How to improve paediatric clinical trial design: a sponsor's perspective

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Het Lam Gods

Jan Van Eyck

Source: Historiek.net

(https://historiek.net/het-lam-gods-in-honderd-miljard-pixels/14942/

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PAEDIATRIC CLINICAL TRIALS

Continuous **high off-label use** of medicines in children, estimates of **50% (90% neonatal)**

1 out of 5 paediatric trials fails
due to **suboptimal experiment planning, inappropriate study design** or inadequate participant enrollment

Regulatory

2007: Regulation for Paediatric Investigational Plans (PIPs), low completion

Enpr-EMA: guideline for preparedness of clinical trials in paediatrics (August 2020, EMA/56009/2019) identify site modifications for paediatric trials

Paediatric clinical trial networks

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ECRIN – EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

PedCRIN

Innovative Therapies for Children with Cancer – ITCC – European consortium

ESCAPE network

TEDDY NETWORK – European Network of Excellence for Paediatric Research

Enpr-EMA: European Network of Paediatric Research

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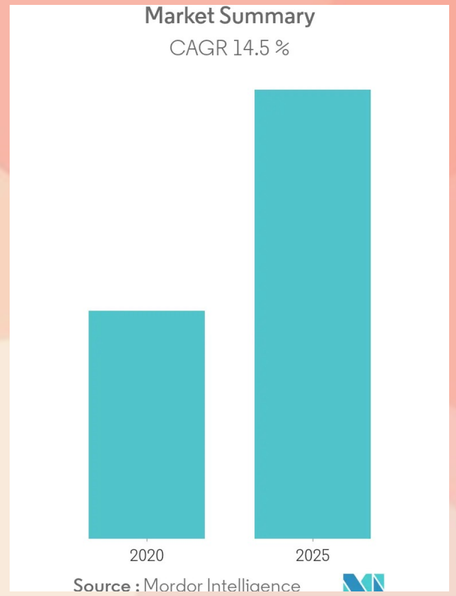
INDUSTRY GROWTH

- **Vast growing interest and commitment** in paediatric clinical trials for both small and big industry partners.

- **Shift** from in-house clinical research to site set-up through pan-European **networks** and **global** collaborations, including use of CRO (clinical research organisation).

- Market **growth** expected (compound **annual** growth rate) was **14,5%** in 2020**, overal market increase with 50% in the EU over the last decade**.

Market Summary of Paediatric Clinical Trials in 2020 and prediction of 2025



Are we there yet?

27% of the world's population are children,
*yet **16.7%** of the clinical trials are in **children** (cfr. 2015).*

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CONECT4CHILDREN (C4C)

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COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

2018 - present

- c4c is an Innovative Medicines Initiative 2 **(IMI2)**

  funded program, including:

  - **20 European countries**
  - **+2000 sites**
  - **10 EFPIA partners**
  - 3 academic sponsors, 5 industry sponsors

1. More efficient trial implementation through the set-up of **national hubs** and qualified sites
2. Business cases for **sustainability** beyond IMI funding
3. Input in clinical trial design and implementation from **pilot expert advisory groups** and other fora.
4. Identification of **data standards** and performance metrics
5. **Educational program** for health professionals and **awareness raising campaigns** for the general public

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imi innovative medicines initiative

efpia

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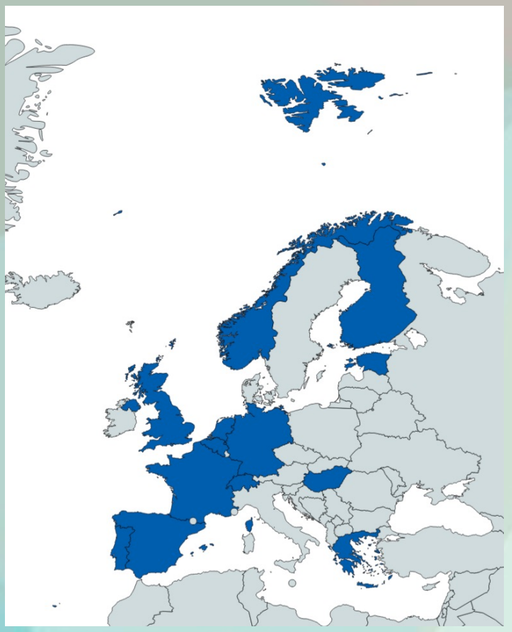
C4C NATIONAL HUB SURVEY – PAEDIATRIC SPECIFICITIES



