Chapter 2

Being invited to take part in research: evidence and law

Chapter 2 – Being invited to take part in research: evidence and law

Chapter 2: overview

The first contact that most children and young people, and their families, will have with clinical research is when they are approached and invited to participate in a particular study. This chapter reviews first the empirical evidence of how, in practice, children and families make decisions about research participation, and then the role played by national law, international declarations, and good practice guidance.

Empirical evidence: the way in which children, young people and parents respond to the possibility of participating in research often depends on three broad factors:

- **The nature of the research**: for example, whether it relates to a child's own condition, and the severity of that condition; whether the need for a decision arises at a particularly traumatic time, and how much time is available to think about it; the degree of risk or discomfort involved; and time and opportunity costs in taking part.
- **The situation of children and their families**: their existing knowledge of research, and their attitudes towards both research and risk in general; their desire to help others through participation in research; and their perception of potential health or other benefit deriving from participation.
- **The relationships between researchers and families**: the extent to which there are trusting relationships between children / young people, parents and researchers; and the quality of the communication between them.

Children and young people themselves are involved in participation decisions in very different ways: from no involvement at all, to joint decision-making with parents, to being 'final' decision-makers. These differences do not simply correlate with age, but appear to be influenced by many other factors including the severity of any illness, the suddenness of either the diagnosis or the opportunity to take part in research, children's and young people's prior experiences, and general family dynamics in decision-making.

Law and guidelines: in contrast with the context-specific nature of decision-making emerging from the empirical literature, regulatory approaches focus very much on the role and status of the decision-maker. In most cases, 'children' or 'minors' are, by default, assumed to be unable to make their own decisions, and authorisation is required instead from a parent or another legally-authorised proxy. International declarations, regulations and guidance take diverse approaches to the extent to which children or young people should, nonetheless, be *involved* in the decision. Most, but not all, make specifications relating to the information that children and young people should receive, and the importance of involving them in the consent process in a manner appropriate to their maturity.

The term **'assent'** is used widely within both international declarations on research ethics and in some national legislation to encompass this involvement, but with very different meanings and implications. These vary from "the emergent capacity to agree" of a three year old, to the "knowing agreement" of an adolescent who has not yet reached the legally established age of consent but who nevertheless has the capacity to make their own decisions. Unlike consent, assent has no legal force, but some guidelines require documentation that a child has assented to take part. There is similar variation in how a child's **'dissent'** should be handled: in particular whether it should be 'considered', or 'respected'.

Introduction

2.1 The first contact that most children and young people and their families will have with clinical research is when they are approached and invited to participate in a particular study. We therefore begin our review of the empirical evidence relating to the experiences of children, young people and their parents in clinical research at this point of recruitment. We go on to consider the role of domestic law, international declarations, and good practice guidance, in shaping families' experiences of being recruited to take part in clinical research, before turning in Chapter 3 to look at the many requirements that researchers must meet before they are able to reach this point of recruitment. As we note in paragraph 2.62, there are a number of inconsistencies and uncertainties at present with respect to the role of children and young people in making decisions about research involvement, and having outlined these in this chapter, we set out our own approach in Chapter 6.

How children, young people and families make decisions in practice

2.2 Our exploration of children's and young people's lived experiences of taking part in research draws both on the published literature (primarily, but not exclusively concerned with practice in the UK), and on the additional insights we gained from the many people who contributed directly to this project: respondents to our call for evidence, members of our stakeholder group, and participants at our factfinding meetings, and school and community projects (see Appendix 2). These direct contributions illuminate and bring to life the general themes arising in the published literature, and examples (chosen to illustrate the range of views expressed) are quoted at the beginning of each section, and in Box 2.1 below.

2.3 The issues that emerge as important to children and families in deciding whether or not to take part in research fall into three broad categories, and we have followed these in our summary below. We look first at influences relating to the nature of the research itself; second, at influences relating to the situation of children and their families; and third, at the relevance of the relationships between researchers, children and young people, and their families. We conclude with a review of the (limited) evidence relating to the respective roles of children and their parents in making the final decision to participate or not.

2.4 It is important to note at the outset that, inevitably, the evidence referred to in the following section paints only a partial picture. Much of the literature about how families make decisions in practice draws on the use of hypothetical questions: asking families who may have no first-hand experience of participation in clinical research what they think they would do in a given scenario. Many more research studies have been carried out with parents than with children and young people themselves; and research seeking parents' opinions features less input from fathers than from mothers.

Box 2.1: Examples of research involvement from our stakeholder group

The Working Party's initial meeting with its stakeholder group of parents and young people provided a vivid snapshot of the various ways in which decisions about research involvement may be made, and the factors that may influence these decisions:

- One young person started making their own decision about research involvement from the age of 13: this was the point at which the balance of decision-making shifted from the parent (with their child's involvement/agreement), to the young person (with the involvement of their parent).
- Another child had been involved in a trial at age four. It would have been good if they had been given simple, jargon-free information – after all it was *their* bone marrow being taken. They were subsequently withdrawn from the study because of deterioration in their condition.
- One parent refused consent for their child to take part in a trial because the protocol included too many blood tests, to be taken by a non-specialist nurse rather than a phlebotomist.
- Consent was refused to another trial because it involved a blood test, and the child had needle phobia.
- Very positive experiences of being involved in a trial were reported in a case where the researcher / clinician involved knew the patient well, and made them feel their opinions counted. Knowing that involvement in research has helped to make a new treatment available for people worldwide is a "proud moment".
- Participation in a trial was refused because of a failure to provide adequate information for parents. This arose in a context where a parent was invited to sign a form that said that they *had* been given the opportunity to discuss concerns with a named individual – whom they had never met.
- It was reported that, at one clinical trials unit, parental consent forms that were unaccompanied by any documentation about children's assent would be queried in order to explore with researchers why this had arisen.

Participation decisions: the relevance of the nature of research

2.5 The decision whether or not to take part in research may first of all be influenced by the *nature* of the particular clinical research study, and the demands it may place on children and their families. In some cases, these demands may be inherent in the nature of the research; in others, however, they may be amenable to change. We note examples, both in the literature and in our own evidence gathering, of where suggestions for such changes have been made.

