one member was affected in most of the families we examined. Genomic DNA was extracted from peripheral blood lymphocytes using the MagCore® HF16 Automated Nucleic Acid Extractor. Next, we applied either PCR followed by Sanger sequencing of the entire *GLI3* coding sequence or targeted next-generation sequencing of a custom gene panel containing genes linked to congenital limb defects.

## Results

We detected eleven variants in the GLI3 gene out of which nine caused GCPS and two caused PHS. Four of these variants have not been reported in the medical literature to date.

## Conclusions

We described as of yet unreported additional clinical features in GCPS and PHS. Moreover, we detected novel GLI3 variants and expanded the mutational spectrum of both GCPS and PHS. This study may be valuable for geneticists consulting patients affected with disorders within the limb defects spectrum.

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### STUD 10.

## EUROlinkCAT study on survival and morbidity among European children with Klinefelter syndrome

Rud Andersen A.-L.

EUROlinkCAT study group

### Introduction

Klinefelter syndrome is a sex chromosomal aneuploidy in males, which may not be diagnosed at birth. As a result of an unspecific spectrum of stigmata there may be a delay in diagnosis with less than one out of ten diagnosed before puberty. Most of the published studies describe the adult population. There is a lack of knowledge regarding survival and morbidity among children with Klinefelter syndrome.

Klinefelter syndrome may be diagnosed prenatally through screening or examinations for more severe chromosomal anomalies. Accurate parental counselling is very important but is currently limited due to the limited number and scope of studies on children.

### Objectives

To broaden knowledge on survival and morbidity of European children diagnosed with Klinefelter syndrome in the first 10 years of life.

### Materials and methods

The study used EUROlinkCAT data on survival and morbidity of children up to 5 years old with major congenital anomalies. Data on survival was analyzed for 14 European registries. Data on hospitalization and surgeries were available for 9 and 8 European registries respectively.

All children diagnosed with Klinefelter syndrome (cases) and born between 1995 and 2014 in the registry areas were included. Data on live born children with any major congenital anomaly or without a congenital anomaly (reference children) born during the same time-period from the same population area covered by the registry were included for comparison.

European meta-analyses of the outcome measures were performed by two age groups, <1 year and 1–4 years.

### Results

A total of 291 children diagnosed with Klinefelter syndrome were included and a total of 6,937,995 children were born in the same geographical areas. This gives a prevalence of Klinefelter syndrome of 4.2 per 100,000 births.

Ten children with Klinefelter syndrome died during the first year of life giving a mortality of 3.44%. No children with Klinefelter syndrome died between the ages of 1 and 4.

In terms of hospitalization and surgeries, a total of 196 and 154 children with Klinefelter syndrome were included from 9 and 8 registries respectively. Meta-analyses of the outcome measures will be presented, and the results include the percentage of children hospitalized, median length of stay and number of surgeries for children with any congenital anomaly, Klinefelter syndrome and reference children in the 0–1 years old and 1–4 years old age groups.

### Conclusion

Infant mortality for children with Klinefelter syndrome is higher than for reference children, but there were no deaths between the ages of 1 and 4.

Children with Klinefelter syndrome are more likely to be hospitalized compared to reference children but are less likely to be hospitalized compared to all children with a congenital anomaly.

These results can be applied to the children diagnosed prenatally and shortly after birth, and most likely represent the most severe cases, given that most of the children do not show any symptoms of the syndrome before puberty.

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### STUD 11.

## Social limitations related to the COVID-19 epidemic and the work structure of associations of patients with rare diseases and their families – the pilot study

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### Introduction

The COVID-19 pandemic and the related limitations affect many aspects of everyday life and the functioning of

institutions. An example is related to the various associations working for people suffering from rare diseases. These organizations intend to support their charges not only medically and educatively but also socially by establishing a sense of community. The limitations due to the epidemiological situation forced these associations to change the structure of their work.

### Objectives

The aim of the study was to evaluate how the changes related to the functioning of associations during the pandemic influenced their work and what changes were most significant for them. In addition, an analysis of the methods of coping with stress was assessed. The subjective assessment of one's own disease and evaluation of social support was also analyzed.

### Materials and methods

52 people (31 patients and 21 caregivers) participated in the study. The respondents were members of the Polish Association of People with Haemophilia, Gdansk Association of Friends of Children with Phenylketonuria, FRA X FAMILY, More Loved, Haemophilia and Related Haematological Disorders, Marfan Polska Association or Ehlers-Danlos Polska Association.

The study was conducted using an anonymous online questionnaire. Respondents were asked to fill in the Author-Designed Questionnaire. It included questions on subjective opinions about the work of the association before and during the restrictions and a Mini-COPE inventory to measure the assessment of typical ways of reacting and feeling in situations of severe stress. The modified Own Disease Assessment Scale to measure the perception of their own/ child's disease and the Berlin Social Support Scales to assess the type of subjectively perceived social support were also used in the study.

### Results

Associations were evaluated to engage in less work during the restrictions caused by the pandemic than before. Among the study group, active stress coping was the most frequent way of reacting in situations of severe stress. People suffering from rare diseases more often perceived their illness as a benefit and also as an obstacle in comparison to caregivers. 100% of caregivers were women. Emotional support was the most observed type of provided support. In relation to the functioning of an association, most respondents indicated that the main disadvantage is the lack of face to face meetings.

### Conclusion

The pandemic-related restrictions influence the functioning of associations. Providing support, including emotional support may be difficult currently, due to the lack of face to face meetings for example. In the face of the pandemic, it is particularly important to monitor the needs of patients and their close relatives and to look for solutions aimed at improving the work of associations

during the pandemic for the better functioning of their members.

## STUD 12.

### The current state of genetic care for children with congenital anomalies in Wielkopolska province – data from the Polish Registry of Congenital Malformations (PRCM)

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### Introduction

Genetic care is one of the elements of medical care for children with congenital anomalies (CA). It confirms a clinical diagnosis, predicts patient's future health complications, helps choose the appropriate medical care and is necessary for genetic counselling. PRCM started in Wielkopolska in 1997. Over the following years it grew to cover the entire territory of Poland. From the very beginning, PRCM aimed to evaluate and improve genetic care for children with CA in Poland. Between 2000 and 2006, PRCM clinical geneticists analyzed all notifications to the Registry regarding indications for genetic care and letters were sent to the families in question. In 2007 an analysis of 40,263 children born with CA between 1998 and 2006 showed that less than 10% of all children with CA had genetic consultation between 1998 and 1999. After the action, an increase to 15.2% was observed. Among children with multiple CA (excluding Down syndrome), about 12% of children had genetic consultations between 1998–1999. Furthermore, this figure increased to 34.5% in the following years. Children with Down syndrome had a genetic consultation in almost all cases. Now, after 25 years of running PRCM, there is no data on the state of genetic care for children with CA in Poland.

