CORE-MD

Coordinating Research and Evidence for Medical Devices

Evidence from clinical trials on high-risk medical devices in children: A scoping review

Kathrin Gürlich, Bernadeta Patro-Golab, Paulina Dworakowski, Alan G. Fraser, Michael Kammermeier, Tom Melvin, Berthold Koletzko

Webinar, December 14, 2023

Background and Objective

- Medical Device Regulation (EU 2017/745): changed regulatory requirements
- Paediatric devices context: number of patients limited, rarity of events, ethical considerations, parental concerns, high financial regulatory costs
- *Challenge:* **Obtain best possible documentation of safety and efficacy AND provide access to innovative medical devices for children**

- *Objective:* To review existing **published evidence from clinical trials** on high-risk medical devices in children to identify and describe methodologies applied in this research area

→ Review protocol published at OSF: https://osf.io/uzekt

Methods

Participants:

- Paediatric population covering the age range from 0 to < 21 years
- Mixed populations including both children and adults

Context:

- No restrictions in terms of study setting

Type of sources:

- Clinical trials of any design

Methods

Concept:

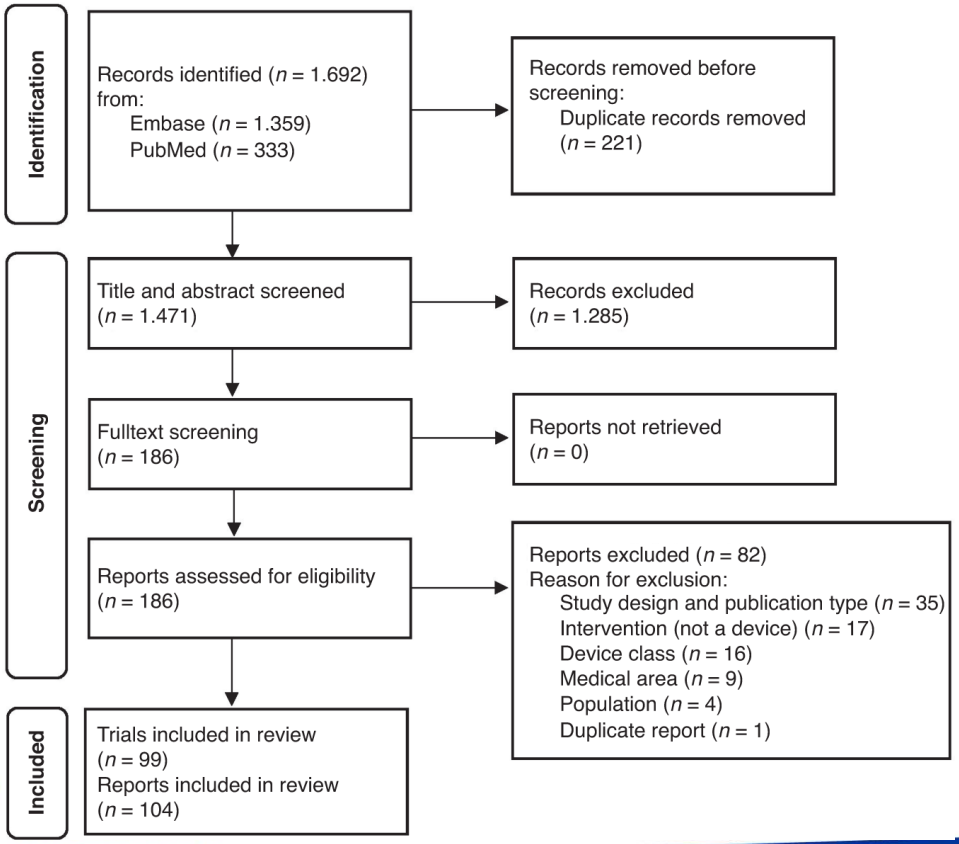
- Clinical specialties of interest: cardiology, diabetology, orthopaedics and surgery
- Focus on high-risk medical devices
- No central database of (paediatric) medical devices in Europe