A **European-wide survey** was conducted within the **c4c network**

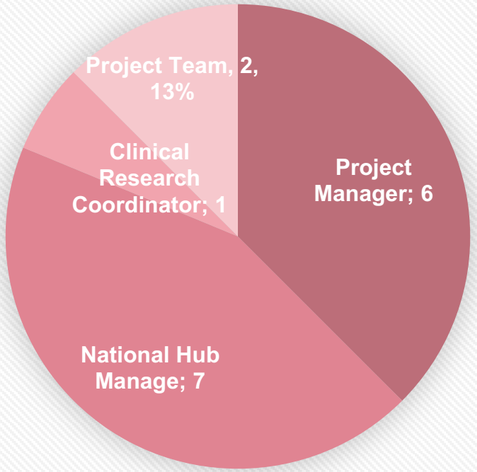
In 12 countries gathering a total of 13 unique responses and a cumulative total of **24 responses**.

The role of responders were primarily project manager and national coordinators, located in **North to South-West Europe**.

The responders' **median of experience** conducing paediatric clinical trials ranged from **beginning to 30 years,** with **a median of 10 years** of experience.

Each hub's response was gathered from direct or indirect team discussion, having a median of 5 members per National Hub

Responders of the survey per role performed in c4c



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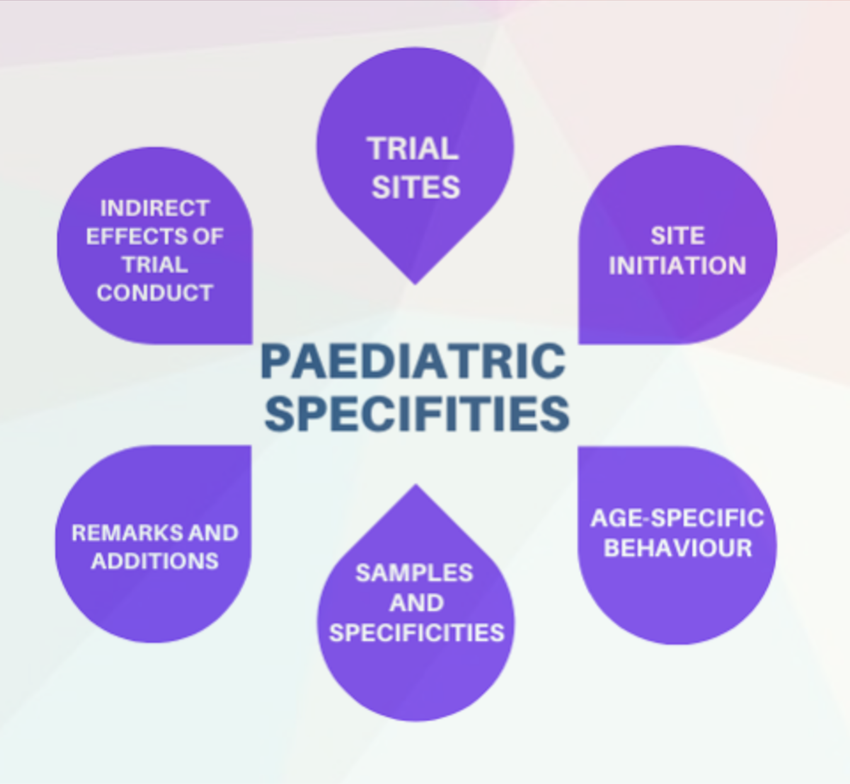
OUTLINE: PEDIATRIC SPECIFICITIES TO CLINICAL TRIALS FOR DRUG DEVELOPMENT



The survey was constructed of
37 open questions.

