

1. What do you consider to be the main obstacles to recruiting children to research? How might these be overcome?

To my opinion, the pediatric population is heterogeneous, and obstacles vary according to for example the chronic or acute nature of condition, which strongly determines the minors' and parents' experience with deciding on trial participation, the criticism in reading patient information, and with the frequency of being invited to participate in studies. It is to be expected that many factors affect the willingness to participate in trials, ranging from altruism or an a priori positive stance towards scientific activities, to despair (as I also have observed in my own research).

We will be able to elaborate more on this topic in the near future, as in a current research project at the ErasmusMC Rotterdam (for which I am the project leader), we investigate the motivations of minors and their parents for participating in clinical trials at various pediatric wards. At this point, results are still preliminary and data are still being collected.

2. Who should make the final decision as to whether a child participates, or continues to participate, in clinical research when parent and child disagree? What responsibilities do health professionals or researchers have in such cases? (You may wish to distinguish between children at different stages of development and/or the different ways in which disagreement may arise or be expressed.)

If minors truly disagree with the objectives/aims/content (e.g. risks) of the research: minors. Such dissent implies true understanding, and there is no reason to disrespect dissent merely because one has a certain age. If minors are only resistant to undergo certain trial interventions but do not fundamentally disagree with the objectives/aims/content (e.g. risks) of the research, it could be considered whether there are sufficiently good reasons not to respect the dissent (which is not easy), taking the level of risks and burdens, the importance of the research, potential direct benefit and the opinion of parents into account.

Health care professionals should always take children seriously, and make sure that they have a voice (which is listened to), even in the case where children are not the final decision-makers. Even in young children, it is important that dissent is considered, even if it is not respected.

If a child wishes to participate and the parents disagree, it must be very well and transparently argued why the minor's opinion overrules that of the parent, before respecting the minor's wish. If this is not possible, the parent should have the final decision.

3. How useful is the concept of assent? Is it helpful to distinguish between consent and assent for young people?

It is useful, both because it reminds professionals that minors do have a voice that is of key importance and because it is truly respectful to children. For mature minors, it may underestimate their decisional abilities, certainly in specific types of research.

On the other hand, I have observed minors who do not wish to be involved in decisions at all, notwithstanding their age, their excellent capabilities of understanding information and making decisions. They might consider assent as a burden, and just wish to be cared for without having to make decisions at all, and not showing any interest nor objection to participate in clinical trials. (For example, I have observed minors who were exhausted at the moment of inclusion, having experienced a recent diagnosis of a very serious condition, while inclusion cannot be delayed due to the inclusion criteria of the protocol – they might wish to delegate the decisions to their parents altogether, without being involved at all – it think it makes sense to be respectful of such requests)

4. A ‘shared’ or ‘collaborative’ decision-making model is often advocated for decisions about a child’s research involvement, involving the child, relevant family members and professionals. Is this a helpful approach? How might any problems arising in this model be overcome?

Depends on what is pre-existing. Within the family, cultures of shared decision making may exist, and if these work well and entail sufficient respect for the minor, this shared decision making culture of families could to large extent be used/respected in the setting of clinical trial participation. To introduce completely novel ways of making decisions may not always be feasible or workable. And obviously, respect for the minor and protection of the most vulnerable individual in the decision making process should be safeguarded, although the way to do this may vary on a case-to-case basis.

5. Parents’ views on whether (and how) children should be involved in decisions vary enormously both within and beyond the UK. How should the law and professionals take account of such different parenting approaches?

The law: should leave the discretion to deal with such variety to others involved, incl. professionals and children (e.g. by assent or respecting dissent). Not everything can be arranged by law.

Professionals: make sure that competent children at least have an opportunity to express their opinion on trial participation, and respect such opinion unless clear arguments for overruling the expressed wish of a minor exists. Such arguments may for example include full incompetence to understand what the trial is about.

6. Rewards (such as vouchers) for children participating in research may be welcomed as an appropriate way of saying ‘thank you’, or criticised as a form of undue incentive (to either child or parent). What forms of compensation/reward/expression of gratitude for research involvement do you think acceptable, and why?

No cash – small amounts of cash are of disproportionate value to children.

A voucher or small gift can be an appropriate way to say thank you. However, I would prefer that the value of the voucher does not represent the risks or burdens, but is merely a token of gratitude (kind of a fixed value for any research) and I would highly recommend that it is not mentioned in the patient information (only in the protocol that is reviewed by the EC/IRB)

to avoid decision bias, and that it is given to all participants, even if participation is discontinued at a certain point.

7. How helpful is the notion of the best interests of the child participant? How would you define 'best interests'?

The notion is not helpful at all.

8. How can the rights and interests of individual children (potential participants in research) be balanced against the rights and interests of all children (potential beneficiaries of the knowledge gained by the research)?

There is no duty to participate in research whatsoever, it is truly voluntary. So 'all children' cannot claim anything of the individual. The individual is free to contribute to the welfare of 'all children', although there are clearly limits to for example the risks that can be reasonably taken in this process (which does not automatically imply rigorous risks thresholds)

9. Are there any situations in which you think it would be acceptable for a child to be invited to participate in clinical research when there will not be any personal benefit to them? If so, please give examples.

Yes. In Belgium the law does not distinct between beneficial and non-beneficial research. Personal benefit cannot always be expected. Earlier stages of drug research, research in rare diseases etc... cannot always be expected to generate a direct benefit.

10. Are there any circumstances where it would be right for a research ethics committee to approve research involving risks they would usually regard as too high, if parents and young people had clearly expressed their willingness to accept these?

It cannot be left entirely to minors and parents, but committees might decide that in certain cases, risks that would otherwise be considered problematic can still be justified. For example, in Belgium, the law makes no distinction between therapeutic and non-therapeutic research, and by consequence, there is no minimal risk minimal burden threshold for non-therapeutic research, as there is in many countries.

11. Do you think the current regulations strike the right balance between promoting clinical research in children, protecting child participants, and involving children in decisions about their own participation? What (if anything) would you like to change?

There's regulation and there's practice. I think regulation is sufficient. But there is few to no support in implementing the regulations in practice, and cultivating good practice in these matters.

12. With limited resources, how would you decide which childhood conditions should be the priorities for research? Who should be involved in making these decisions?

Emotional and mediatized claims should be strongly avoided. Also rewarding by means of extension of market exclusivity (cf. regulation 1901/2006EC), which rewards the drugs that already are the most profitable the most, which is a missed opportunity in spending public resources.

13. What responsibilities do funders, researchers and stakeholder groups have to encourage the coordination of children's clinical research?

14. What responsibilities do researchers have towards child participants and parents when the study is over?

If the study is successful, supply of the drug until it is available in the pharmacy.

Any other comments?

Please highlight any relevant areas you think we have omitted, or any other views you would like to express about the ethical issues arising in clinical research involving children.