→ List of paediatric medical devices of interest developed based on FDA sources

Search strategy:

- Two databases: Embase (Ovid), Medline (PubMed)
- Timeframe: 1st January 2017 – 9th November 2022

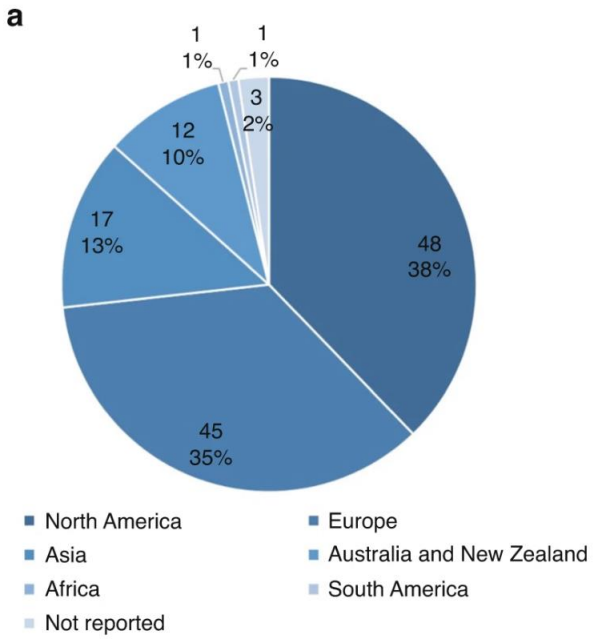
Results – Flow chart



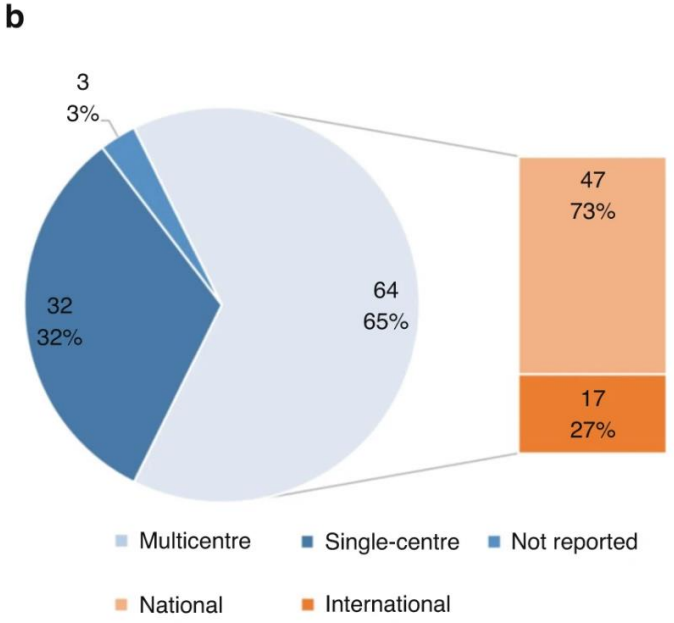
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Results – Study settings

Trials distribution by continent



Trials distribution by centre



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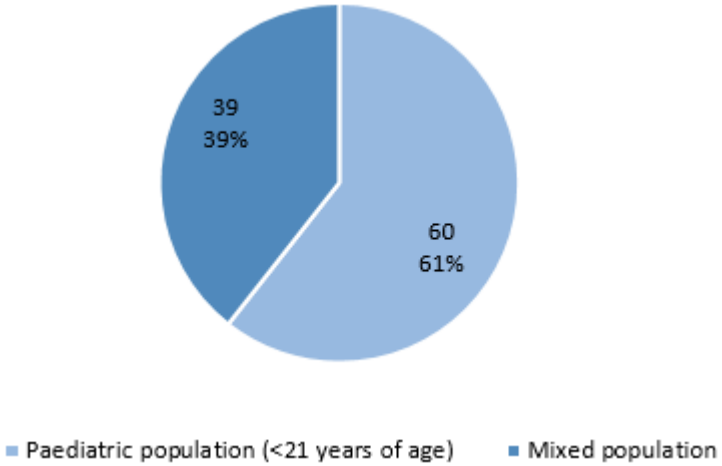
Results – Evaluated medical devices

