

## Are Children Vulnerable in Research?

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### Abstract

*The Nuffield Council on Bioethics' 2015 report, Children and Clinical Research: Ethical Issues, explores how ethical anxieties with respect to the involvement of children and young people in clinical research can be managed and mitigated with the help of children, young people and parents themselves. In so doing, the report challenges many of the assumptions that underpin the classification of children and young people as necessarily constituting a "vulnerable group", arguing that vulnerability is primarily present in situations, rather than in individuals, and that much can be done to design worthwhile research in ways that minimise the risk of individual children and young people being placed in a vulnerable situation. Partnership between researchers and children, young people and their families is essential, not only at the point of recruitment to a study, but also much earlier in the development stages of research studies.*

*Keywords: children, research, vulnerable, clinical research, ethical issues, young people, Nuffield Council*

### Introduction

In May 2015, the Nuffield Council on Bioethics launched its latest report, *Children and Clinical Research: Ethical Issues*.<sup>1</sup> This was the culmination of nearly two years of work by a multi-disciplinary working party that worked closely with the Council to consult widely, collect and interrogate evidence, and develop

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a rigorous ethical approach to the issues raised by the participation of children and young people in clinical research.<sup>2</sup>

Initially, the Council's working party perceived the main ethical challenge in terms of the dilemma presented by two competing demands: the need, on the one hand, to provide children and young people with access to evidence-based healthcare; and the requirement, on the other, of ensuring that the children and young people participating in research are properly protected. In other words, it started from the traditional assumption that children and young people, by their nature, constitute a vulnerable population, on whose behalf others exercise beneficent protective duties. The challenge was thus how best to balance these two competing threats to the well-being of children and young people—threats posed by participation in research, and those (often ignored) posed by unresearched care.

However, at our first meeting with young people and parents, it rapidly became very clear that a third issue needed to come upfront in our thinking and analysis: the question of the role of children and young people themselves. Crucially, in considering this perspective, we should be concerned not just about the role that children and young people should play in decisions about their *own* participation in research, but also their capacity to play a significant part in shaping the research agenda in the first place. At that very first meeting, our initial assumptions about the inherent and inevitable “vulnerability” of children and young people in research were turned on their heads.

## **The Need for Clinical Research with Children and Young People**

The “ethos” that should underpin our analysis emerged relatively early in the working party's deliberations. In a policy environment where there is a broad consensus on the value of evidence-based healthcare, the level of off-label prescription of medicines for babies, children and young people stands out as an anomaly.<sup>3</sup> Care regarded as “standard” may turn out to be far from optimal when compared with alternatives in a properly conducted study,<sup>4</sup> and qualitative research with parents suggests both that most parents are unaware of the limitations of the evidence underpinning their children's care, and that when informed, are concerned.<sup>5</sup> So in the first chapter of our report, we take the clear stance that scientifically valid and ethically robust research that addresses questions of importance to the health of children and young people should be seen as intrinsically good and as a necessary part of a healthcare system. It should not

be seen as a threat to children, as something to be apologised for, nor indeed as anything unusual.

## Children's and Young People's Capacity for Agency

However, in making this claim, it is necessary to elucidate the second part of our ethos, which is that research must be carried out *with* children and young people, and not *on* them. This is far from being a semantic quibble. If we understand research as taking place *on* children and young people (or indeed *on* anyone of any age), then we are implicitly assigning them a passive, dependent, even incapacitated role in which responsibility for their welfare is entirely entrusted to others. In contrast, by conceptualising research as taking place *with* children and young people, we are immediately forced to recognise their potential capacity for active agency and positive engagement. The same argument underpins preference for the term “research participant” over “research subject”. Such an understanding of the capacities of children and young people to take an active part in determining their role within research calls for a reframing of the question as to how *we*, in a range of adult roles, should protect them, and hence in what way we respond to their potential or perceived vulnerability.

