Providing medical devices for children

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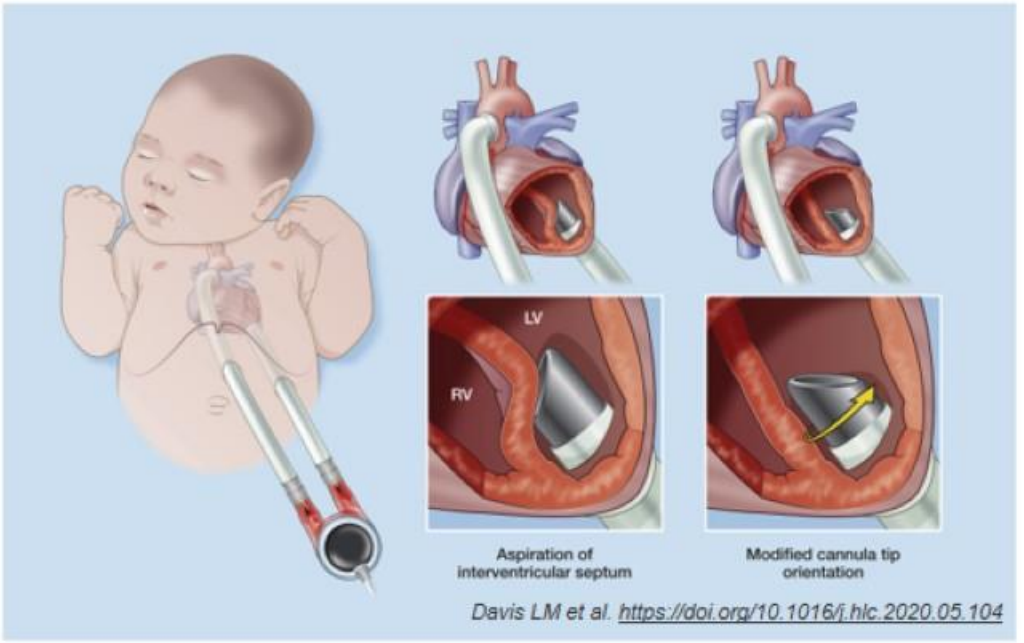


Declarations

- BK, KG and BPG declare NO CONFLICT of interest
  No funding received from any commercial entity related to medical devices
- Our work in this area is financially supported in part by the EU Horizon 2020 research & innovation programme, project CORE-MD *(Coordinating Research and Evidence for Medical Devices, grant agreement 965246)*
- On behalf of the European Academy of Paediatrics, the Biomedical Alliance in Europe and the Stiftung Kindergesundheit/Child Health Foundation, we led the paediatric medical devices task in the CORE-MD project

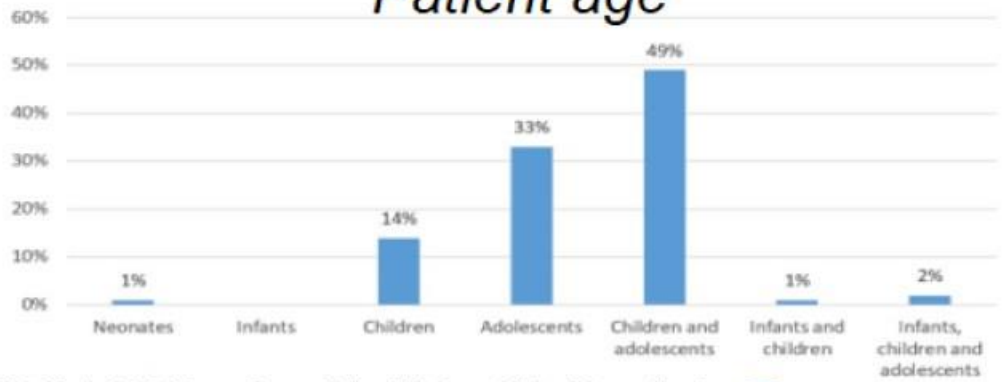
Background

- EU MDR 745/2017: strengthen clin. evaluation & safety, part. high-risk MD
- EU MDR **markedly increases barriers, time requirements, and costs** for bringing MD to *(or keeping them on)* the market
- Particularly challenging for MD sold in small numbers *(paediatric & orphan devices)*
- **Paediatric & orphan MD increasingly disappear** from the EU market
- **Loss of essential MD** needed for appropriate care of sick children and other patients with orphan disease *(NB: 7 of 10 orphan diseases manifest only in childhood, a further 18% occur both in children and adults!)*