- 88% of the trials from diabetology, 12% from cardiology

Clinical specialty	Medical device	N (%)
Diabetology	Closed loop system	24 (24)
	(Advanced) hybrid closed loop system	22 (22)
	Open loop control system	1 (1)
	Predictive low-glucose management (PLGM) system	4 (4)
	Continuous glucose monitoring (CGM)	27 (27)
	Continuous subcutaneous infusion of insulin (CSII), insulin pump	9 (8)
Cardiology	Atrial septal defect occluder	4 (4)
	Transcatheter pulmonary valve	3 (3)
	Transcatheter heart valve	1 (1)
	Ablation catheter with mini-electrodes	1 (1)
	Covered stent	1 (1)
	Fully bioabsorbable pulmonary valved conduit	1 (1)
	Novel expanded polytetrafluoroethylene-based valved conduit	1 (1)

Results – Population

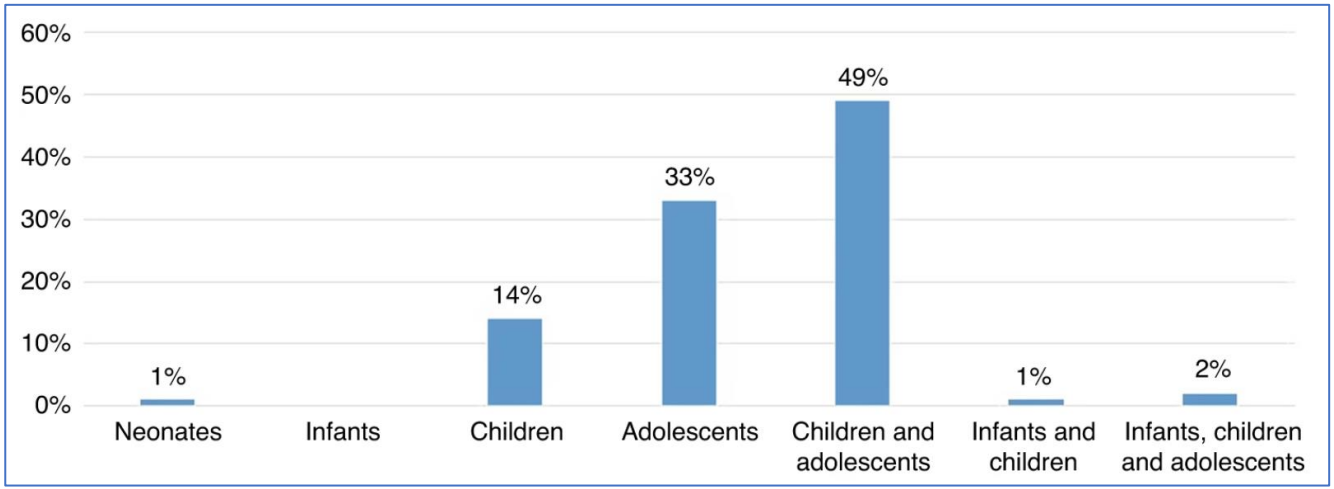
Trials distribution by population



→ Within mixed populations, 25 trials (64%) reported exact number of children

→ Proportion ranging from 10%-89%

Results – Distribution of age groups



Age groups categories[1,2]: Neonates (first 28 days), Infants (29 days-2 yrs), Children (2-12 yrs), Adolescents (12-21 yrs)