Not every child, of course, is able to exercise this potential capacity for active agency in the context of research, and we return to this question below in our presentation of three paradigm cases of decision-making in research with children and young people. Neither does the recognition of children's potential for agency act to undermine the important responsibilities of adults (whether as parents or professionals), a point to which we also return. However, it is striking to note how very uncontroversial this claim of social agency seems *outside* the context of clinical research. As any parent of a toddler will attest, children from a very young age clearly express the desire, and an evolving ability, to take an active part in managing their own lives.<sup>6</sup> Looking after children, from babyhood on, is not a “one-way” process in which children are the passive recipients of care and protection, but rather a two-way relationship involving constant and evolving forms of negotiation.

The extent to which, and manner in which, children's capacity for agency is encouraged, will of course vary substantially both between and within cultures. Children in some societies and families may be actively encouraged to express preferences and make choices in a way that would be regarded as quite inappropriate in others. Similarly, children in some societies may be expected to take on significant levels of responsibility for themselves, and for younger siblings,

at an age when in other societies they would not even be permitted to walk home from school alone. Despite this diversity, however, children in any culture will be aware of different expectations placed upon them in terms of accepting and managing responsibility between their early childhood and their adolescence, in recognition, however expressed, of their developing capacity for agency.

From a similarly young age, children are routinely encouraged and expected to develop social awareness and respond to the wishes and needs of *others*, whether in terms of learning to play and share with other children, or in terms of responding to adults' expectations of behaviour. As one of our consultation respondents put it succinctly, "A child is already part of society—not a trainee adult." The determination of the age of criminal responsibility by individual jurisdictions—which may be as low as ten (in England)<sup>7</sup> or eight (in Scotland)<sup>8</sup>—represents a further, if less benign, stance with respect to children's capacity for agency, and hence potential responsibility for their own actions. There are thus many diverse contexts, outside that of clinical research, where children's and young people's capacity to express and take responsibility for personal and social agency appears well-established.

## Children and Young People as Part of Their Families

This recognition of children's and young people's capacity for agency must be seen and understood alongside another important aspect of children's lives: their situation within their families. One of the important differences, both legally and ethically, between children/young people and adults is the role of their *parents* (in which we include anyone performing a parental role, as recognised by law in their jurisdiction). Children are not (usually) alone. Complementing the developmental nature of childhood, from newborn baby to relatively self-sufficient young adult, parents have the responsibility to make decisions for and with their children, until those children reach the age of majority recognised by their national law.

It is, of course, a truism to recognise that the parental role does not, in practice, change overnight at this point, and that indeed many young people will continue to rely on their parents, whether emotionally or financially, well into young adulthood.<sup>9</sup> However, parents' *legal* powers and responsibilities change fundamentally at the point when their child is recognised as "adult", and we suggest that these responsibilities of parents towards their minor children are of ethical, as well as legal, significance. Drawing both on empirical evidence of parental decision-making<sup>10</sup> and the literature on "good" parenting decisions,<sup>11</sup> we set out in the Council's report a number of ethical considerations that

parents should take into account when making decisions with, or on behalf of, their children:

- Respect for children as *individuals*, regardless of their age or capacity, expressed, for example, through consideration of the children's wishes.
- Recognition of children's *developing capacity* for autonomous agency, and parents' supportive role in helping their child develop decision-making skills and confidence.
- Concern for children's *immediate and longer-term welfare*.<sup>12</sup>

The question of how we understand "welfare" is particularly important in our analysis of children and young people's capacity for agency, and the role of parents in encouraging and mediating that capacity. We argue for an understanding of welfare that is concerned with children's and young people's immediate and future "good": including, but not limited to, what is "best" for them in terms of their physical health or personal interests. It is our claim that parents, as well as protecting their children from harm, also have a responsibility to seek to influence the values that their children acquire as they grow up, and to "shape" the adults they become.