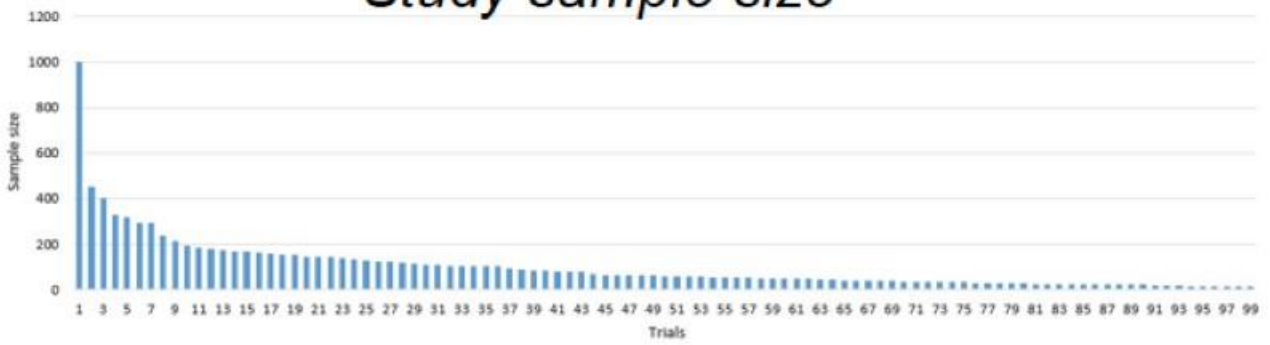
Scoping review, paediatric clinical trials on MD

- Scoping review on clinical trials investigating selected high-risk paediatric medical devices in patients aged 0-21 yrs, published 2017- 2022
- Mostly **small sample size** *(median 59; 65% <100)*
- Most studies *(≈90%)* in children with **diabetes** *(common disease, ≈same MD as adults, high financial turnover)* but **hardly in other disorders**
- **Lack of studies** in **infants & young children**

Patient age



Study sample size



Guerlich K et al. Evidence from clinical trials on high-risk medical devices in children: a scoping review. Pediatr Res. 2024 Feb;95(3):615-624. doi: 10.1038/s41390-023-02819-4.

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Recommendations on clinical investigation & evaluation

European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children

ACTA PÆDIATRICA WILEY

Experts from various child health specialties, representatives of **24 medical associations** *(Eur Acad Paediatrics, Child Health Foundation-Stiftung Kindergesundheit, Assoc Eur Paed Congen Cardiol, Biomed Alliance Eur, Cardiovasc Intervent Radiol Soc Eur, conect4children, Eur Ped Dialysis WG, Eur Ped Surgeons Assoc, Eur Rare Kidney Dis Ref Network, Eur Ref Network Rare Endocrine Conditions, Eur Ref Network Hereditary Metabol Disorders, Eur Soc Cardio, Eur Soc Developm Perinatal Paed Pharmacol, Eur Soc Emergency Med, Eur Soc Endocrinol, Eur Soc Ped Nephrol, Eur Soc Paed Neonatal Intens Care, Eur Soc Paed Gastro Hepatol Nutrition, German Soc Paed Adolescent Med, Int Ped Nephrol Ass, Royal College Paed Child Health UK, Royal College Physicians Ireland, Int Ped Nephrol Assoc, Soc Study Inborn Errors Metabol)*, a national **regulatory authority** *(Health Products Regulatory Authority Ireland)* and the **European Commission** Directorate General Health and Food Safety - Health Technology Unit B6

Gürlich K et al. European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children. Acta Paediatr. 2023 Nov;112(11):2440-2448. doi: 10.1111/apa.16919. Epub 2023 Aug 15

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Recommendations on clin. investigation & evaluation

- Development of **recommendations for investigation** of high-risk MD for **children**, building on participants' expertise and the results of the scoping review of clinical trials on high-risk MD in children
- Propose approaches for **evaluating and certifying high-risk MD** for children for market introduction