Severity of health condition being researched

> *"You know… a child can be involved in research when he is sick... Now there as the parent, you accept immediately because you want… your child to get well."*[100]

[100] Community representative, contributing to Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

> *"My child has a chronic condition and I would happily allow her to participate in a research study that might improve the treatment options for other children (even her own in the future)."*[101]

2.6 We noted earlier that an important aspect of the context in which children are invited to take part in clinical research relates to the extent to which the research is associated with, or divorced from, care for children's own health conditions (see paragraph 1.9). In the case where research relates to a child's existing health condition, considerable diversity exists with respect to the seriousness of that condition, the availability of acceptable treatment options, and the extent to which it is sudden and acute, or chronic and long-standing.

2.7 Where research relates to treatment for a severe condition with no 'standard care' treatment options, parents have indicated that they feel they have little, if any, choice in making decisions about their child's participation in a clinical trial.[102] The experience of parents whose children have untreatable life-threatening conditions is captured vividly by the comment that "there was not a decision to make really – save my daughter. You save my daughter and I will do anything it takes."[103] Such an experience forms a stark contrast not only with the situation in which parents of healthy children find themselves, but also those of children who have a chronic, but stable, condition.[104] Mothers of children with diabetes, for example, who had lived with the diagnosis and reality of their child's illness for some time, described themselves as being confident about making their own choices as to what would be right for their child, and would make the decision based on their perceptions of the risks, benefits and opportunities presented by the proposed study.[105] These distinctions may, however, be less important in connection with survey-based research, where parents may feel more unconstrained in their choices, irrespective of the severity and acuteness of their child's condition.[106]

2.8 Two particular areas of research with children appear to have particularly high participation rates: those of cancer and neonatology.[107] Indeed, as many as 70 per cent

---

[101] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[102] Deatrick JA, Angst DB, and Moore C (2002) Parents' views of their children's participation in phase I oncology clinical trials *Journal of Pediatric Oncology Nursing* **19(4)**: 114-21; Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9.

[103] Stevens PE, and Pletsch PK (2002) Ethical issues of informed consent: mothers' experiences enrolling their children in bone marrow transplantation research *Cancer Nursing* **25(2)**: 81-7, at page 84. See also: Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9; Fisher HR, McKevitt C, and Boaz A (2011) Why do parents enrol their children in research: a narrative synthesis *Journal of Medical Ethics* **37(9)**: 544-51. Attendees at Nuffield Council on Bioethics (2013) *Factfinding meeting: making research decisions: who decides and how?* (London, 9 September: Nuffield Council on Bioethics) reiterated the message that parents may be willing to do anything to get a particular new treatment for their child where serious illnesses have been diagnosed.

[104] Fisher HR, McKevitt C, and Boaz A (2011) Why do parents enrol their children in research: a narrative synthesis *Journal of Medical Ethics* **37(9)**: 544-51, which compared the perception of 'choice' between parents with terminally ill children will do 'anything that might help', and parents of healthy or stable children.

[105] Pletsch PK, and Stevens PE (2001) Children in research: informed consent and critical factors affecting mothers *Journal of Family Nursing* **7(1)**: 50-70, at page 61.

[106] See, for example, Liaschenko J, and Underwood SM (2001) Children in research: fathers in cancer research - meanings and reasons for participation *Journal of Family Nursing* **7(1)**: 71-91. Fathers of children engaged in cancer research were found to focus on possible benefit for their child when considering 'experimental' studies, but cited altruism as a reason for participation in survey research.

[107] Snowdon C, Brocklehurst P, Tasker R *et al.* (2014) Death, bereavement and randomised controlled trials (BRACELET): a methodological study of policy and practice in neonatal and paediatric intensive care trials *Health Technology Assessment* **18(42)**: 1-410 identified 50 RCTs as having enrolled babies or children from 2002-6; approximately 50 per cent of UK NICUs and PICUs participated in at least one of these trials. Collectively, they enrolled over 3,000 children.

of children and young people diagnosed with cancer may be included within trials.[108] It has been suggested that these high participation rates may be influenced by the value placed by both professionals and parents on research in connection with these serious health conditions, but may also reflect possible parental reluctance to say 'no' to the clinical team on whom their child's care depends (see also paragraph 2.27).[109] However, severity of condition does not guarantee the existence of a professional culture conducive to research: there are many other serious health conditions affecting children where the need for research into more effective treatments may be as acute as in cancer but where a strong research culture, in which most clinicians are also involved in carrying out research, has not yet emerged.[110]

Research proposed in traumatic, highly emotional, or sensitive situations

> *"There are particular difficulties in carrying out research in neonatal palliative care, largely because parents of newborns may not have had time come to terms with their baby's poor prognosis and the introduction of a palliative care approach, let alone considering participation in research studies."*[111]
>
> "*… research into the use of drugs or sexual relationships, where involvement of the parents or other family members may be problematic*".[112]

2.9 Associated closely with research that addresses severe conditions are circumstances where participation decisions about clinical research are made in traumatic or highly emotional situations. In the context of neonatal clinical research, for example, 'fear' has been identified as the dominant parental emotion, underscoring almost all elements of decision-making.[113] Attendees of a factfinding meeting with the Working Party highlighted a set of circumstances where a baby could be born, enrolled into a research study, and die, within 24 hours. Since a baby who is thought to be highly unlikely to live will not usually be recruited into research, the invitation to consider research may be a source of (false) hope for parents.[114] At the same meeting, it was suggested that finding out that a child or young person has a long-term or serious

---

[108] Ablett S, and Pinkerton C (2003) Recruiting children into cancer trials - role of the United Kingdom Children's Cancer Study Group (UKCCSG) *British Journal of Cancer* **88(11)**: 1661-5; Byrne-Davis LMT, Salmon P, Gravenhorst K, and Eden TOB (2010) Balancing high accrual and ethical recruitment in paediatric oncology: a qualitative study of the 'look and feel' of clinical trial discussions *BMC Medical Research Methodology* **10**: 101.

[109] Shilling V, and Young B (2009) How do parents experience being asked to enter a child in a randomised controlled trial? *BMC Medical Ethics* **10(1)**: 1-11, at page 4.

[110] See, for example, the argument put forward in Davies JC (2013) Cystic fibrosis: bridging the treatment gap in early childhood *The Lancet* **1(6)**: 433-4 that cystic fibrosis research in very young children should become the norm, not the exception, as in oncology – there are almost no evidence-based treatments for this age group.