### Aim

To determine the current state of genetic care for children with CA and attempt to identify influencing factors. As aCGH and NGS are not reimbursed in Poland, it is crucial to evaluate the state of Polish genetic care before both methods become widely available (planned for the second half of 2022).

### Materials

We obtained data on children with CA from PRCM – born in Wielkopolska in 2019 (EUROCAT FM; covers 10% of

births in Poland). Genetic care information was obtained from the PRCM database. We checked if the children reported to PRCM had a consultation (by January 2022) at the Medical Genetics Centre Genesis in Poznan (the only such genetic center in the region). Information from other genetic clinics in Poland was also collected.

## Results

In 2019, 1209 children with CA were born in Wielkopolska. By 2022, 115 of them were under genetic care (9.5%). Genetic care was provided to 100% of children with Down syndrome (n=55) and Edwards or Patau syndromes (n=11), 80% of children with multiple CA (n=44), 14.5% of children with CA and a family history of CA/genetic diseases (n=11) and in 20.8% cases of children with CA born after 2 or more miscarriages (n=5). We observed higher alertness to the importance of genetic care among mothers with education to a higher level, yet a history of CA/genetic diseases or miscarriages seems to have a low impact. Distance from the genetic clinic or the mother's place of residence do not matter.

## Conclusion

There has been no overall improvement in medical care for children with CA over the past 20 years. The only notable advance in medical care is for children with multiple CA. We believe the main barrier to proper medical care for children with CA in Poland is lack of reimbursement for new methods of genetic diagnostics.

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### STUD 13.

## Treatment challenges of severe congenital hydrocephalus in India

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### Introduction

A new law regarding the legality of abortion in cases of severe and lethal embryo malformations has been implemented in India. This amendment was introduced in 2021. In this study we explore the realities of palliative care in cases of severe CNS malformations, focusing on extreme hydrocephalus, resulting in nervous tissue compression, which leads to irreversible brain damage and atrophy. The advancement of medicine enables vital functions in patients born with lethal CNS malformations to be maintained. Patients can live long lives with appropriate care and specialized pediatric treatment even though their quality of life and that of their relatives may be very low.

### Materials & Methods

The retrospective study was carried out on 11 children hospitalized due to extreme congenital hydrocephalus between 2013 and 2021. Based on medical histories,

we analyzed treatment strategies and outcomes. We decided to carry out a follow-up study based on a questionnaire interview with the parents and an examination of the children. The questionnaire focused on analyzing children's disabilities, daily functioning, family dynamics as a result of the disease, socioeconomic problems, and social perception of the child and family.

## Results

Past medical history analysis uncovered multiple health conditions besides CNS malformations and hydrocephalus. Spinal muscular atrophy, drug-resistant epilepsy, difficulties in feeding, and serious cognitive abnormalities were the main medical problems. One patient died due to an infection of their ventriculoperitoneal shunt. All patients required multiple surgical interventions and multiple hospitalizations.

## Conclusion

Severe CNS malformations result in extreme changes in the daily lives and routines of affected families. Sufferers require 24/7 palliative care and, sometimes, artificial life support and multiple medical interventions. Therefore, early prenatal detection which enables parents to undergo psychological and medical counselling should be followed by a well-informed decision on whether to keep or terminate the pregnancy.

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### STUD 14.

## Cardiac arrhythmias after the closure of Secundum Atrial Septal defect (ASD II)

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### Introduction

Atrial septal defect (ASD) is one of the most common types of congenital heart defects. It occurs when communication between the right and left atria does not close successfully. Small atrial septal defects usually spontaneously close in childhood while large defects that do not close spontaneously may require percutaneous or surgical intervention to prevent further complications. Transcatheter closure of atrial septal defect (ASD) is an alternative to open-heart surgery and has become the method of choice to manage most patients with secundum ASDs. Although transcatheter closure of ASD with the Amplatzer septal occluder is considered a safe and feasible method in pediatric patients, there is a risk of provoking arrhythmias following transcatheter device closure of secundum ASD.



## Case report

A 10-year-old female patient with a history of percutaneous closure of secundum atrial septal defect (ASD II) with the Amplatzer Septal Occluder at the age of 4 and consequent multiple attacks of supraventricular and ventricular tachycardias, hypothyroidism, treated with various combinations of antiarrhythmic drugs was admitted to an ICU due to sudden cardiac arrest which occurred after swimming. Ventricular tachycardia and impaired cardiac contractility on echocardiography were diagnosed. One month later, after a subsequent episode of tachycardia, the patient was scheduled for ECG telemonitoring. Family history of DCM was positive (father – DCM, father's brother – death after heart transplant at the age of 23, father's mother – sudden death), but a genetic test excluded the involvement of genetic factors in the etiology of the disease with a high probability. Two months later, after the second EPS, which failed to differentiate the ventricular tachycardia, a decision to implant an endocavitary cardioverter-defibrillator system was made. A left-sided sympathectomy (Th2–Th5) was also performed. During a subsequent EPS examination, left atrial fibrillation was recorded. The performed cardioversion did not stop the attack. At the age of 14 foreign consultation in a reference center in Munich (Germany) was conducted. The outcome was a change of treatment and a decision was made to perform heart mapping. Current echocardiography presents no cardiomyopathy or hypertrophy of the cardiac muscle.

## Conclusions

In children, arrhythmias have an etiology, evolution and treatment strategy that often differs from that of adults. Although most arrhythmias in children have a benign outcome, recurrent arrhythmic events have a significant impact on quality of life.

Recognition of the right cause is essential for appropriate treatment. In this case, we want to highlight the importance of attempting to establish personalized management workflows that can help clinicians when facing specific arrhythmias in children.