1. Lee SJ, Cho L, Klang E, Wall J, Rensi S, Glicksberg BS. Quantification of US Food and Drug Administration Premarket Approval Statements for High-Risk Medical Devices With Pediatric Age Indications. JAMA Netw Open. 2021;4(6):e2112562.
2. US Food and Drug Administration. Pediatric medical devices [Available from: https://www.fda.gov/medical-devices/products-and-medical-procedures/pediatric-medical-devices

Results – Study designs

- **38 RCTs**

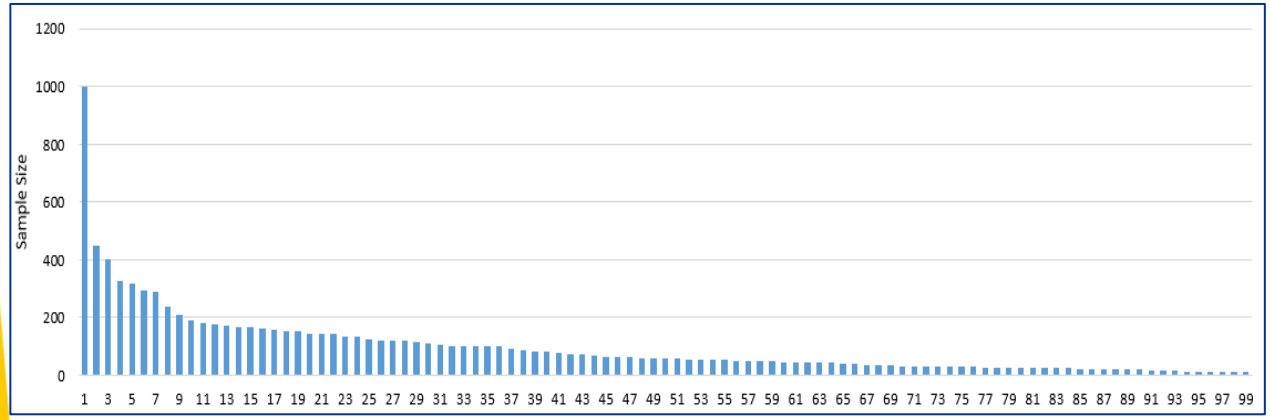
- 90% of controlled and crossover trials randomized
- All crossover trials and most of RCTs open-label
- 13% of all RCTs single or double blinded

Study design	Trials: n (%)
Randomized controlled trials, RCTs	38 (38)
Nonrandomized controlled clinical trials	4 (4)
Crossover trials	20 (20)
Before–after studies	22 (21)
Clinical performance studies with reference device	7 (7)
Uncontrolled trials	4 (4)
Cluster randomized controlled trials	1 (1)
Interventional studies with historical controls	1 (1)
Qualitative studies on intervention being trialed	2 (2)

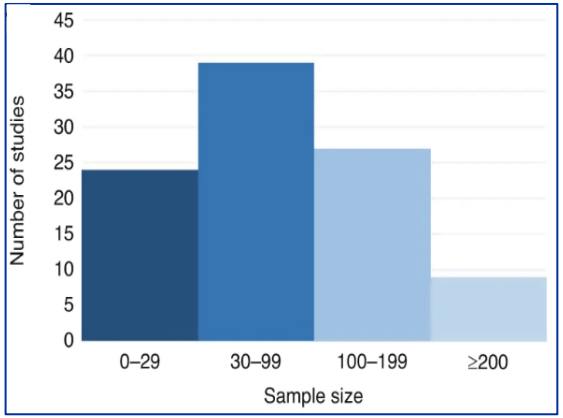
Results – Sample size

- Median number of study participants: 59 (IQR 30-124.5, range 10-1000)
- 64% of studies with a sample size <100 participants