[111] Together for Short lives and Association for Paediatric Palliative Medicine Joint Research Group, responding to the Working Party's call for evidence.

[112] Health, Ethics and Law, University of Southampton (HEAL UoS), responding to the Working Party's call for evidence.

[113] Snowdon C, Elbourne D, and Garcia J (2006) "It was a snap decision": parental and professional perspectives on the speed of decisions about participation in perinatal randomised controlled trials *Social Science & Medicine* **62(9)**: 2279-90.

[114] Nuffield Council on Bioethics (2013) *Factfinding meeting: making research decisions: who decides and how?* (London, 9 September: Nuffield Council on Bioethics). See also: Snowdon C, Brocklehurst P, Tasker R *et al.* (2014) Death, bereavement and randomised controlled trials (BRACELET): a methodological study of policy and practice in neonatal and paediatric intensive care trials *Health Technology Assessment* **18(42)**: 1-410, where parents had to make a rapid decision about taking part in a RCT which sought to assess the effect of whole-body cooling for babies who had suffered perinatal asphyxia following complicated deliveries. Whole body cooling was only available to babies of parents who agreed to take part in the RCT; but only 50 per cent would be allocated to the intervention arm of the trial; the remaining 50 per cent in the control arm did not receive whole body cooling. The authors of this study note, at 62, that "where babies are critically ill and the trial intervention may offer some hope, allocation to the control arm can be a very disappointing experience for parents." See also: Embleton ND, and Rankin J (2014) The BRACELET study: implications for the design of randomised controlled trials in neonatal and paediatric intensive care *Archives of Disease in Childhood - Fetal and Neonatal Edition* **100(2)**: F97-8.

illness has the potential to change fundamentally the nature of family relationships, and what it is to be a parent.[115] It is therefore very important for researchers to have a real understanding of how decisions about research are made in this 'new world' of parenting a seriously-ill child, and this can only be obtained through research with those parents, even at this very difficult time.[116]

2.10 Participation decisions may also be influenced by the sensitivity of the proposed research question,[117] such as research that addresses young people's sexual behaviour or use of drugs. The challenging question of parental involvement in decisions about young people's participation in such research was highlighted by respondents to the Working Party's consultation both in the UK and in Africa.[118] In some cultural contexts, it might also be the case that parents prefer to consult respected members of their community before making a decision about providing consent for adolescents to take part in sexual and reproductive health research.[119] There is considerable diversity in what may be considered a 'sensitive' research topic: other sensitive areas of research, for example, may include questions surrounding a child's weight,[120] or appearance.[121]

Time pressures at point of recruitment

> *"Children in particular need time, they need to know that we value their opinion…"*[122]

2.11 A significant factor affecting how both children and parents approach the possibility of participation in research is that of the time pressure under which they are asked to make the decision. In cases where research protocols are closely intertwined with treatment options, decisions about participation might have to be made almost immediately after a diagnosis has been made: the experience of young people with cancer and their families has been described as a "whirlwind of consent activities immediately after diagnosis".[123] The importance of parents having time to think about

[115] See, for example, Bluebond-Langner M, Belasco JB, Goldman A, and Belasco C (2007) Understanding parents' approaches to care and treatment of children with cancer when standard therapy has failed *Journal of Clinical Oncology* **25(17)**: 2414-9.

[116] Nuffield Council on Bioethics (2013) *Factfinding meeting: making research decisions: who decides and how?* (London, 9 September: Nuffield Council on Bioethics).

[117] See, for example, Modi N, Vohra J, Preston J *et al.* (2014) Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees *Archives of Disease in Childhood* **99(10)**: 887-91, which observes that "in most instances, the child's assent or consent should be underpinned by parent consent, but this can be problematic where sensitive subjects, such as sexual health, contraception, and adolescent behavioural studies are involved, and there is a duty to preserve confidentiality."

[118] For example, Morenike O Folayan, Obafemi Awolowo University and the New HIV Vaccine and Microbicide Advocacy Society, and Health, Ethics and Law, University of Southampton (HEAL UoS), both responding to the Working Party's call for evidence.

[119] Folayan MO, Haire B, Harrison A *et al.* (2014) Ethical issues in adolescents' sexual and reproductive health research in Nigeria *Developing World Bioethics*: Published online first (9 June 2014).

[120] Barratt R, Levickis P, Naughton G, Gerner B, and Gibbons K (2013) Why families choose not to participate in research: feedback from non-responders *Journal of Paediatrics and Child Health* **49(1)**: 57-62 notes, at page 61, that "a primary objective of any study is to do no harm. Overweight and obesity in childhood are sensitive issues and some parents were particularly conscious of the impact of the study on their child." See also: Warren JM, Golley RK, Collins CE *et al.* (2007) Randomised controlled trials in overweight children: practicalities and realities *International Journal of Pediatric Obesity* **2(2)**: 73-85.

[121] See, for example, Williams LBDSM, Dures EP, Waylen AP *et al.* (2012) Approaching parents to take part in a cleft gene bank: a qualitative pilot study *The Cleft Palate - Craniofacial Journal* **49(4)**: 425-36.

[122] Professor Faith Gibson, responding to the Working Party's call for evidence.

[123] Stevens PE, and Pletsch PK (2002) Ethical issues of informed consent: mothers' experiences enrolling their children in bone marrow transplantation research *Cancer Nursing* **25(2)**: 81-7, at page 84. See also: Deatrick JA, Angst DB, and Moore C (2002) Parents' views of their children's participation in phase I oncology clinical trials *Journal of Pediatric Oncology Nursing* **19(4)**: 114-21.

participation decisions, and also having time to discuss it with their partner,[124] and the researchers,[125] has been noted by several commentators. Children and young people have also commented on tight timelines within which participation decisions need to be made, and have highlighted the importance of having someone to explain to them *why* research (in a general sense) is undertaken, *before* being asked to enrol into a study (see also paragraphs 2.17–2.18).[126] Clearly, this urgency for decisions to be made does not apply for all forms of research, and other studies have indicated that parents and children have been given plenty of time to consider participation decisions.[127]

Discomfort and risk

> *"Operationally, one of the main obstacles for recruiting young children is the thought of blood sampling."*[128]
>
> "*Concern over painful or uncomfortable procedures, many of which are technically more challenging in children such as venepuncture..."*[129]
>
> "*I would be very worried if any new drug is to be administered. Any drug that has been approved and has been used for other conditions would make me feel more relaxed*."[130]

2.12 Participation decisions may also be affected by perceptions of discomfort, pain or risk. As the quotations above indicate, the use of needles in blood sampling is often raised as a particular concern.[131] Discomfort from blood sampling can be alleviated, for example, through the use of anaesthetic creams,[132] or by taking blood at the point at which children visit clinics for a 'standard' blood test, so that there are "no extra pokes, no extra pain".[133] However, anxieties about these procedures may still persist.