## STUD 15.

### Identification of the molecular background of hypophosphatemic rickets in Polish patients

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## Introduction

Hypophosphatemic rickets (HR) are a rare group of clinically and genetically heterogeneous genetic disorders. To date, seven chromosomal loci associated with HR have

been described. X-linked dominant hypophosphatemic rickets (XLHR), caused by loss-of-function mutations in the *PHEX* gene, are the most common type of HR responsible for approximately 83% of cases. Due to similar clinical manifestations, differential diagnosis of distinct types of HR is challenging. The large size of *PHEX* gene coding sequence and lack of hot-spot pathogenic mutations also contribute to delayed diagnosis and implementation of proper treatment in this group of disorders.

## Objectives

The main objective of the study is the identification of HR's molecular background in affected patients, which will contribute to proper clinical diagnosis. We aim to provide a differential diagnosis to the patients and a better understanding of physiological and pathological phosphate homeostasis, as well as to discover and describe novel pathogenic variants.

## Materials and methods

The study involved 16 patients, of which 13 were screened for pathogenic mutations using Sanger sequencing in two causative genes: *PHEX* and *FGF23*. Three additional patients from this cohort were tested with the use of whole genome sequencing (WGS). All identified variants were analyzed using bioinformatics tools. Data was interpreted with the use of online genetic databases and programs.

## Results

We have established the molecular cause of HR in 9 affected patients, defined by pathogenic mutations in the *PHEX* gene. In 4 cases, we have identified variants that were previously described as pathogenic: a missense (rs1064795106) and a nonsense (rs1569442206) mutation and the same splicing variant (rs886041225) in two unrelated patients. Additionally, we have identified previously unreported pathogenic mutations in 5 patients: a duplication of 4 nucleotides in exon 9 (c.972-976dup), a missense mutation (c.1229T>G), a deletion of 5 nucleotides in exon 3 (c.208\_212delGTAAA) and two intragenic deletions encompassing exon 22 and exons 21–22 respectively. The last three variants were detected using the WGS approach, which enabled the establishment of precise breakpoints of duplications. The evaluation of pathogenic variants was carried out with the use of the Varsome database.

## Conclusions

So far, the sequence analysis of the *PHEX* and *FGF23* genes allowed an XLHR type disorder to be diagnosed in 9 patients from the cohort. The next diagnostic tier will involve screening for intergenic deletions and duplications in the two causative genes by means of an MLPA assay. Patients with negative results of the preliminary molecular screening will be subjected to an NGS gene panel dedicated to hypophosphatemic rickets and other genetic disorders with signs of rickets. We plan to apply this diagnostic algorithm to a larger cohort of patients with a similar phenotype.

## STUD 16.

### An unusual case of 18 trisomy in the usual world – follow-up of a 4-year-old boy with Edwards Syndrome

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#### Introduction

Edwards Syndrome (ES) is the second most common trisomy following trisomy 21, with an extra chromosome 18 present on the standard G-banded karyotype. More than 95% of fetuses with trisomy 18 die in utero. What about the remaining 5%? From this group, only 10% of infants turn one year old. Trisomy 18 symptoms mainly include pre- and postnatal growth retardation, hypotonia, limb anomalies, and visceral malformations (heart disease in 90% of cases). Although ES has been described as a lethal defect, more recent studies report long-term survival of more than 5 years is possible through the application of surgical intervention.

#### Case report

A presented boy was born on the 38th week of gestation by caesarean section, due to a risk of birth asphyxia. During the pregnancy no abnormalities were found on the USG. His APGAR score was assessed at 4 points at the 1st minute and 8 points at the 5th minute mark. The parameters at birth were as follows: weight: 1950 g; length: 40 cm; occipitofrontal head circumference (OFC): 33 cm; thorax circumference (THC): 26 cm. All of them were below the 3rd centile. Dymorphologic examination showed craniofacial abnormalities, bone defects including the absence of radius and thumb of the right upper limb and absence of both forearm bones and thumb of the left upper limb, bilateral clubfoot, cleft lip, and palate, right inguinal hernia. Postnatal ECHO demonstrated atrial as well as a ventricular septal defect, mitral valve defect, and dextroposition of the aorta. Initially it was hypothesized to be Roberts syndrome, but the karyotype confirmed a non-mosaic trisomy 18, which prompted the diagnosis of ES. Throughout his life, he was hospitalized many times due to severe pneumonia. Currently, he is in home hospice care. He has hydrocephalus, epilepsy, and requires persistent respiratory support and parenteral nutrition via PEG tube. Because ES is fatal, he was disqualified from cardiac surgery.

#### Conclusions

Despite a poor prognosis for trisomy 18, the boy with a severe disability is now almost 5 years old. We should ask how can we help these unusual people with ES to live as best as possible in the usual world? Is palliative care the only way to support children with trisomy 18? It seems that each patient should be considered on an individual basis and the decision to perform surgical repair

of birth defects should be made in collaboration with clinicians and parents.

## STUD 17.

### Analysis of phenotype of patients with a rare disease – CHARGE syndrome

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#### Introduction

Rare diseases have already affected 300 million people worldwide, which means that 8% of the population suffers from them. Worldwide, one in every 25 children is born with a rare disease. About 8,000 diseases have been described in the literature so far. CHARGE syndrome is one of them. It is a rare monogenic birth defect syndrome. The name of the syndrome is an acronym of first letters of the English words describing congenital defects occurring in CHARGE syndrome: C coloboma, H heart defects, A atresia choanae, R retarded growth and development, G genital abnormalities, E ear anomalies.

#### Material and methods

Phenotype analysis was performed on 29 patients with CHARGE syndrome confirmed by molecular tests. The study group consisted of 15 boys and 14 girls, between 2 and 18 years old.

Parents of children with CHARGE syndrome completed a self-administered questionnaire designed to explore in detail the patient's medical history and the diagnostic process as well as a PedsQL 2.0 family impact questionnaire.

#### Results

Twenty-four patients were diagnosed before the age of 2, 4 patients were diagnosed before their 5th birthday, and one patient received a diagnosis at the age of 15. 16 natural births. 2 patients were hospitalized up to 1 week postpartum, the remaining patients stayed more than 2 weeks in the hospital. Twenty-four patients had heart defects. 10 patients had choanal atresia/stenosis and 10 patients were diagnosed with cleft lip. Hearing loss was diagnosed for 24 patients. Craniofacial dysmorphic features typical for CHARGE syndrome were present in all patients.