It is thus open to parents (depending, of course, on their own values and attitudes) to encourage their children to participate in activities that may not necessarily be of direct benefit to themselves, on the grounds that those activities are of social value, and hence represent a "good thing to do". Such activities could, in the right circumstances, include taking part in research. Bearing in mind the parallel parental responsibility to consider what is physically and emotionally good for their children, parents also need to be confident that what is entailed in such activities of social value is, at the least, *compatible* with their children's personal interests. We avoid the commonly-used term "best interests" on the grounds that "best" unhelpfully implies that only one possible course of action can be "best", when this will rarely be the case in research participation.

*How* different parents balance the three considerations listed above (respect for individuals, recognition of developing capacity and concern for welfare) in their decision-making will depend on many contextual factors, including the situation of their child at the time, the nature of the particular decision, and the nature of family relationships and approaches to parenting in this particular family. We discuss this below. We then go on to consider professional responsibilities with respect to creating "the right circumstances" in which research participation may constitute a potential "good" for children and young people, which brings us back full circle to the question of vulnerability.

## Paradigm Cases of Decision-Making

We alluded earlier to the fact that not every child and young person will be able to exercise agency, whether with respect to involvement in clinical research, or indeed in any other sphere. Recognising the fact that “children and young people” are a far from homogenous group, the working party identified three paradigm cases or situations arising in childhood which raise distinct ethical issues with respect to decision-making in research, for children, parents and professionals alike. These paradigm cases draw not only on the capacities associated with particular stages of childhood development, but also on important *situational* factors—including the complexity of the decision to be made, and the physical, mental and emotional state of particular children and young people at the time that a decision needs to be made. Thus:

- **Case One** arises when children and young people are not able at the time to contribute their own view as to whether they should take part in research. This case covers all babies and very young children, but may also apply on a temporary basis to older children or young people if they are unconscious or very unwell. Children in Case One may, of course, express physical and emotional reactions to the *procedures* involved in research, but cannot actively participate in an initial decision as to whether they should undertake them. In Case One, parents’ main focus will be their child’s welfare, although respect for their child as an individual will also be important. This may be expressed, for example, in terms of the parents’ judgement as to whether, and to what degree, particular procedures might distress *this* particular child, in *these* circumstances.
- In **Case Two**, children and young people *are* able to form views and express wishes, but are not yet able to make their own decisions about research involvement without assistance. Many children will be able to express wishes and preferences in this way from a relatively young age. The sophistication of those views will, of course, vary significantly. Parents will again be concerned for their child’s welfare, but will also want to give some weight to their children’s wishes (which in this case they are able, in some form, to express) and support them, to the degree the parents think appropriate, in starting to make decisions for themselves.
- **Case Three** covers the situation of children and young people who potentially do have the intellectual capacity and maturity to make their own decisions about taking part in a particular research study, but who are still considered to be “minors” in their domestic legal system. “Capacity” to make a particular decision should be understood both in terms of the intellectual capacity to

understand what is involved and the emotional maturity and experience to understand the wider picture—for example, the likely impact on their future life. The parental role in Case Three is primarily one of support and advice. However, parents do still retain responsibility for their child’s welfare. In this respect, we draw an important distinction between competent children and adults. Children, however intellectually capable, do not have full adult powers—and the corollary of that is that they also do not have full adult responsibilities. Parents are there, both ethically and legally, to share that responsibility until the agreed threshold of adulthood is reached. This threshold is—as diverse ages of majority in different jurisdictions demonstrate—at least in part, culturally determined.<sup>13</sup>

## Situational Vulnerability

As will be clear from the account above, the Nuffield Council’s working party took the view that there *are* circumstances in which parents may legitimately agree that their children should take part in clinical research: in brief, in circumstances where they are satisfied as to the potential social value of the research, and consider the procedures involved in the research to be compatible with their child’s interests. (We return, at the end of this article, to the distinct question of children’s own role in that decision.) This, then, brings us to the question of the role of research professionals, both in designing and reviewing research proposals, and in recruiting children and young people to those studies, once approved. In particular, we need to consider their responsibility to make sure that they do *not* place children and young people in a position where they feel vulnerable.