---

[124] Cartwright K, Mahoney L, Ayers S, and Rabe H (2011) Parents' perceptions of their infants' participation in randomized controlled trials *Journal of Obstetric, Gynecologic & Neonatal Nursing* **40(5)**: 555-65.

[125] See: Vanhelst J, Hardy L, Bert D *et al.* (2013) Effect of child health status on parents' allowing children to participate in pediatric research *BMC Medical Ethics* **14(1)**: 7, where 13 per cent, 29 per cent, and 40 per cent of parents of healthy, ambulatory, and non-ambulatory sick children, respectively, would have like to spend more time with investigators discussing the trial.

[126] See: Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83, at e880. 87 per cent (n=32) of children who participated in this study indicated that this approach would be helpful. See also paragraph 2.30 where we note how children and young people may be removed from participation discussions and decisions in cases where their participation is deemed to be necessary immediately and urgently.

[127] See, for example, Burgess E, Singhal N, Amin H, McMillan D, and Devrome H (2003) Consent for clinical research in the neonatal intensive care unit: a retrospective survey and a prospective study *Archives of Disease in Childhood-Fetal and Neonatal Edition* **88(4)**: F280-6, where 62 per cent of parents of neonates reported that they had enough time to make a decision about their baby's participation in research. See also: Sammons HM, Atkinson M, Choonara I, and Stephenson T (2007) What motivates British parents to consent for research? A questionnaire study *BMC Pediatrics* **7(1)**: 12, where 95 per cent of parents indicated that they were given enough time to make a decision.

[128] EMIG, responding to the Working Party's call for evidence.

[129] Professor Jane C. Davies, responding to the Working Party's call for evidence.

[130] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[131] See: Wolthers OD (2006) A questionnaire on factors influencing children's assent and dissent to non-therapeutic research *Journal of Medical Ethics* **32(5)**: 292-7, where 46 per cent of dissenting children made their decision because of worries about having a blood sample taken.

[132] Modi N, Vohra J, Preston J *et al.* (2014) Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees *Archives of Disease in Childhood* **99(10)**: 887-91.

[133] Thomas M, and Menon K (2012) Consenting to pediatric critical care research: understanding the perspective of parents *Dynamics* **24(3)**: 18-24.

2.13 Parents and children will, of course, be concerned about the possible risks associated with research compared to the known outcomes of previous treatment,[134] and be put off by possible side effects.[135] Parents may also have particular concerns about the 'unknown' risks of participation.[136] Research proposals that are perceived to be low risk, or involve painless procedures, by contrast, have been shown to make it easier for parents to agree to participate.[137] Approaches to risk when making participation decisions may differ according to whether a protocol is considered by a parent or a young person: young people have been observed to agree to higher risk research more willingly than their parents.[138] However, this willingness to take risks in the context of research needs to be considered alongside the well-established evidence that risk-taking behaviour peaks in adolescence.[139] In particular, adolescents are more likely than children and adults to make risky decisions in situations of high emotion and in the presence of peers. The peak in risk-taking during adolescence is believed to be due, at least in part, to asymmetrical development of the brain's reward system, which temporarily becomes more responsive during adolescence, while brain systems involved in impulse and inhibitory control seem to develop more gradually over childhood and adolescence.[140]

Time and opportunity costs

> *"Participation must coincide with treatment schedules and not be in addition. The treatment schedule / office visits, hospital stays for a cancer patient is already extensive, so combining visits should be reasonably easy for the researchers."*[141]

2.14 Parents have commented that hassle and inconvenience play significant roles in their decision to *refuse* to allow their child to take part.[142] Conversely, parents' willingness to

[134] See: Eiser C, Davies H, Jenney M, and Glaser A (2005) Mothers' attitudes to the randomized controlled trial (RCT): the case of acute lymphoblastic leukaemia (ALL) in children *Child: Care, Health and Development* **31(5)**: 517-23, where three mothers stated that they withheld consent for their child to take part in a clinical trial because of concerns about the possible risks associated with a new treatment compared with the success of previous treatment.

[135] See, for example, Harth S, and Thong Y (1990) Sociodemographic and motivational characteristics of parents who volunteer their children for clinical research: a controlled study *BMJ: British Medical Journal* **300(6736)**: 1372-5; Fisher HR, McKevitt C, and Boaz A (2011) Why do parents enrol their children in research: a narrative synthesis *Journal of Medical Ethics* **37(9)**: 544-51.

[136] See, for example, Fisher HR, McKevitt C, and Boaz A (2011) Why do parents enrol their children in research: a narrative synthesis *Journal of Medical Ethics* **37(9)**: 544-51, where reasons for parental refusal tended to cite the unknown risks of the therapies being tested.

[137] Vanhelst J, Hardy L, Bert D *et al.* (2013) Effect of child health status on parents' allowing children to participate in pediatric research *BMC Medical Ethics* **14(1)**: 7. See also: Perez ME, Langseder A, Lazar E, and Youssef NN (2010) Parental perceptions of research after completion of placebo-controlled trials in pediatric gastroenterology *Journal of Pediatric Gastroenterology and Nutrition* **51(3)**: 309-13, where 91 per cent of parents' decision to participate may have been made because of the perception that risk was minimal.

[138] For example, Brody JL, Annett RD, Scherer DG, Perryman ML, and Cofrin KM (2005) Comparisons of adolescent and parent willingness to participate in minimal and above-minimal risk pediatric asthma research protocols *Journal of Adolescent Health* **37(3)**: 229-35 observed that young people were more willing to take part in above-minimal risk asthma research, compared to parents who were asked to assess the same protocol.