Topic 1 TRIAL SITES

a. Site identification
b. Feasibility process
c. Facilities on site

Topic 2 PROCEDURES FOR SITE INITIATION

a. Budget and contracting
b. Ethics Committee
c. National competent authority
d. Site set-up trial

Topic 3 AGE SPECIFIC BEHAVIOUR

a. Screening
b. Consent / assent
c. Study participation withdrawal
d. Trial procedures

Topic 4 SAMPLES AND SPECIFICITIES RELATED TO THE SIZE OF PARTICIPANTS

a. Blood sampling Specificities
b. Blood sample Assays
c. Other trial procedures

Topic 5 INDIRECT EFFECTS OF TRIAL CONDUCT

a. Financial
b. Family planning
c. Education

Topic 6: OTHER COMMENTS AND REMARKS

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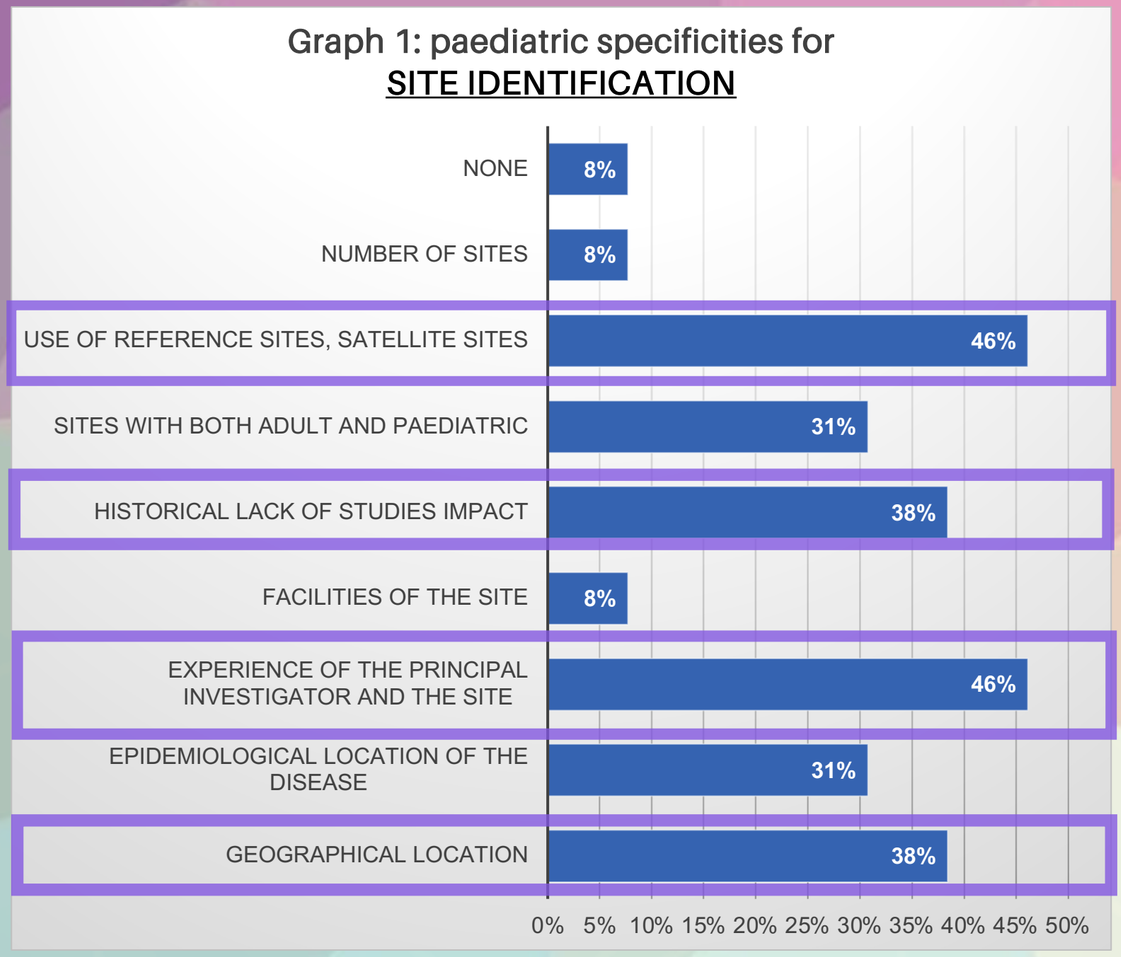
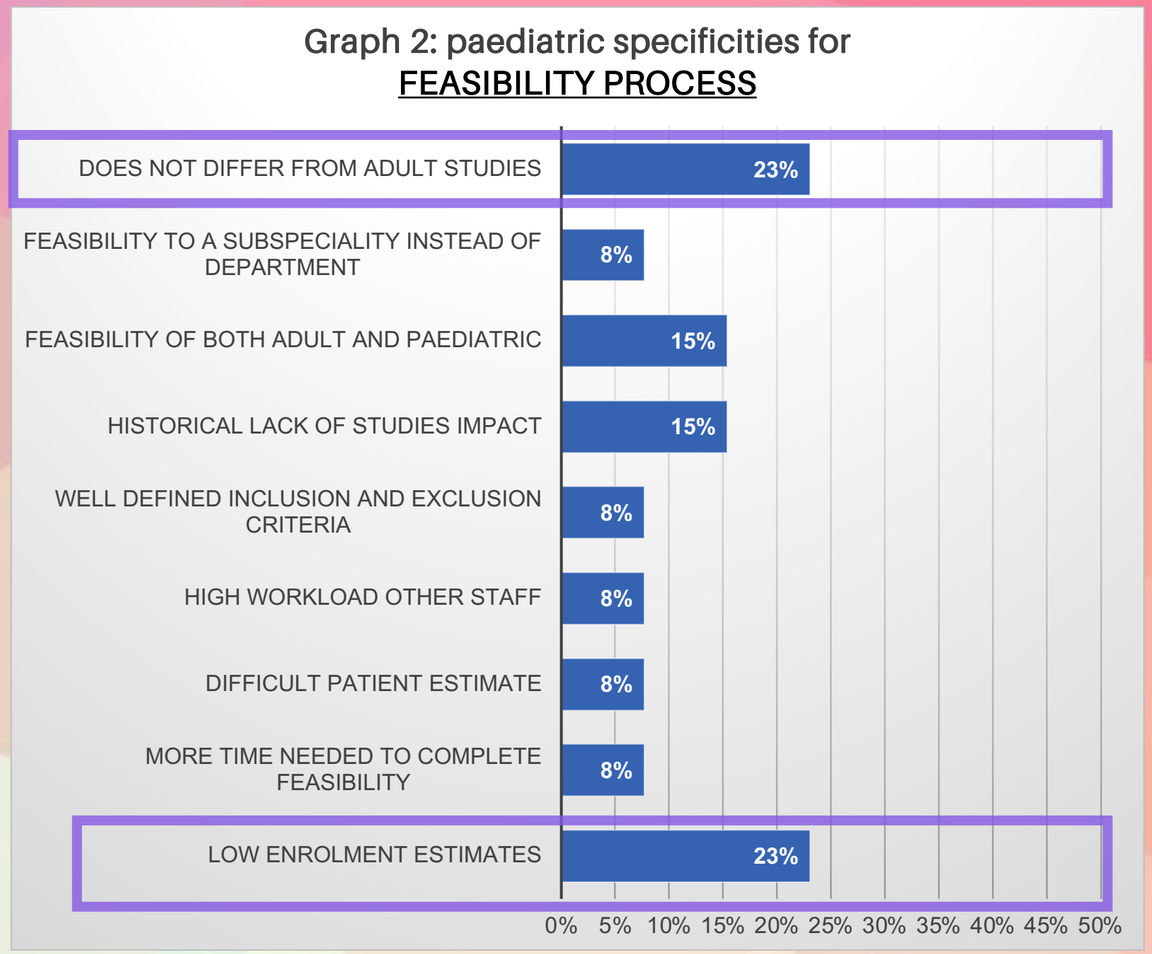
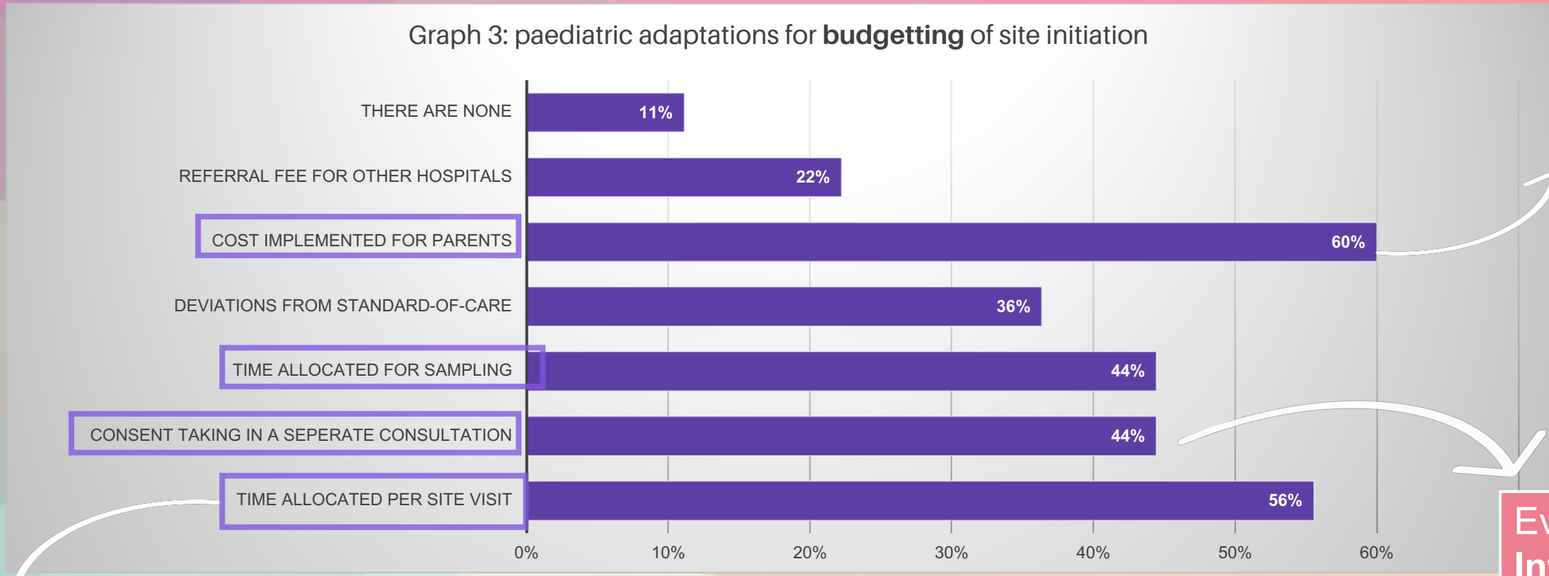
PAEDIATRIC SPECIFICITIES: SITE DOCUMENTATION