Parents of children with CHARGE syndrome completed the PedsQL Family Impact Questionnaire (quality-of-life questionnaire). Twenty-five patients often or sometimes experience fatigue throughout the day. 18 parents were too tired to do the things they enjoy, felt isolated and found it difficult to talk to medical staff about their child's illness.

## **Conclusions**

Diagnosis of a rare genetic disease is a long process which is often associated with long-term stress for parents and patients. Conducting phenotype-genotype cor-

relation studies will improve the diagnostic process. Dissemination of knowledge on rare diseases will increase the knowledge of health care professionals and enable parents to have access to reliable information.

## General Posters

POSTER NUMBER	POSTER CATEGORY	TITLE	AUTHORS
G1.	General	Corrective classes for people with motor dysfunctions based on the activities of the Capoeira Konin Academy	Andrzejak J. <sup>2</sup> , Łukowski K. <sup>1</sup> <i><sup>1</sup>Andrzejak J. from the State Higher Vocational School in Konin and International Association for Health Promotion, <sup>2</sup>Łukowski K. from the University of Łódź and International Association for Health Promotion, Poland</i>
G2.	General	Artistic activities in the education of students with Down syndrome as a determinant of social inclusion	Krawiecka K. <i>Uniwersytet Kardynała Stefana Wyszyńskiego w Warszawie Wydział Nauk Pedagogicznych, Poland</i>
G3.	General	Alternative and augmentative communication – a tool for inclusion and participation of people with complex communication needs	Świeczkowska K., Kwiatkowska A. <i>Polskie Stowarzyszenie na Rzecz Osób z Niepełnosprawnością Intelektualną PSONI Koło w Gdańsku, Poland</i>
G4.	General	Polish Registry of Congenital Malformations – support for children with congenital anomalies and their families	Materna-Kiryłuk A. <sup>1</sup> , Jamsheer A. <sup>1</sup> , Jamry-Dziurla A. <sup>1</sup> , Wiśniewska K. <sup>2</sup> , Latos-Bieleńska A. <sup>1</sup> and PRCM Working Group <i><sup>1</sup>Chair and Department of Medical Genetics, Poznan University of Medical Sciences, Poland; <sup>2</sup>Epidemiology Unit, Department of Preventive Medicine Poznan, University of Medical Sciences, Poland</i>
G5.	General	The good start – support for carers of people with disabilities	Zglińska P. <i>Assosiation FOR YES (Stowarzyszenie Na Tak), Poland</i>
G6.	General	It is easier with “DOROTKOWO”. Fundacja na Rzecz Doroty Targowskiej i Jej Przyjaciół	Targowski M., Słupkowska J. <i>Foundation DOROTKOWO, Poland</i>
G7.	General	Birth defect as a symbol. The prospect of communicative anthropology	Żuraw H. <i>Instytut Pedagogiki UPH w Siedlcach, Poland</i>
G8.	General	Foundation for Developmental Support JA TEZ (Fundacja Wspierania Rozwoju “JA TEŻ”)	Bulczak M. <i>Foundation for Developmental Support JA TEZ, Poland</i>
G9.	General	Challenges in counseling and therapy for adolescent diagnosed with ASD and with comorbid behavioral and mental health problems in the context of school and parenting conditions. Case study	Stefańska-Klar R. <i>State Higher Vocational School in Raciborz, Poland</i>

G1.

### Corrective classes for people with motor dysfunctions based on the activities of the Capoeira Konin Academy

Andrzejak J.<sup>2</sup>, Łukowski K.<sup>1</sup>

(1) Jakub Andrzejak from the State Higher Vocational School in Konin and International Association for Health Promotion; (2) Karol Łukowski from the University of Łódź and International Association for Health Promotion

The poster presents the Capoeira Academy Konin, run by Piotr Lobo Glapa, a member of the International Association for Health Promotion. Apart from regular training sessions, Piotr is involved with activating disabled people at various centers, associations and institutions. Physical rehabilitation in the form of Capoeira entails participants trying their hand at this activity. Capoeira is different from other martial arts in the fluidity of dance. This is why it could become an interesting form of physical therapy. A martial art, capoeira is a fighting style with a completely different origin and symbolism. It is becoming increasingly similar to classical martial arts and is slowly becoming an area of physical recreation. K. Kołbowska, *Capoeira in Poland. Wanderings of cultural threads*, Warsaw 2010, p. 80.

Physical activities as part of physical rehabilitation take the form of games and movement games. The main aim of these activities is to improve the motor system of the person exercising. Corrective gymnastics, loosens, activates, strengthens and improves stiff and stagnant parts of the body. For people with movement dysfunctions corrective gymnastics is part of their everyday activities, which they perform in order to learn how to lift their legs properly during gait, maintain a straight posture, squat or stand up from a lying position. Corrective-motor gymnastics is used in diseases of locomotive organs. Exercises such as these are used in medicine, rehabilitation, motor recreation, relaxation exercises, motor therapy and physical culture. When talking about the classification of movement games, according to the degree of difficulty and complexity, it should be remembered that all games that today have standardized and internationally accepted rules, are very simple in their original form. The rules of movement therapy, should be simple and adapted to the participants. These rules were standardized in different parts of the world, until they were given their present form.

G2.

### Artistic activities in the education of students with Down syndrome as a determinant of social inclusion

Krawiecka K.

Uniwersytet Kardynała Stefana Wyszyńskiego w Warszawie  
Wydział Nauk Pedagogicznych

The artistic activities presented herein constitute a transition process from students' creative work strategy to creative and effective cooperation of students with Down syndrome: students, teachers, educators, parents.

The aim of the presented topic is to implement an original idea for organizing and conducting various forms of artistic cooperation, enabling the participants to gather experiences through exploration, expression and aesthetic experience.

Within the scope of the artistic activities, I used visual and sound materials and applied various work methods: expressive, metalinguistic, metaphorical, as well as unconventional work techniques and surprising surfaces: did you ever paint pictures on the surface of water?

The artistic activities based on the cooperation of students with Down syndrome, teachers, educators, parents and students yielded musical and artistic works: Musical trees of emotions (preparation for the meeting), literary and artistic works: Educational art books (action "for the benefit" of students with Down syndrome) and paintings using the metaphor "Masks" (inclusive potential).