[139] Spear LP (2013) Adolescent neurodevelopment *Journal of Adolescent Health* **52(2)**: S7-S13.

[140] Van Leijenhorst L, Moor BG, Op de Macks ZA *et al.* (2010) Adolescent risky decision-making: neurocognitive development of reward and control regions *NeuroImage* **51(1)**: 345-55.

[141] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[142] See, for example, Harth S, and Thong Y (1990) Sociodemographic and motivational characteristics of parents who volunteer their children for clinical research: a controlled study *BMJ: British Medical Journal* **300(6736)**: 1372-5; van Stuijvenberg M, Suur MH, de Vos S *et al.* (1998) Informed consent, parental awareness, and reasons for participating in a randomised controlled study *Archives of Disease in Childhood* **79(2)**: 120-5; Hayman R, Taylor B, Peart N, Galland B, and Sayers R (2001) Participation in research: informed consent, motivation and influence *Journal of Paediatrics and Child Health* **37(1)**: 51-4.

participate in clinical research may increase if inconveniences decrease.[143] Young people have also suggested that hassle plays a key role in participation decisions,[144] a point emphasised by those who took part in the Working Party's stakeholder event.[145] Practical suggestions put forward in response to these obstacles to participation include the advantage of researchers offering flexible start times, and making time commitments more transparent from the start of the process.[146]

2.15 Time spent participating in clinical research may also lead to commensurate opportunity costs for families, such as less time to play or socialise; such factors may have a direct effect on participation decisions.[147] Suggestions for how such issues may be addressed include providing services such as child-friendly play areas, but also reducing waiting times,[148] and exploring the possibility of undertaking research procedures at home, rather than in clinics.[149]

Participation decisions: the situation of children and their families

2.16 While the factors outlined above focus on features of the research itself or the clinical circumstances in which the need for research arises, these will be experienced in diverse ways by children and their families, depending on their own situation. This section focuses on those factors shown to affect participation decisions that stem from the particular situation, knowledge or attitudes of children and young people, and their families. As such, these are not generally factors that can be changed by researchers although, as indicated below, some may potentially be influenced by higher levels of awareness about clinical research in the population as a whole, and by good communication (see also paragraphs 2.28–2.29).

Knowledge and attitudes with respect to research and risk

> *"Although attitudes to research are generally positive amongst the general public, some parents may have pre-existing concerns or misconceptions about research in general, that their child would*

[143] Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9.

[144] For example, Brody JL, Annett RD, Scherer DG, Perryman ML, and Cofrin KM (2005) Comparisons of adolescent and parent willingness to participate in minimal and above-minimal risk pediatric asthma research protocols *Journal of Adolescent Health* **37(3)**: 229-35 found that just under 35 per cent of adolescents indicated that hassle played a role in participation decisions.

[145] Nuffield Council on Bioethics (2014) *Note of stakeholder group meeting*, available at: http://nuffieldbioethics.org/wp-content/uploads/Stakeholder-meeting-note.pdf. Factors identified by participants as likely to put them off research participation included: "things that affect your daily life or things you like doing, like sport"; "if it goes on too long or gets boring", and "inconvenience for parents".

[146] Barratt R, Levickis P, Naughton G, Gerner B, and Gibbons K (2013) Why families choose not to participate in research: feedback from non-responders *Journal of Paediatrics and Child Health* **49(1)**: 57-62. This suggestion was echoed by a response to our call for evidence from the University of Cambridge Department of Paediatrics which noted that this obstacle might be overcome by "making [it] more convenient for busy parents and children to participate in research studies." See: Nuffield Council on Bioethics (2015) *Children and clinical research: ethical issues - summary of consultation responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/, at page 9.

[147] See, for example, Barratt R, Levickis P, Naughton G, Gerner B, and Gibbons K (2013) Why families choose not to participate in research: feedback from non-responders *Journal of Paediatrics and Child Health* **49(1)**: 57-62, which observed that families are less likely to take part in research if time commitments are too onerous. Hein IM, Troost PW, de Vries MC *et al.* (2015) Why do children decide not to participate in clinical research: a quantitative and qualitative study *Pediatric Research*: (Accepted article preview published online 9 April) similarly found that "many children mentioned that participating would impact on their time-schedule, and children of all ages mentioned they did not want to miss school." See also: Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9.

[148] Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9, at page 558.

[149] Chantler TE, Lees A, Moxon ER *et al.* (2007) The role familiarity with science and medicine plays in parents' decision making about enrolling a child in vaccine research *Qualitative Health Research* **17(3)**: 311-22.

> *be used as a 'guinea pig'[...] Addressing misconceptions regarding the purposes of clinical research more generally may be helped by publishing good practice or positive case examples."*[150]
>
> *"I would not want to subject my child to something that would potentially harm them and I would not want their privacy to be at risk."*[151]
>
> *"I would have no concern. Research can only be a good thing."*[152]

2.17 Participation decisions can be influenced by families' attitudes to and understanding of research, and the threat it may pose to their children. As the last two quotes above illustrate, these anxieties differ substantially from family to family. Parents may find participation decisions less stressful where they themselves have medical backgrounds, or are more familiar with the language of science and medicine (either professionally or as healthcare consumers);[153] if they have higher levels of understanding of standard research procedures or the right to withdraw from clinical research; or if they are more confident in their abilities to evaluate the research being proposed.[154] Conversely, the way families make participation decisions in clinical research may be affected by conceptual and communication ambiguities, or lack of knowledge. Many families may be unfamiliar with the concepts of 'randomisation' and 'control arms',[155] or even the term 'research' itself.[156]

2.18 The NIHR Clinical Research Network: Children, responding to our call for evidence, suggested that "publicity and training to highlight the benefits of and opportunities to undertake paediatric research" could be beneficial in supporting recruitment of children into research. The Oxford Vaccine Group noted that the same problem of a lack of knowledge can arise in clinicians too, observing that if clinicians are "better informed, they may be willing to partake or encourage families to become involved in research." Members of the Working Party's stakeholder group similarly placed particular emphasis

[150] British Medical Association, responding to the Working Party's call for evidence.

[151] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[152] Ibid.