Children and young people may indeed feel vulnerable in the context of clinical research, and where this arises, it is a matter of deep ethical concern. However, if the *source* of this vulnerability is unpacked, we often find that it lies not in the inherent nature of childhood, nor in innate aspects of research with children, but rather in the context or situation in which those children may be placed. Anyone, of any age, can be *rendered* vulnerable; for example, by being placed in alien surroundings, without support, with insufficient information, at a time of emotional upheaval, or (worst of all) all of these at the same time. However, most, if not always all, of these factors are amenable to change. Classifying a *group* as vulnerable, rather than a *situation* as creating vulnerability, acts simply to disguise the possibility of amelioration.

Moreover, classifying all children and young people as a “vulnerable group”, on the same basis as groups as diverse as older people, pregnant women or

prisoners, tells us nothing, either about the actual vulnerability of any particular member of that group, or of the particular way in which they may (or may not) happen to be vulnerable. Even if we try to identify particular ways in which “children” as a group may be vulnerable (for instance, with respect to assumptions of lack of decision-making capacity), we risk underestimating the capacities of many children and young people, and also lose sight of the important fact that, in many cases, children and young people will be well-supported by their families and, with that support, will be as well-placed to make a decision as many an adult.

The children and young people who contributed to the Council’s project were robust in telling us that, while some children in some circumstances could certainly be vulnerable, it was wrong to assume that all children were necessarily so.<sup>14</sup> They expressed concern that describing children as vulnerable could simply “stop the conversation” about whether research with children should be allowed to go ahead, and also identified ways in which they felt they could be made to feel more or less vulnerable in the context of research. “Being prepared” and “being empowered” were both cited as important factors in avoiding or minimising vulnerability, with proper information for both children/young people and parents playing a critical role in such preparation. Poor relationships with researchers, poor communication, or being given too *much* responsibility, on the other hand, would make them feel more vulnerable.

## **Responding to Vulnerability: Working in Partnership**

At the start of this article, we set out our understanding of children as people who, from an early age, can take an active role in determining the direction of their lives, in the context of a life shared with others. In light of this understanding, we suggest that an appropriate response by professionals towards concerns about children’s potential vulnerability in research is to ensure that they work in *partnership* with children, young people and parents throughout the whole endeavour of research. Such a partnership approach will ensure that, whenever children and young people are invited to take part in research, the procedures to which they are being invited to consent have been developed with the input of others in a similar situation to themselves. In other words, concerns about the (potential) vulnerability of children in research should trigger not an automatic brake on the research but rather the question: “Does this research raise particular ethical challenges and what (with the help of children, young people and parents) can I do about them?”

The “ICAN” network of young people’s groups, including groups in the UK, United States, Canada and France, provides one practical means by which researchers may be able to obtain such input.<sup>15</sup> Condition-specific family support groups provide other ways of obtaining the expert knowledge of children, young people and parents who live on a daily basis with particular conditions or disabilities. Where it is not feasible to seek direct input from children in similar situations (that is, for some of the children in Case One, e.g. babies), researchers should seek input and advice from parents, such as those with past experience of being invited to enrol their young children in research. However, as we discussed earlier, parents also continue to play a role as their children develop through Case Two and Case Three, and hence there is also a place for input and advice from parents, as well as from children and young people, in studies involving older children.<sup>16</sup>

## **The Role of Ethics Committees: The “Fair Offer”**

And what about the role of research ethics committees or institutional review boards—in particular with respect to determining whether or not a research study involves risks that are too high to sanction? A number of those who shared their views with the Council’s working party expressed concern that ethics committees tend to be too cautious, or “parentalist” when asked to scrutinise research involving children, although clear evidence on this is hard to obtain.

The working party developed the concept of a “fair offer” to describe what an ethics committee should be aiming to secure on behalf of potential participations. The notion of a “fair offer” recognises that potential participants will respond differently to the invitation to participate, especially because people adopt very different views concerning what constitutes acceptable burden or risk for themselves or their children, and hence will respond in diverse ways to the “offer”. At the same time, it emphasises that there is also a proper role for a layer of professional scrutiny, to provide the assurance to those subsequently receiving that “offer” or invitation that it is “fair” and can be trusted. Such an approach contrasts with the claim, sometimes made, that the role of the ethics committee should be limited to scrutinising the quality of information provided, on the basis that potential participants should be free to make their own choices. This claim, the working party felt, wrongly characterises the relationship between professionals and patients as one of “buyer beware”, rather than one of professional concern and trust.