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Developing recommendations

- Invitation to paediatric and other related medical associations, regulators, European Commission, and renown experts to join expert panel
- Evaluate systematic review on current status of clinical investigation of MD intended for children
- Review of current approaches to support R&D, and review of current approaches to certification for market introduction
- Face to face panel meeting and an additional online meeting, plus further digital communication
- Conclusions adopted by consensus, publication & dissemination

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Clinical investigation: recommendations

- No “one size fits all” solution – one and the same approach to clinical investigation of all MD intended for paediatric patients cannot be applied
- **Different levels of clinical evidence** are required depending on
  - specific research question
  - type of MD
  - identification of potential hazards and expected risks
  - nature and prevalence of conditions treated with the MD
  - intended age group

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Clinical investigation: recommendations

The approach to clinical investigation of MD in children should consider

- **RCTs are the gold standard** for evaluating therapeutic benefits of medical interventions and should be performed whenever feasible.
- **RCTs in children are mostly not feasible** to evaluate MDs for ethical or practicality reasons. Other study designs must be considered to generate clinical data on device performance and safety. **Strive for the highest achievable level of clinical evidence**.

  Hierarchy of evidence:
  1) RCT (highest level)
  2) Comparative prospective study with concurrent controls (experimental or observational)
  3) Comparative study without concurrent controls (e.g. with historical control)
  4) Prospective case series with documentation of either post-test or pre-test/post-test outcomes

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Clinical investigation: recommendations

- **Mixed population studies** *(both adults & children)* can optimize sample sizes and resource use in case of a shared indication for MD use *(include subgroup analyses)*
- **Extrapolation** of data obtained from trials in adults can be considered for devices with the same intended use in children, if treated condition is similar and no indication points to different effectiveness and safety of the device in children
- Post-marketing surveillance needs European **patient registries supervised by competent paediatric associations** systematically collecting relevant and informative data on paediatric patients treated with MD of interest
- **Define and enhance quality** of existing registries, establish new registries
- **Funding** to be secured from public and private sources

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Clinical evaluation: recommendations

- Establish an **expert panel on paediatric MD**, with **paediatric experts** to provide scientific and clinical advice
  - to developers of new and high-risk MD according to MDR Art. 61(2)
  - to EU MD Coordination Group with respect to consistent application of the MDR on MD for children according to MDR Art. 106
- **Require notified bodies** certifying paediatric MD to **seek advice from competent paediatric experts**
- **Transparency** needed regarding 1) **advice** of expert panels re clinical evidence expectations provided to MD developers according to MDR Art. 61(2), and 2) **clinical data** relied upon by manufacturers for paediatric MDs to ensure predictable evidence requirements, and clinicians have access to MD related data

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Clinical evaluation: recommendations

- **Designation of "orphan MD" status** should be based on a case by case evaluation, taking the following criteria into account
  - Intended use in a life-threatening or chronically debilitating disease with a prevalence of <1 per 2,000 people, based on the accepted definition of rare diseases in the EU
  - Existence of an unmet medical need, and
  - Absent or insufficient suitable / equivalent alternative therapeutic options with similar clinical safety

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Interim solutions for paediatric and orphan MD

- **Ensure continued access** to essential paediatric and orphan MD
- **Establish systematic monitoring** on MD that are about to disappear or have already disappeared from the market *(currently lacking!)*
- Implement efficient & fast process to assign a “paediatric device” or “orphan device” status, leading to a **simplified, fast** and **low-cost conformity assessment**
- Proactively support bringing MDs to market also for small and particularly vulnerable patient groups, e.g. **public funding, other incentives** *(cf. drugs for children)*
- **Until final solution is achieved:** paediatric or orphan MDs that have been marketed for at least 3 years without reported problems to get permission for continued use; MDs approved with credible evaluation in other jurisdictions to be permitted for market access, to support patient safety and well-being with access to essential MDs

Potential interim solution for EU children in need

- UK and Switzerland *(both non-EU)* apparently accept using medical devices for children with market approval in the USA
- Switzerland accepts single use of medical devices without regulatory approval
- Sick children from the EU requiring treatment with medical devices withdrawn or not approved in the EU could be treated in Switzerland or the UK until adequate solutions are established in the EU