PAEDIATRIC SPECIFICITIES: SITE INITATION

73% noted **budgetting** to be the **biggest adaptations** for clinical trials in children for **site initiation.**
52% noted a need for contract **templates**.



Day care for other siblings, missing **holiday** day, **work** leave; indirect cost for **education** loss

Evolutions in **Patient Information Folders** (e.g. infographics, video) that are study specific and can be taken home with the patients.

The potential for **remote nursing/consultations**, including combining trial and motivation visits, should be investigated, according to **46% of the respondents.**

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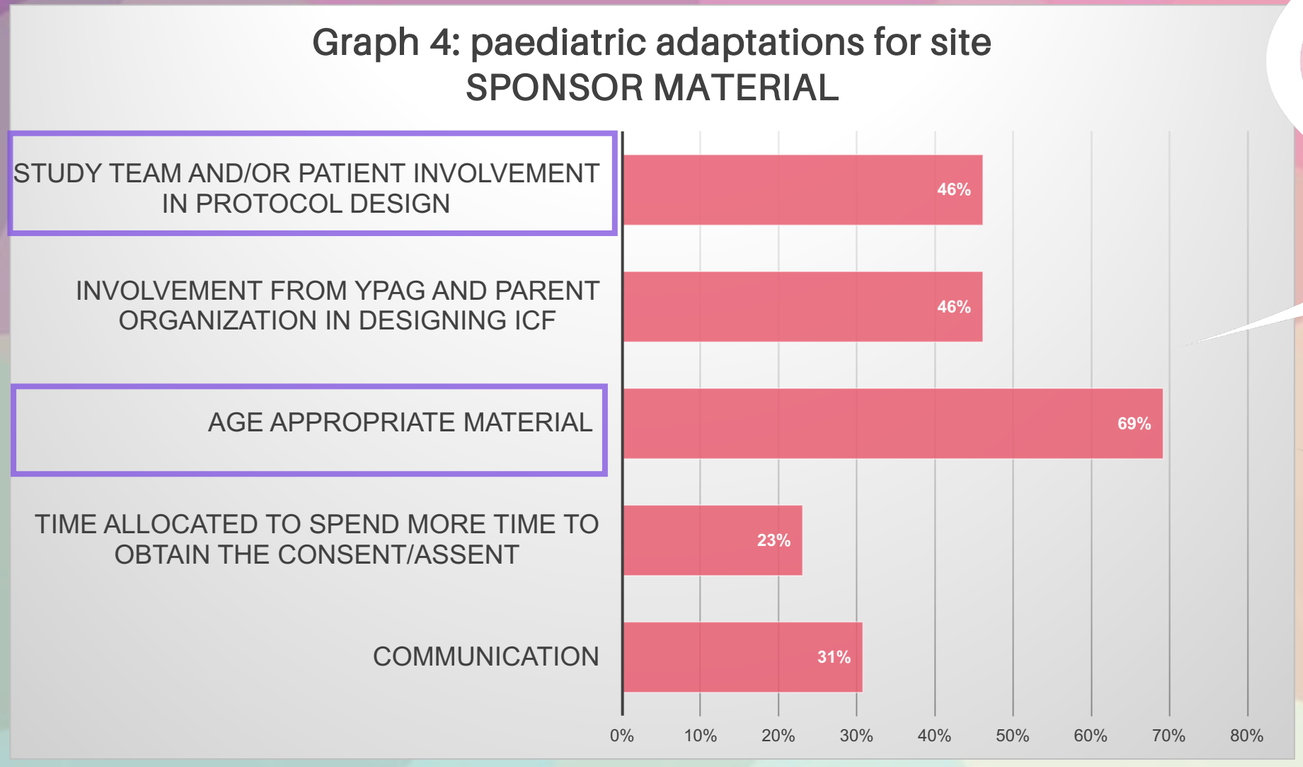
PAEDIATRIC SPECIFICITIES: SITE INITATION