The main conclusions concern the need to provoke meetings between various entities and to organize various forms of cooperation in order to build authentic relationships that constitute the basis for mutual functioning not only in the educational environment, but also in a broader sense of the social environment. The main impact of artistic activity carried out in the field of education with Down syndrome students is greater openness and involvement of the subject in cooperation, acceptance of personal cognitive limitations, understanding of needs and interests, and willingness to be active on a common level of interpersonal meetings. Just as exclusion is real and stands for a social problem, inclusion, due to its specific nature and potential value, should identify this problem and generate strategies of actions – without losing sight of the other side of the scale.

### G3.

#### Alternative and augmentative communication – a tool for inclusion and participation of people with complex communication needs

Świczowska K., Kwiatkowska A.

Polskie Stowarzyszenie na Rzecz Osób z Niepełnosprawnością Intelektualną PSONI Koło w Gdańsku, 80-371 Gdańsk, ul. Jagiellońska 11

#### Objectives

The objective of the poster is to present a way of introducing and practicing alternative and augmentative communication to empower and include people with complex communication needs.

#### Target audience

Parents, physicians, occupational, speech, language and developmental therapists, multi-disciplinary teams

#### Summary

Communication is one of the most important aspects of our life. We use communication to interact socially, to build relationships, to express personal preferences and feelings, to make comments and share opinions, make choices, ask for and give information (Communication Bill of Rights National Joint Committee for the Communication Needs of Persons with Severe Disabilities (NJC)). By interacting with others, children encounter and solve problems, communicate, and learn to consider the perspectives of others'. Children, who suffer from severe motor and communication impairments, often lack the opportunities to play and interact with peers due to limitations in their speech or movement.

In our poster we would like to present how ICF and F-words based AAC interventions empower our students, allow them to participate in social life and to feel included. We would like to discuss ways of implementing AAC in everyday school practice and everyday school life, present the most important elements of the support system we have built and discuss the meaning of team work in developing AAC users' communication skills. Assimilation of AAC in our schools is essential for providing communication opportunities for the students. This process included providing knowledge and skills to the school staff. Teachers' attitudes, AAC-knowledge and practicable abilities are crucial issues in AAC support system we have built at ZNPO. We will also discuss the impact of the communication partners' engagement on the development of communication skills among AAC users.

### G4.

#### Polish Registry of Congenital Malformations – support for children with congenital anomalies and their families

Materna-Kiryłuk A.<sup>1</sup>, Jamsheer A.<sup>1</sup>, Jamry-Dziurla A.<sup>1</sup>, Wiśniewska K.<sup>2</sup>, Latos-Bieleńska A.<sup>1</sup> and PRCM Working Group

(1) Chair and Department of Medical Genetics, Poznan University of Medical Sciences, Poland; (2) Epidemiology Unit, Department of Preventive Medicine Poznan, University of Medical Sciences, Poland

The Polish Registry of Congenital Malformations (PRCM, rejestrwad.pl), established in 1997, has been monitoring congenital anomalies in Poland. The PRCM is located within the Chair and Department of Medical Genetics of the Poznan University of Medical Sciences. The PRCM has been a member of EUROCAT since 2001 (European network of population-based registries for the epidemiological surveillance of congenital anomalies). Congenital anomalies of children between the ages of 0–18 are reported to the PRCM. Since 2015, notification of congenital anomalies to PRCM is mandatory.

The most important purpose of the PRCM is to collect reliable data on the prevalence and type of congenital anomalies throughout the country. This data is used for etiological and clinical research, indicating the need for medical care, diagnostics, therapy and rehabilitation for children with congenital anomalies. The PRCM conducts activities related to increasing public awareness of the occurrence, prevention and treatment of congenital anomalies.

An additional aspect of PRCM's activity is the creation of an environment where families of children with congenital anomalies can find the necessary information about these anomalies. This includes listings for genetic clinics and foundations. The PRCM participates in numerous Polish and international research projects, thus enabling children with congenital anomalies and their parents to participate in genetic tests, focus groups, surveys, meetings and conferences.

By offering children with specific congenital anomalies the possibility of genetic testing (using the best methods, including next generation sequencing, on a scientific basis, as part of research projects), the PRCM improves genetic care for children with these conditions as well as their families. To date more than 340 patients with limb anomalies and more than 3,000 patients with kidney anomalies registered with the PRCM have benefited from the genetic testing.

Access to the PRCM Database has assisted in the drafting of 87 original papers, 7 monographs, 2 habilitation theses, 9 doctoral dissertations, 5 BA and MA theses and 187 conference reports. Members of the PRCM Central Working Group act as experts within many specialist

teams, e.g., Medical Ration of State and Working Group for Rare Diseases Plan (Ministry of Health). They also collaborate with foundations and associations to provide epidemiological data on congenital anomalies and support their efforts to improve medical care. An example of such cooperation is the collaboration with the Spina Foundation to obtain full reimbursement of hydrophilic catheters for children with spina bifida and support for the SOS Program for Spina Bifida. In recognition of the work carried out by the PRCM, the PRCM Chairwoman (ALB) was awarded the title of SOS Program Ambassador by the Spina Foundation.

The PRCM is not only an epidemiological registry, it also provides help in various forms to children with congenital anomalies as well as their families.

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**G5.**

### **The good start – support for carers of people with disabilities**

*Zglińska P.*

Association FOR YES (Stowarzyszenie Na Tak)

The 'Na Tak' association supports people with intellectual disabilities, people with Down syndrome and their families – at every stage of life. We shape positive attitudes in the local community. We have been working for 30 years so that people with disabilities and their families could live normal lives. We are helping about 1000 families from Wielkopolska. We run institutions and units for children, adolescents and adults with neurological and genetic disorders, families and the local community. These include Occupational Therapy Workshops, special school, special kindergarten, Art Gallery, information portal, Agency of Supported Employment, Community Self-Help Centre, specialist counselling center, Short Stay House and assist with supported housing. We have the following organizational, communication, substantive skills: managing a big NGO; promoting a positive image of people with disabilities (conducted actions, campaigns), trust of families of people with disabilities, authorities, media; we employ about 200 people – specialists, therapists and assistants. We create new social services, change the local assistance system across various fields of activity: institutions, assisted living facilities, self-help activities as well as promotion of positive attitudes towards people with disabilities and their families. We work mainly with the residents of Poznań and its surroundings.