Increasing awareness, support political decisions

- Clinical experts and paediatric associations in Europe increase awareness on consequences of the EU MDR and its implementation for medical care of sick children, due to increasing unavailability of essential MD for children

Open Letter to EU Health Commissioner signed by 27 organizations

copy by e-mail:
cab-kyriakides-contact@ec.europa.eu

Commissioner Stella Kyriakides
European Commissioner for
Health and Food Safety
European Commission
Rue de la Loi / Wetstraat 200
1049 Brussels, Belgium

Date 27/6/2023
Open letter: Urgent action needed to secure continued access to essential medical devices for children and for patients with orphan diseases

Response by European Commission President

Ref. Ares(2023)5981983 - 04/09/2023

EUROPÄISCHE KOMMISSION
Kabinett der Präsidentin Ursula von der Leyen

Berater zum europäischen Grünen Deal

Brüssel, 04. September 2023
Ares (2023) 4514198

Sehr geehrter Herr Professor Koletzko,

Präsidentin von der Leyen dankt Ihnen für die Übermittlung des an Kommissarin Kyriakides gerichteten offenen Briefes, den Sie gemeinsam mit 28 anderen europäischen Verbänden im Bereich der Kindermedizin und der medizinischen Versorgung unterzeichnet haben. Sie äußern darin Ihre Besorgnis über die Auswirkungen der Umsetzung der Verordnung (EU) 2017/745 über Medizinprodukte (MDR) auf die Verfügbarkeit bestimmter Medizinprodukte, insbesondere solcher zur Behandlung von

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Motion for a resolution of the Eur. Parliament on ensuring access to medical devices in paediatric care in the EU (Dec 2023)

pursuant to Rule 143 of the Rules of Procedure - Sunčana Glavak MEP, December 2023

European Parliament, - having regard to the "EU for Health" program 2021-2027, - having regard to the Medical Devices Regulation (EU 2017/745), - having regard to article 143 of its Rules of Procedure,

A. Whereas the provisions of the **Medical Devices Regulation may lead to the unavailability of key medical devices, putting paediatric and rare disease patients at risk**;

B. Whereas maintaining **uninterrupted access to vital medical devices is essential for optimal health care and protection**;

C. Whereas the **EU does not have an effective surveillance mechanism** to actively monitor the availability and potential withdrawal of essential medical devices from the market;

Motion for a resolution of the Eur. Parliament on ensuring access to medical devices in paediatric care in the EU (Dec 2023)

1. Calls for the **amendment of the EU Medical Devices Regulation** to ensure continued access to devices essential for advanced paediatric care and treatment of rare diseases;

2. Calls for the **expansion of monitoring** of shortages and the availability of certain medical devices, with the aim of avoiding potential shortages;

3. Calls for the **establishment of temporary measures** to protect patients during the transition, including automatic authorization for the continued use of high-risk paediatric medical devices that have been proven safe in the EU for at least 3 years;

4. Recommends that **conformity checks for devices for paediatric patients** be carried out by **subsidized public bodies** or by **limiting the fees** charged by private bodies;

5. Instructs its President to forward this Resolution to the Commission, the Council and the Governments and Parliaments of the Member States.

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Next steps

- Very constructive collaboration with the EU Medical Device Coordination Group – Task Force on Orphan Medical Devices aiming to promote solutions possible within the existing legal framework
- EAP and its members continue advocacy activities at European and national levels to support political decisions beyond the existing legal framework *(e.g. lower cost hurdle for conformity assessment of paediatric devices that cause market withdrawal)*
- EU4Health Project DeCODe *(2024-2026)* develops a pivotal platform for developing safe and effective paediatric and orphan medical devices to accelerate development of novel, innovative paediatric and orphan medical device solutions at all stages of the product lifecycle towards implementation
- We need to continue making the voice of children heard

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The rights of children must be protected with priority

UN Convention on the Rights of the Child ratified by all EU member states:

- Children have the right to enjoy the **highest attainable standard of health** and to be provided with the necessary medical assistance and **health care** *(Art. 24)*
- The **best interest of the child** shall be the **primary consideration** in all actions concerning children, whether undertaken by public or private social welfare institutions, courts of law, administrative authorities or legislative bodies *(Art. 3)*