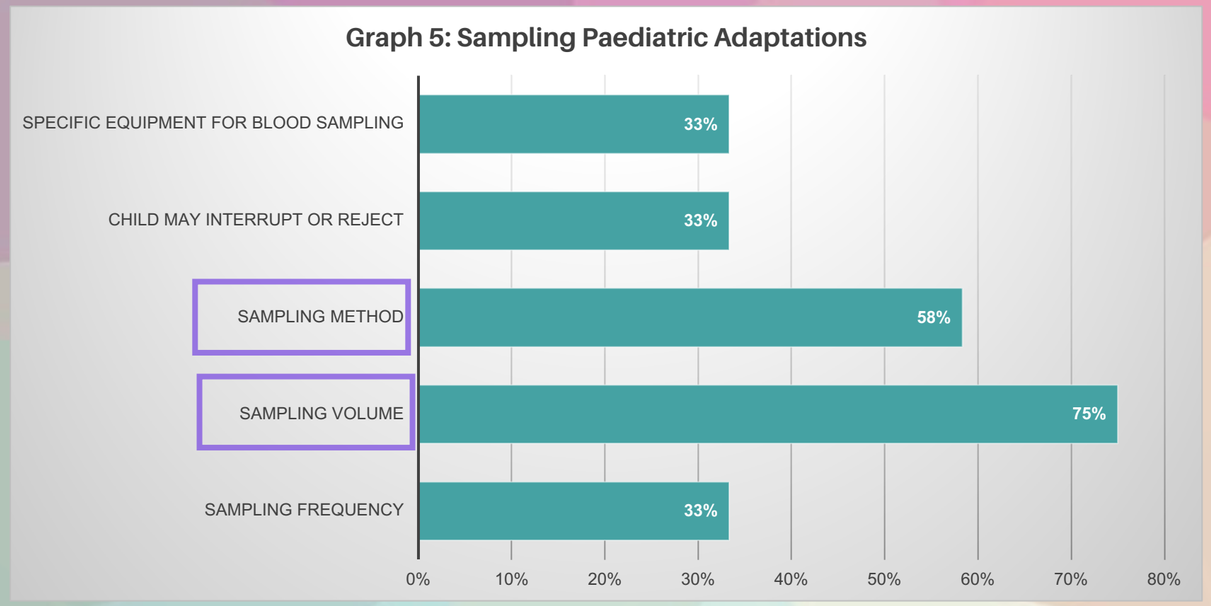


"It is more difficult to enroll babies and young children than older patients, because the parents are usually more difficult to give their consent for enrollment of their very young child. The neonates are an extreme example for whom the parents are unwilling to have them participating in the study."

"A protocol should take into account all potential social, financial and other burden (indirect effects) for the participant as well as the parents and should address / anticipate to this in the best possible way. Therefore study staff experts and parents and study participants could give valuable feedback in the process of protocol creation."

PAEDIATRIC SPECIFICITIES: SAMPLING AND IMAGING

61% of the responders: adapting the **imaging** requirements needs **prioritization** in current study designs.



Buzzy tool, price 50 dollars. Source: Amazon

Imaging: responses

- Timing of imaging: when a baby is sleeping. A child of 20kg needs to receive proper explanation and to be asked not to move during.
- Devices adaptation for the child: lower **doses** of contrast, age specific (also in the **protocol**).
- **All imaging must be stated on the IFC.**

(blood) sampling: responses

- Use of dried blood spots or **alternative** non-invasive samples.
- Thoroughly considering the **volume** that will be drawn.
- Considering alternatives: urine, saliva, hair or other ways.
- Spare sampling combined with routine care.
- Adapted to patient size, including **pain relief and distraction methods.**

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TAKE HOME MESSAGES

- Paediatric adaptations should be further incorporated by **sponsors**, in order to **improve the success rates**.
- Improvements are required predominantly in the domains of **budgeting**, **study visits**, and **technical** improvements.
- **Input** of patients, parents and staff is essentially, especially in the **protocol** and IFC writing phase.
- **International collaboration** stimulate higher site count, and higher principal investigator and site **experience**; lowering the overarching cost per site.

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Thank you for your attention.

Q&A

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c4c_BPCRN

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