"A good start" project entails self-help and self-advocacy activities by a group of parents/guardians of people with disabilities in Poznań. It consists in the developing a form of support for carers that does not yet exist in the region, combining mutual aid and self-advocacy. The aim is to assimilate the group, strengthen it, exchange experienc-

es and promote active attitudes in the local community.

Methods used: self-help group, self-advocacy, volunteer respite care program, media activities. The activity engages the Parents Movement, stimulates exchange of intergenerational experiences, supports early parenthood (up to 2 years old). Parent/guardian groups will develop self-advocacy activities related to selected parenting issues. Groups will work with specialists in areas such as law, care, psychology. A range of activities will be developed including: a film about the carers' environment, public speaking, meetings, workshops.

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**G6.**

### **It is easier with „DOROTKOWO”. Fundacja na Rzecz Doroty Targowskiej i Jej Przyjaciół**

*Targowski M., Słupkowska J.*

Foundation DOROTKOWO

"Dorotkowo". Fundacja na rzecz Doroty Targowskiej i Jej Przyjaciół (Dorotkowo. Foundation for Dorota Targowska and her Friends) is a private foundation established in 2008. Its mission is to support medical treatment, rehabilitation, personal development and functioning of people with disabilities (especially those suffering from Down syndrome) and to provide help to their families. The Foundation is located in Toruń, Kujawsko-Pomorskie Voivodeship, Poland.

Since its establishment, the Foundation has been striving to provide all beneficiaries with complex, regular and long lasting therapy paid for using public funds. The therapy is based on both conventional as well as modern methods.

During more than 13 years of its operation, the Foundation has developed an integrated, original organizational system of physical and intellectual therapy, mainly for persons with Down syndrome, but also those suffering from other disabilities. It resulted in an impressive number of individual therapy hours (over 50,000) conducted with more than 350 disabled persons in several regions of Poland over a period of a year (2020). State funds, mainly from Państwowy Fundusz Rehabilitacji Osób Niepełnosprawnych are used to support this project as it provides different forms of care, such as speech and intellectual therapy, physical therapy, psychological therapy, music therapy, dog therapy, sensory integration therapy, training of social communication skills and EEG Biofeedback therapy. All these activities are carried out either at a subject's home, or a therapist's offices under the supervision of coordinators employed by the Foundation.

AZt its headquarters, the Foundation also provides additional activities for individuals who live in Toruń and

its vicinity. These include various group therapy meetings which support integration and activation of people with disabilities (dog therapy, music therapy, psychological therapy, social communication, theatre and dance). The Foundation also runs a job preparation school and a kindergarten for children with intellectual disabilities. There is also a theatre and a dance group operating under the supervision and support of the Foundation. Plays performed for a wider audience are prepared there. Furthermore, "Dorotkowo" also organizes multiple trips and tours with a high educational and integration value.

Providing support for families of persons affected by Down syndrome or other congenital diseases by helping them in raising funds for therapies and medical treatments, offering professional assistance of by the Foundation's consulting unit and organizing meetings, where parents and family members of Down syndrome individuals can exchange their experiences, network and support each other is another important part of the Foundation's activities. The Foundation is also extremely proud to be an organizer of numerous training courses for parents, therapists and medical professionals working with Down syndrome children.

The Foundation also actively aims to stimulate integration of people with genetic anomalies with their environment, but also to inform a wider audience about Down syndrome and other diseases, in particular using its own website [www.dorotkowo.pl](http://www.dorotkowo.pl), but also number of different Facebook profiles.

The "Dorotkowo" Foundation staff is a team of experienced professionals, who specialize in various kinds of therapies (about 300 people in Poland) supported by an administration unit, which is also a place for work for a group of people with disabilities, including four persons with Down syndrome. Mainly children and young people under 30 years old benefit from the Foundation's efforts.

Costs of the Foundation's activities are covered using funds obtained from the Polish State Fund for Rehabilitation of Disabled People (PFRON), local self-government authorities, sponsors, charity donations and other forms of financial support.

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## G7.

### Birth defect as a symbol. The prospect of communicative anthropology

Żuraw H.

Instytut Pedagogiki UPH w Siedlcach

#### Introduction

Anthropology is a field broadly understood as a description of ubiquitous human existence, stretching back to the time when homo sapiens emerged from a commu-

nity of humans until present-day society. Anthropology provides a description of integration mechanics at work within societies and how they distance themselves from certain groups and individuals. It describes permanence and changes of the culture order. It exhibits the value of creating a framework for the lives and existence of disabled and non-disabled people through applying criteria of human evaluation. An anthropological approach allows one to provide evidence against the 'that is natural !' belief. According to anthropology, human beings have relatively little inherent survival mechanisms. They subsist and remain being still alive for a long time, although we can say – for a short time – if we compare to dinosaurs' life time, mankind owes to something what is called culture. What is the culture ? It is some kind of gained possession which is passed on successive generation.

However, just the culture is blamed for creation of disability, there is no way you deny its ubiquitous influence. It manifests itself even in the area of study on ideology at given stage of human life of the certain group. It deals with the genesis of division in societies.

In some area the separation of human life there is more obvious than in others. But as modern prophets say: they will increase 'irrespectively of official ideology of chances equalisation and apologising otherness' (Bauman). Keeping it on-going is derivative of life features, which constitute cultural order under circumstances of individualisation, competing and uniformisation (i.e. understood as banned to be different) (Barnes and Mercer).

It happens like that because in European culture 'yours' means still masculine human being, intellectual, finding science and progress valuable. He is characterized by moral self-control and familiarity with good manners, acquaintance, conventional bourgeois lifestyle. The way of his thinking and activity is characterized by self-control, rationalism, individualism, proper evaluation of beauty and order. And what is more he should be healthy and fit man /Barnes and Mercer, Heathertorn, Kleck, Hebl, Hull /. Therefore who is 'the other' ? He is like an alien – in opposition to presented vision of European man i.e. ideal man. 'The other' is characterised by controversial instinctive behaviour, features arousing contradictory feelings like fear, anxiety and on the contrary fascination. The 'alien' expresses his sexuality too much, with excessive emotion and his mentality or spirituality is primitive. It is associated with magic, animism and animal instinct / Fanon 1992/. He may earn admiration for his taboo abilities (hidden and protected) and also for his art, spirit and erotica. And on the contrary he brings feeling of fear due to be contradictory between omnipotent science, rationalism and his spiritual intuition. It shows different system of value, undermine status quo and elicit fear emotion of chaos in West culture. Exotic 'the other' threatens intellect, morality and order which is mollycoddled in the area of West Law /Joffe after Sztompka 2008/. In the



past human race was barrier which may provide feeling of fear and give reluctance /sic historical typology Gobi-neau/. Nowadays various kind of disability arises different level of fear and social reaction.