Sample size distribution of the included studies



Sample size distribution of the included studies per category

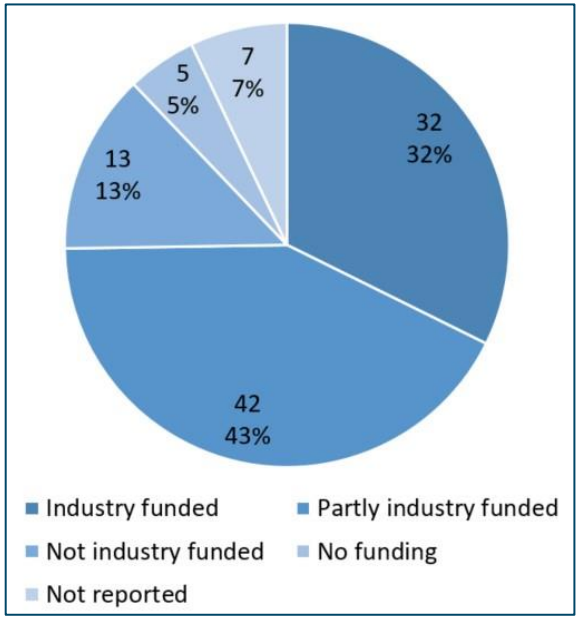


Results – Assessed outcomes

- 79% of trials assessed efficacy & effectiveness, 73% safety outcomes

Types of the study outcomes assessed	Trials: n (%)
Efficacy/Effectiveness	78 (79)
Safety/Adverse events	72 (73)
Patient reported outcomes, PROM	24 (24)
Performance/Accuracy	23 (23)
Usability/User experience	19 (19)
Feasibility	6 (6)
Cost evaluation/cost-effectiveness	2 (2)
Interoperability	1 (1)
Other	6 (6)

Results – Sources of funding



→75% of studies were fully or partly industry funded

Summary of findings

In the assessed sample, clinical trials on high-risk medical devices in infants, children and adolescents were:

- mostly **multicentre** conducted in Europe and North America
- performed with **small sample sizes**
- mostly in adolescents or older children, with a **low number in infants and young children**
- using **variable study designs** (often without concurrent control group)
- dominated by devices from the clinical specialty of **diabetology**

Conclusions

- Paediatric devices require specific considerations and have unique barriers to their development
- Findings may assist regulators and competent authorities in setting achievable and context-tailored requirements for clinical evidence supporting device conformity

Further reading

APS European Society for Paediatric Research Society for Pediatric Research www.nature.com/pr

SYSTEMATIC REVIEW OPEN

Check for updates

Evidence from clinical trials on high-risk medical devices in children: a scoping review

Kathrin Guerlich[1,2,7], Bernadeta Patro-Golab[1,7], Paulina Dworakowski[3], Alan G. Fraser[4], Michael Kammermeier[1], Tom Melvin[5] and Berthold Koletzko[1,2,6]✉

BACKGROUND: Meeting increased regulatory requirements for clinical evaluation of medical devices marketed in Europe in accordance with the Medical Device Regulation (EU 2017/745) is challenging, particularly for high-risk devices used in children.
METHODS: Within the CORE-MD project, we performed a scoping review on evidence from clinical trials investigating high-risk paediatric medical devices used in paediatric cardiology, diabetology, orthopaedics and surgery, in patients aged 0–21 years. We searched Medline and Embase from 1st January 2017 to 9th November 2022.
RESULTS: From 1692 records screened, 99 trials were included. Most were multicentre studies performed in North America and Europe that mainly had evaluated medical devices from the specialty of diabetology. Most had enrolled adolescents and 39% of trials included both children and adults. Randomized controlled trials accounted for 38% of the sample. Other frequently used designs were before-after studies (21%) and crossover trials (20%). Included trials were mainly small, with a sample size <100 participants in 64% of the studies. Most frequently assessed outcomes were efficacy and effectiveness as well as safety.
CONCLUSION: Within the assessed sample, clinical trials on high-risk medical devices in children were of various designs, often lacked a concurrent control group, and recruited few infants and young children.

Pediatric Research; https://doi.org/10.1038/s41390-023-02819-4

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CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

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For more information, visit: www.core-md.eu

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