In determining whether or not a particular research proposal constitutes a fair offer to potential participants and their families, ethics committees should ensure

that they hear both from those able to provide the perspective of potential participants (for example, through the partnership work of researchers with young people and parents in developing the protocol) and, as necessary, from those with expertise in the relevant area of children's healthcare. However, the judgement (and hence the responsibility) as to whether or not the likely risks, burdens and benefits have been carefully weighed and hence whether the "offer" is one that should be put to participants, must remain one for the committee alone. Parents and children should be enabled to contribute their experience and perspectives, but should not be burdened with the ultimate responsibility of judgement.

## **The Role of Children and Young People in Decision-Making**

Finally, we return to the question of the role of children and young people themselves in making decisions about their own participation in research. Earlier, we argued that if researchers develop their studies with the assistance of children, young people and parents, and if ethics committees routinely expect such involvement, then the risks of children and young people being placed in vulnerable situations are radically reduced. However, the "fair offer" as approved by the ethics committee must critically also be extended fairly to each individual child or young person and their family: thus, the *manner* of the recruitment process plays an essential part in ensuring that children and young people are not placed in a vulnerable position.

Just like parents, researchers have a responsibility to demonstrate respect for children and young people as individuals, to recognise their developing ability to participate in the research decision, and to be concerned for their welfare. This demands not only age-appropriate information, but also sensitive and skilled communication, to provide that information in a way that meets the needs of each particular child, in their own particular situation. Any concerns that children and young people have about research should be taken seriously and never brushed aside. While the researchers and ethics committees may rightly have concluded (drawing on the advice of the children, young people and parents involved in developing the study) that particular aspects of the research constitute a "fair offer", this does not mean that they will be acceptable to every child and young person. A child who is terrified of needles might well feel highly vulnerable if coerced into taking place in research involving blood sampling, even if others are well able to cope.

Requirements that children's "assent" be sought for research participation appear in a range of international declarations and in the regulatory arrangements of

some jurisdictions, but little consensus exists on how, in practice, it should be obtained. Guidelines vary from specifying that assent should be sought from children as young as three,<sup>17</sup> to the definition of assent as the “knowing agreement” of children and young people able to understand what is entailed.<sup>18</sup> There is similar diversity in how active dissent should be handled, and whether it should always be “respected” or just “considered”.<sup>19</sup>

The Council’s working party took the view that the key ethical imperative, underpinned by researchers’ responsibilities to respect children and young people of any age as individuals, is to ensure that children and young people are as *involved* in a research decision as they are able and wish to be. Assent should be understood as no less, and no more, than this proper involvement. The fact that children and young people have been involved should then be recorded in some way (e.g. in writing or drawing, using audio or video recording, or electronically), but it is the (ongoing) process of involvement, and not the form of record-keeping used, that is ethically significant.

“Involvement” in a decision should not be confused with making the final decision. Where children and young people fall into Case Two, on the basis that they are able to contribute to a particular decision but not make it themselves, then the final decision will be made by their parents. In contrast, where children and young people fall into Case Three, because they have the capacity to make their own decision but are not yet treated by law as independent decision-makers, then ethically, they should be invited to give their *consent*, not their assent, to research participation. The law may additionally require parental consent, but this does not undermine the ethical centrality of the child’s or young person’s own consent before research participation may proceed.