This presentation actually shows prospect typical for anthropology. It focuses on sociocultural mechanism and social reaction as a feedback in response to portray people of different behaviour. It is analysis under my own research of utterances of people from environment of disabled people and people with mental disability. I would like to draw special attention to commonality of discursive analysis of otherness in everyday life of ordinary people.

I present the way of evaluation and its criteria applied for needs of community. In this way I want to exam chances for integration of this society and normalisation of social livelihood for mental disabled people. I would like to emphasize vitality of bond between local society and every inhabitant stigmatized by otherness. And I also portray some ways of coping with otherness in behaviour of mentally disabled and mentally ill people (sometimes people suffer from both of these stigma).The value of anthropological facet is connected with anthropocentric approach, assuming vision of human being as entity of being type of homo eligens (Siciński 1982), mentally unrestrained creature with ability to be autonomous, self-reliant and independent in creation of meaning of facts, experience and phenomena. This approach allows researcher to learn something new and interesting in a given area from every member of this community. Researcher is a specific authority on custom and manners, competent evaluator. His private independent opinion is affected by creation of criteria of people evaluation and transferring their image. Third party appropriately according to their competence, motivation and systems of value build verbal communication, so that is their 'micro-world'. It works like word magic. and motive power, due to the fact that language i.e. builder of reality is the kingdom of human being (Folkierska).

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**G8.**

### **Foundation for Developmental Support JA TEZ (FUNDACJA WSPIERANIA ROZWOJU "JA TEŻ")**

*Bulczak M.*

Foundation for Developmental Support JA TEZ

The JA TEZ (ME TOO) Foundation for Developmental Support) was founded in 2012 by concerned parents with the aim of supporting both children with disabilities – primarily but not exclusively suffering from Down syndrome – as well as parents and caregivers. Presently our organization encompasses approximately 200 families from the Pomeranian area and the rest of Poland.

In September 2021, we launched our new educational and rehabilitation center for people with Down syndrome in Gdańsk as well as an integration kindergarten. In the center we have prepared 5 therapy rooms (speech therapy, pedagogy, psychology and neurobiology), 2 rooms for physical rehabilitation and sensory integration and 3 rooms for group work (for rhythmic, dance, communication and dialogue classes, creating support groups for parents, a meeting place for young people).

The "TO JA" (IT'S ME) kindergarten is based on open education the assumptions. For every 20 children in a group, 5 are children with Down syndrome.

In September 2021, we began a 4th class, where children with Down syndrome will be participate in lessons at a public school. Joint education and implementation of new work and activity methods allow all children to develop a sense of success, self-confidence and respect for other people.

As a foundation we strive to provide care and support for families and the professional establishment which serves these families. We do this by providing educational opportunities for both parents and medical professionals, where they are both provided with a perspective and learn how to best work together in supporting these children. These opportunities include workshops, conferences and other formal and informal gatherings where ideas and concerns are shared among all those who provide care and support.

We also actively help people with disabilities find employment. Our aim is to facilitate their integration into the workplace and help them become active members of the society. The foundation's activities include networking and discussions with cultural organizations and businesses in the Tricity area. We also support other entities throughout Poland which are interested in duplicating our project. We would like to find jobs for people with disabilities at different businesses and entities.

The Foundation's primary activities:

- Therapy center for the psychological, sociological and physical development of disabled children
- Training and guidance with employment in different institutions in the Tricity area
- Sharing experiences in exploring employment opportunities and know-how with other non-profit organizations and institutions throughout Poland
- Supporting training sessions and workshops
- Guidance for parents and other professionals working with children with disabilities
- Therapy workshops for parental training
- Social events for inclusion in the community
- Mainlining school programs for educational integration

More information: <https://jatez.org.pl/>

## Challenges in counseling and therapy for adolescent diagnosed with ASD and with comorbid behavioral and mental health problems in the context of school and parenting conditions. Case study

Stefańska-Klar R.

State Higher Vocational School in Raciborz, Poland

### Introduction

Adolescents with ASD often experience problems and difficulties at school and at home, as well as in other social situations. ASD is often associated with other psychiatric disorders, such as anxiety disorders, ADHD, OCD, depression and behavioral disorders. They result from difficulties in regulating relations with the world and coping on a personal level with the challenges of life and biological determinants of ASD, which may intensify in adolescence. Particularly difficult problems arise when they are combined with factors such as childhood violence, living in an orphanage or with a foster family. A child's unresolved problems can cause serious complications in later years, resulting in failures at school, family and non-family conflicts, anti-social behavior, and problems with the law. Inclusion of a counseling psychologist in a child's programme may bring about beneficial changes, provided that the therapy is conducted in an ASD and trauma informed manner and that all parties involved in the change process cooperate fully.

### Objectives

Recognition and analysis of the challenges associated with counseling a teenager diagnosed with ASD, suffer-

ing from coexisting behavioral problems (externalizing as well as and internalizing) and diagnosed with depression and anxiety disorder (actual counselor recognized symptoms of PTSD additionally) in a foster family setting.

### Materials and Methods

A case study entailing a 15-year-old boy participating in counseling due to serious behavioral problems, which could result in him being placed in a MOW facility (special youth educational center), was investigated. An attempt was made to describe the processes and changes taking place within the *child – foster family-school-other institutions – counselor system*.

### Results

The results of a five-month therapy were summarized. Analysis of the course in close connection with the course of events in the boy's environment (family, school, peers, institutions) and the results of the counselor's cooperation with these places are presented.

### Conclusion

Cooperation and coordination within a child's external environment as well between a child and counsellor are essential for a successful intervention. Therapy leads to changes that result in crises in all types of the child's environment and within the child as well. The external environment reacts to this. If done unskillfully, it usually exacerbates the crisis and also blocks positive changes rather than reinforcing them. Cooperation and coordination of interventions between all elements of the *child – environment – counseling system* is necessary to achieve positive and lasting effects of therapy and to prevent serious crises with undesirable prognoses.