[153] Chantler TE, Lees A, Moxon ER *et al.* (2007) The role familiarity with science and medicine plays in parents' decision making about enrolling a child in vaccine research *Qualitative Health Research* **17(3)**: 311-22; Cartwright K, Mahoney L, Ayers S, and Rabe H (2011) Parents' perceptions of their infants' participation in randomized controlled trials *Journal of Obstetric, Gynecologic & Neonatal Nursing* **40(5)**: 555-65.

[154] Hoberman A, Shaikh N, Bhatnagar S, and et al. (2013) Factors that influence parental decisions to participate in clinical research: consenters vs nonconsenters *JAMA Pediatrics* **167(6)**: 561-6.

[155] For example, Woolfall K, Shilling V, Hickey H *et al.* (2013) Parents' agendas in paediatric clinical trial recruitment are different from researchers' and often remain unvoiced: a qualitative study *PLoS ONE* **8(7)**: e67352 found that despite practitioners explaining how the randomisation process worked, some parents were confused. For example, some mistakenly believed that researchers made the decision about which arm of the trial their child was allocated to, rather than allocation being conducted by computer randomisation. However, Kupst MJ, Patenaude AF, Walco GA, and Sterling C (2003) Clinical trials in pediatric cancer: parental perspectives on informed consent *Journal of Pediatric Hematology/Oncology* **25(10)**: 787-90, at page 789, highlight that one of the reasons for parents' distress during the consent process was due to "the computer choosing – randomization."

[156] Molyneux C, Peshu N, and Marsh K (2004) Understanding of informed consent in a low-income setting: three case studies from the Kenyan Coast *Social Science & Medicine* **59(12)** 2547-59; Participants in the Community Engagement Consent Workshop: Kilifi; Kenya (2013) Consent and community engagement in diverse research contexts *Journal of Empirical Research on Human Research Ethics: An International Journal* **8(4)**: 1-18.

on the importance of action to address poor levels of knowledge about research in society as a whole.[157]

2.19 As we noted above (see paragraphs 2.12–2.13), concerns about possible pain or discomfort, and any risks involved in the research, are an important factor in decision-making about research. Parents will come to different conclusions about what is acceptable to ask their child to do, with some perhaps understandably adopting an approach that researchers should "do it on someone else".[158] Children and young people similarly take diverse approaches to risk. While young people have been observed to agree to higher risk research more willingly than their parents (see paragraph 2.13), this approach to research is naturally not adopted by every child or young person. One young person who responded to our Survey Monkey question about what should happen if they *didn't* want to take part in research, but their parents thought that they *should*, highlighted the role of fear in decision-making: "you shouldn't have to [take part] because you could be scared, and you're the one who is taking part, not your parents."

Desire to help others

> *"… it will have the possibility of helping children and may even save lives/change for the better."*[159]
>
> *"… the research would still be done with other children, and I wouldn't be at risk. Selfish, but that would be what I would do."*[160]
>
> *"It depends how it would help them, because if they had cancer, I would. If they had chicken pox I wouldn't".*[161]

2.20 The desire to help others is cited as a factor influencing the participation decisions of some children and young people.[162] This emerged as a strong theme in the direct engagement the Working Party had with children and young people through its stakeholder group, school workshops and online survey. However, as indicated in the quotations above, concerns about risk, or doubts about the likely value of the research, may also play an important role.

2.21 A desire to help others may also play a part in *parents'* deliberations about research participation. A high percentage of parents participating in neonatal research, for example, believe that their baby's participation in research will improve the care of

[157] Nuffield Council on Bioethics (2013) *Stakeholder meeting* (London, 17 July: Nuffield Council on Bioethics). See also: Participants in the Community Engagement Consent Workshop: Kilifi; Kenya (2013) Consent and community engagement in diverse research contexts *Journal of Empirical Research on Human Research Ethics: An International Journal* **8(4)**: 1-18.

[158] Caldwell PHY, Butow PN, and Craig JC (2003) Parents' attitudes to children's participation in randomized controlled trials *The Journal of Pediatrics* **142(5)**: 554-9, at page 557.

[159] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of young people's responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[160] Ibid.

[161] Ibid.

[162] See, for example, Broome ME, Richards DJ, and Hall JM (2001) Children in research: the experience of ill children and adolescents *Journal of Family Nursing* **7(1)**: 32-49; Wolthers OD (2006) A questionnaire on factors influencing children's assent and dissent to non-therapeutic research *Journal of Medical Ethics* **32(5)**: 292-7; Wendler D JT (2008) Children's and their parents' views on facing research risks for the benefit of others *Archives of Pediatrics & Adolescent Medicine* **162(1)**: 9-4; Cherrill J, Hudson H, Cocking C *et al.* (2010) Clinical trials: the viewpoint of children with a chronic illness compared with healthy children *Archives of Disease in Childhood* **95(3)**: 229-32; Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83.

future babies,[163] while a parent whose child was taking part in a phase 1 oncology trial similarly comments: "if nothing else, it will help somebody else down the road."[164] These altruistic instincts might be directed towards other families in similar situations,[165] or more generally be understood as part of "being a good citizen" and associated actions of social responsibility.[166] Parents might also recognise that their child benefits from the participatory altruism of other children in the past.[167] For bereaved parents – for example, those whose baby took part in neonatal research – participation may also be a source of satisfaction, or even pride; that their baby, however short his or her life, made a contribution to the world.[168]

Perceived health or other benefit to participants

> *"I have a child with congenital heart defect and I happily enrol him in studies which could be beneficial for him and cast more light on his condition."*[169]

> *"I was glad that they had asked because I knew it was probably his only chance of survival because of the level of intensive care that he was being given once he got there… just having the chance of him surviving, I was grateful."*[170]

> *"Ok with me you see I will enjoy because I will be able to interact with the different people from different back grounds also… you will enjoy that."*[171]

2.22 Participation decisions are also affected by the perception (from both parents and young people) that a young person's condition will improve if they take part in a study.[172] The prospect of 'direct benefit' for their child is a major factor influencing parents' decisions to enrol their children in research, particularly where their child is seriously ill.[173] There may be additional expectations that children will receive

---

[163] See, for example, Morley C, Lau R, Davis P, and Morse C (2005) What do parents think about enrolling their premature babies in several research studies? *Archives of Disease in Childhood-Fetal and Neonatal Edition* **90(3)**: F225-8, where 94 per cent of parents whose premature babies had been invited to join several studies believed that their baby's participation would improve future neonatal care.