Parents themselves will take very diverse approaches with respect to the acceptability of their child’s involvement in decision-making (in research, as in many other situations), and researchers need to be sensitive to, and respectful of, this parental role. However, they also have direct professional responsibilities to children and young people. Where parents are entirely unwilling to involve their child in a decision about research participation, or ignore their child’s active dissent or evident distress, then researchers do have the professional discretion not to enrol that child in their study, unless there are overriding welfare reasons as to why it is important for that child to take part. Parental consent provides legal authority for research participation, but cannot *require* it where professionals feel that such participation would breach their own responsibilities to a particular child or young person. Such situations should, however, be very much the exception, rather than the norm. The professional aim of

researchers should always be to seek, and encourage, a shared decision between children and young people, and their families.

## Conclusion

When the Nuffield Council initiated its work over two years ago, we did not imagine that our project would interrogate the notion of vulnerability in quite this way. We invited young people and parents, along with professionals engaged in research in a variety of contexts, to an initial meeting with the aim of hearing from all these different “stakeholders” what they saw as the main ethical challenges and hurdles in research. What we heard at that meeting challenged our underpinning assumptions, and sent us down the path of exploring how a true partnership between, on the one hand, the professionals concerned with research, and on the other children, young people and their parents, could fundamentally reframe our concerns about the potential for research to create vulnerability.

It challenged us, too, in our own processes—the ways in which we engaged throughout our project directly with children and young people, with and without existing knowledge of clinical research; not only listening to them, but also subjecting our own ideas and analysis to their scrutiny; and finally making the central ideas and arguments in our report accessible to children and young people in the form of a magazine and an animated film.<sup>20</sup> The contribution of one nine-year-old child in a school workshop perhaps captures even more succinctly the message to every researcher working with children and young people, highlighting both the willingness of many children to help others, and their capacity to pinpoint what might be challenging for a child in research: “Well, I want to help children—but could they make the tablet smaller?”

## Notes

1. Nuffield Council on Bioethics, *Children and Clinical Research: Ethical Issues*, 2015. Available at <http://nuffieldbioethics.org/project/children-research/>.
2. Ibid.
3. C. Pandolfini and M. Bonati, “A Literature Review on Off-Label Drug Use in Children”, *European Journal of Pediatrics* 164 (2005): 552.
4. See, for example, MedicalXpress, “Morphine following Common Childhood Surgery May be Life Threatening”, 2015. Available at <http://medicalxpress.com/news/2015-01-morphine-common-childhood-surgery-life.html>.
5. T. Mukattash, J. Millership, P. Collier and J. McElnay, “Public Awareness and Views on Unlicensed Use of Medicines in Children”, *British Journal of Clinical Pharmacology* 66, 6 (2008): 838.

6. See, for example, the discussion of “agency” in A. James and A. James, *Key Concepts in Childhood Studies*, 2012.
7. Section 50 of the *Children and Young Persons Act 1933*, as amended.
8. Section 52 of the *Criminal Justice and Licensing (Scotland) Act 2010*.
9. R.I. Hart, H.E. Foster, J.E. McDonagh et al. “Young People’s Decisions about Biologic Therapies: Who Influences Them and How?”, *Rheumatology* (2015). doi: 10.1093/rheumatology/keu523.
10. Summarised in Chapter 2 of Nuffield Council on Bioethics, *Children and Clinical Research*.
11. See, in particular, C. Rosati, “Preference-Formation and Personal Good”, *Royal Institute of Philosophy* Supplement 59 (2006): 33.
12. Nuffield Council on Bioethics, *Children and Clinical Research*, paragraphs 4.10–4.33.
13. *Ibid.*, paragraph 4.47.
14. A note of this meeting is available at <http://nuffieldbioethics.org/news/2014/young-people-assess-progress-of-council-s-project/>.
15. <http://www.icanresearch.org/>.
16. Nuffield Council on Bioethics, *Children and Clinical Research*, paragraphs 4.53–4.61.
17. European Commission, *Ethical Consideration for Clinical Trials on Medicinal Products Conducted with the Paediatric Population*, 2008.
18. Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, 2002.
19. The European Parliament and the Council of the European Union, *Directive 2001/20/EC*, 2001; European Parliament and Council of the European Union, *Regulation (EU) No 536/2014*, 2014.
20. <http://nuffieldbioethics.org/project/children-research/>.