## Gallery of Wanessa Bąkowska

Wanessa Bąkowska – 13-year-old girl with Down Syndrome. A talented artist with **over 3,800 followers** on Facebook ([f Obrazy malowane sercem](#)).





# Connecting People and Places





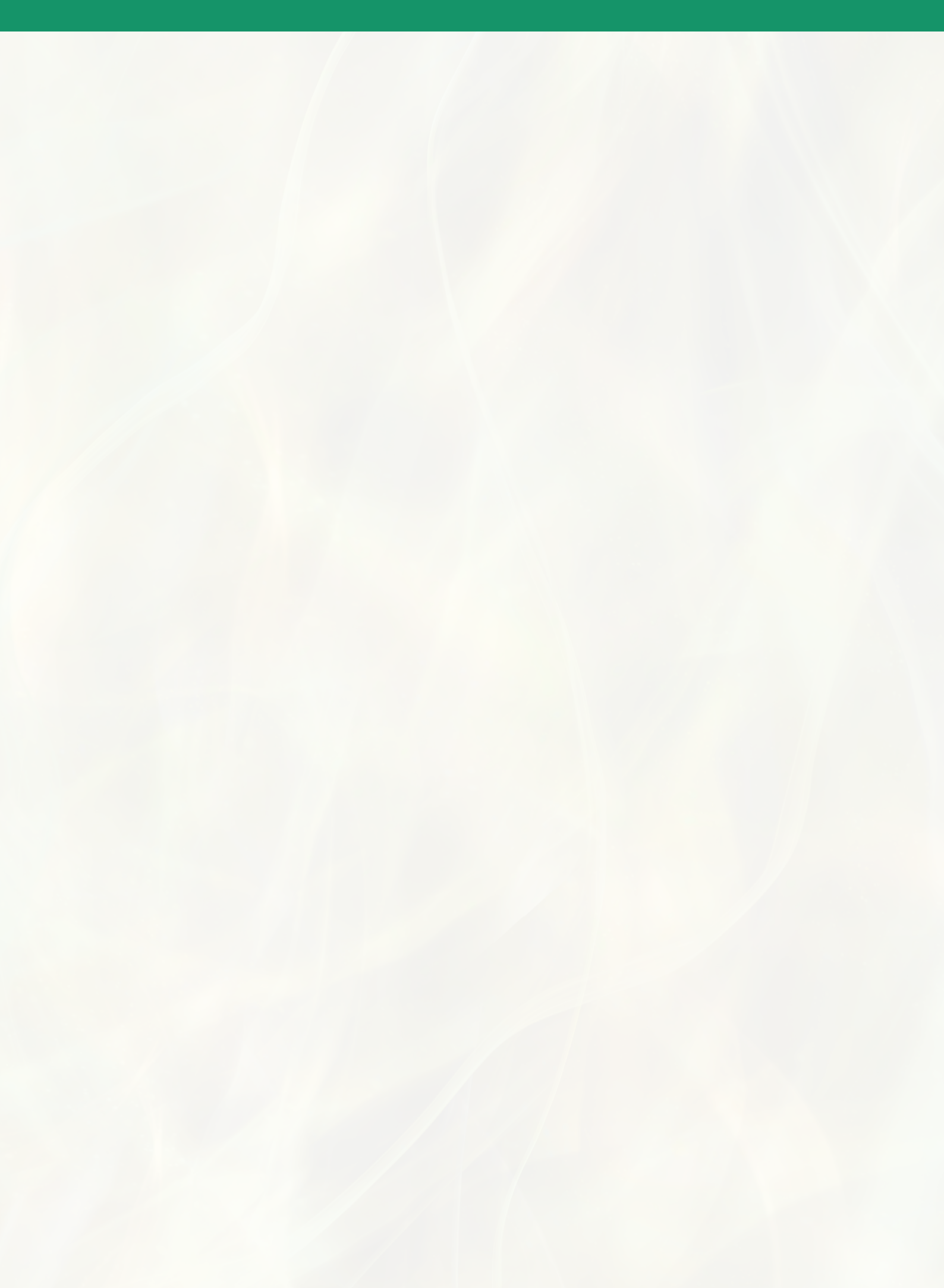






## EUROlinkCAT Working Group: Acronym details

Acronym (partner's number)	Full name
SGUL (1)	ST GEORGE'S HOSPITAL MEDICAL SCHOOL
CARobb	CONGENITAL ANOMALY REGISTER FOR OXFORDSHIRE, BERKSHIRE AND BUCKINGHAMSHIRE
EMSYCAR	EAST MIDLANDS AND SOUTH YORKSHIRE CONGENITAL ANOMALIES REGISTER
WANDA	WESSEX ANTENATALLY DETECTED ANOMALIES REGISTER
UU (2)	UNIVERSITY OF ULSTER
RSD (3)	REGION SYDDANMARK
UNEW (4)	UNIVERSITY OF NEWCASTLE UPON TYNE
UNIFE (5)	UNIVERSITA DEGLI STUDI DI FERRARA
KDB (6)	KLINIKA ZA DJECJE BOLESTI ZAGREB
CNR-IFC (7)	CONSIGLIO NAZIONALE DELLE RICERCHE
UMCG (8)	ACADEMISCH ZIEKENHUIS GRONINGEN
PHW NHS (9)	PUBLIC HEALTH WALES NATIONAL HEALTH SERVICE TRUST
INSERM (10)	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE
FISABIO (11)	FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA DE LA COMUNITAT VALENCIANA
PUMS (12)	UNIwersytet Medyczny im Karola Marcinkowskiego w Poznaniu
THL (13)	TERVEYDEN JA HYVINVOINNIN LAITOS
OMNI NET (14)	INTERNATIONAL CHARITABLE FUND OMNI-NET FOR CHILDREN
OVGU (15)	OTTO-VON-GUERICKE UNIVERSITAET MAGDEBURG
INSA (16)	INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE
CHURéunion (17)	CENTRE HOSPITALIER UNIVERSITAIRE DE LA REUNION
PIH (18)	PROVINCIAAL INSTITUUT VOOR HYGIENE
BIOEF (19)	ASOCIACION INSTITUTO BIODONOSTIA
BIOMED (20)	BIOMEDICAL COMPUTING LIMITED
SU (22)	SWANSEA UNIVERSITY
QMUL (23)	QUEEN MARY UNIVERSITY OF LONDON





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