[164] Deatrick JA, Angst DB, and Moore C (2002) Parents' views of their children's participation in phase I oncology clinical trials *Journal of Pediatric Oncology Nursing* **19(4)**: 114-21, at page 118.

[165] See: Byrne-Davis LMT, Salmon P, Gravenhorst K, and Eden TOB (2010) Balancing high accrual and ethical recruitment in paediatric oncology: a qualitative study of the 'look and feel' of clinical trial discussions *BMC Medical Research Methodology* **10**: 101, where four out of five parents who commented on the scientific imperative of a clinical research trial expressed positive views about helping families in other situations.

[166] Fisher HR, McKevitt C, and Boaz A (2011) Why do parents enrol their children in research: a narrative synthesis *Journal of Medical Ethics* **37(9)**: 544-51.

[167] Ibid.

[168] Nuffield Council on Bioethics (2013) *Factfinding meeting: making research decisions: who decides and how?* (London, 9 September: Nuffield Council on Bioethics).

[169] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[170] Cartwright K, Mahoney L, Ayers S, and Rabe H (2011) Parents' perceptions of their infants' participation in randomized controlled trials *Journal of Obstetric, Gynecologic & Neonatal Nursing* **40(5)**: 555-65.

[171] Secondary school student, contributing to Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

[172] Wagner KD, Martinez M, and Joiner T (2006) Youths' and their parents' attitudes and experiences about participation in psychopharmacology treatment research *Journal of Child & Adolescent Psychopharmacology* **16(3)**: 298-307.

[173] Vanhelst J, Hardy L, Bert D *et al.* (2013) Effect of child health status on parents' allowing children to participate in pediatric research *BMC Medical Ethics* **14(1)**: 7.

enhanced medical care[174] or improved access to medicines[175] if they participate. These expectations of wider health benefits may arise particularly in social contexts where families do not otherwise have routine access to healthcare, or where healthcare associated with research centres is perceived as being of higher quality.[176] There may, however, be significant disparity between professionals' expectations of likely benefit and parental hopes: in the context of cancer treatment, for example, it has been observed that "having explained to parents that there is nothing to offer to combat the disease, the physician cannot expect that parents will stop looking".[177] A parent who responded to our Survey Monkey questionnaire similarly illustrated the role of hope, commenting: "if very lucky, he might happen to be an early beneficiary of a wonder drug."[178] As we note at paragraph 2.17, parents' perceptions of the likelihood of benefit in the context of research may be affected by their work or educational backgrounds, and the insights they have as a result into research practice.[179]

2.23 Participation decisions may also be affected by *non*-health-related motivations, such as an interest in science generally,[180] the chance to learn something new,[181] or because some research processes can be fun.[182]

[174] Morley C, Lau R, Davis P, and Morse C (2005) What do parents think about enrolling their premature babies in several research studies? *Archives of Disease in Childhood-Fetal and Neonatal Edition* **90(3)**: F225-8; Chappuy H, Doz F, Blanche S *et al.* (2006) Parental consent in paediatric clinical research *Archives of Disease in Childhood* **91(2)**: 112-6; Chantler TE, Lees A, Moxon ER *et al.* (2007) The role familiarity with science and medicine plays in parents' decision making about enrolling a child in vaccine research *Qualitative Health Research* **17(3)**: 311-22. The question of a 'trial effect' is debated: see: Braunholtz DA, Edwards SJL, and Lilford RJ (2001) Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect" *Journal of Clinical Epidemiology* **54(3)**: 217-24 and Koschmann C, Thomson B, and Hawkins DS (2010) No evidence of a trial effect in newly diagnosed pediatric acute lymphoblastic leukemia *Archives of Pediatrics & Adolescent Medicine* **164(3)**: 214-7, which disputes the argument that there is benefit *per se* of being in a trial (such as better monitoring leading to better outcomes).

[175] Woolfall K, Shilling V, Hickey H *et al.* (2013) Parents' agendas in paediatric clinical trial recruitment are different from researchers' and often remain unvoiced: a qualitative study *PLoS ONE* **8(7)**: e67352.

[176] This emerged very clearly in the Kilifi consultation: Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme). It is also well-evidenced in the published literature: see, for example, Masiye F, Kass N, Hyder A, Ndebele P, and Mfutso-Bengo J (2008) Why mothers choose to enrol their children in malaria clinical studies and the involvement of relatives in decision making: evidence from Malawi *Malawi Medical Journal* **20(2)**: 50-6; Molyneux S, Mulupi S, Mbaabu L, and Marsh V (2012) Benefits and payments for research participants: experiences and views from a research centre on the Kenyan coast *BMC Medical Ethics* **13(1)**: 13. The challenge for researchers (not necessarily even health researchers) is captured by Nyambedha EO (2008) Ethical dilemmas of social science research on AIDS and orphanhood in Western Kenya *Social Science & Medicine* **67(5)**: 771-9 who reports how, in response to his long-term study on the effect of AIDs on orphans in western Kenya, he is regularly asked "What are you going to do to the orphans after you have studied them?"

[177] Bluebond-Langner M, Belasco JB, Goldman A, and Belasco C (2007) Understanding parents' approaches to care and treatment of children with cancer when standard therapy has failed *Journal of Clinical Oncology* **25(17)**: 2414-9, at page 2418.

[178] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[179] See, for example, Cartwright K, Mahoney L, Ayers S, and Rabe H (2011) Parents' perceptions of their infants' participation in randomized controlled trials *Journal of Obstetric, Gynecologic & Neonatal Nursing* **40(5)**: 555-65, at page 558, where it was observed that parents with a medical background felt that participation in a RCT was of little significance.

[180] See: Bernhardt BA, Tambor ES, Fraser G, Wissow LS, and Geller G (2003) Parents' and children's attitudes toward the enrollment of minors in genetic susceptibility research: implications for informed consent *American Journal of Medical Genetics Part A* **116A(4)**: 315-23, at page 318, where a 12-year-old participant states: "I just like to participate in anything that can help people because I want to be a doctor when I grow up".

[181] Ondrusek N, Abramovitch R, Pencharz P, and Koren G (1998) Empirical examination of the ability of children to consent to clinical research *Journal of Medical Ethics* **24(3)**: 158-65, at page 161, where participants indicated that among "good things [that] might happen to you because you are in this study" was the chance that they might have to know "about calories and/or how much muscle they have".

[182] Ibid., where participants indicated that they could benefit by 'having fun'.

Participation decisions: the relationship between children, families and researchers

2.24 Finally, participation decisions may also be influenced by the nature of the relationship between children, young people, families, and researchers, and in particular the quality of the communication between them. Such relationship factors may be able to be addressed by researchers by changing the way they interact with children and their families.

Good relationship between families and researchers

> *"I think it is really important that the study is as personal as it can be – a personal connection between the researcher and the participants."*[183]

> *"To get people on board they need to feel special and not a sheep and a big herd. It is the little touches for example good manners, nothing is too much trouble, refreshments on arrival, individual care, someone to have done their homework about your child even if it just checking when their birthday is as I say it is the little touches. Researchers also need a good bedside manner :)"*[184]

> *"Like Tambo [community facilitator]… now perhaps, maybe my child has been given those drugs and she took it, knowing Tambo will come, 'How is she doing, no problem?' 'No problem. She is doing well' and he passes by. Then we know we have someone in our midst who cares [other participants: Yes] for us."*[185]

2.25 The ability to feel comfortable with researchers is an important aspect of participation decisions. One study exploring young people's experiences included the suggestion "try and not scare anyone" from one participant,[186] a comment echoed in the Working Party's own online questionnaire for young people where responses included noting that "doctors and nurses being friendly" would put them at ease.[187] Parents may be similarly affected by the friendliness and familiarity of the research team.[188] Confidence in the wider research team has also been shown to be important for parents who are

[183] Nuffield Council on Bioethics (2014) *Be a part of it: what young people think of clinical research*, available at: http://www.youtube.com/watch?v=e2k6eA0dn9Q.

[184] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[185] Community representative contributing to Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

[186] Shilling V, Williamson PR, Hickey H *et al.* (2011) Processes in recruitment to randomised controlled trials (RCTs) of medicines for children (RECRUIT): a qualitative study *Health Technology Assessment* **15(15)**: 1-116, at page 48.

[187] The role of 'bedside nurses' has also been highlighted in good practice guidance on seeking parental permission: for example, Lebet R, Fineman LD, Faustino EVS, and Curley MAQ (2013) Asking for parents' permission to enroll their child into a clinical trial: best practices *American Journal of Critical Care* **22(4)**: 351-6 suggests that nurses are trusted more than other healthcare professionals. In addition, the role of the wider team in research participation, for example statisticians and data managers, has also been acknowledged in the context of leukaemia trials: Moscucci O, Herring R and Berridge V (2009) Networking health research in Britain: the post-war childhood leukaemia trials *Twentieth Century British History* **20(1)**: 23-52.

[188] See: Hoberman A, Shaikh N, Bhatnagar S, and et al. (2013) Factors that influence parental decisions to participate in clinical research: consenters vs nonconsenters *JAMA Pediatrics* **167(6)**: 561-6, which observed that parents were significantly more likely to consent if they thought that the researcher was friendly and professional.

involved with making decisions about their child's participation,[189] as has the reputation of the research institute.[190]

2.26 Conversely, concerns are sometimes expressed by researchers that good relationships with participants might serve unduly to increase their hopes in the possible outcome of the research. Moreover, researchers might find themselves emotionally invested in the outcome, raising concerns that effective professional engagement with participants could potentially lead to "inappropriately high trial expectations" on both sides.[191] Researchers may try to avoid giving advice to children and their parents about participating because of these fears of undue influence; however, this might lead to parents feeling abandoned by the very professionals they expect to advise and support them.[192]

2.27 Professionals may also feel discomfort in the fact that their trusted status can make it hard for families to say *no* to participating in a study;[193] similarly, parents may feel conflicted if they refuse to take part in a study that is being run by their child's doctor.[194] The same issues of discomfort may arise in connection with children and young people's own sense of freedom to refuse to participate.[195]

Quality of communication

2.28 As we note above (paragraphs 2.17–2.18), children and families vary significantly in their background knowledge about clinical research and research procedures at the point when they are first approached and invited to consider research participation. The way such an invitation is communicated by researchers is clearly critical, but the language and terminology used to convey information about research proposals may,

---

[189] Chappuy H, Doz F, Blanche S, Gentet JC, and Tréluyer JM (2008) Children's views on their involvement in clinical research *Pediatric Blood & Cancer* **50(5)**: 1043-6: 41 per cent of parents (n=12) highlighted the importance of having confidence in the investigator. See also: Hoffman T, Taeed R, Niles J *et al.* (2007) Parental factors impacting the enrollment of children in cardiac critical care clinical trials *Pediatric Cardiology* **28(3)**: 167-71, at page 171, which concluded that "the majority of parents believed that being approached about a clinical trial by the patient's primary pediatric cardiologist or cardiothoracic surgeon was most desirable as opposed to being approached by the principal investigator or the research coordinator. Comfort likely plays a significant role in this process."

[190] Nabulsi M, Khalil Y, and Makhoul J (2011) Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective *Journal of Medical Ethics* **37(7)**: 420-3, which observed that "trust in the doctor and in the institution where the study is conducted was mentioned by 14 parents and seemed to play a main role in facilitating or hindering participation."

[191] Peay HL, Tibben A, Fisher T, Brenna E, and Biesecker BB (2014) Expectations and experiences of investigators and parents involved in a clinical trial for Duchenne/Becker muscular dystrophy *Clinical Trials* **11**: 77-85. Three researchers who took part in this study voiced retrospective concerns about having been too positive with the families who participated.

[192] Coyne I (2010) Research with children and young people: the issue of parental (proxy) consent *Children & Society* **24(3)**: 227-37; Gillies K, and Entwistle VA (2012) Supporting positive experiences and sustained participation in clinical trials: looking beyond information provision *Journal of Medical Ethics* **38(12)**: 751-6. See also: Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme), where the dangers of either too much or too little trust by families in researchers are discussed.

[193] Shilling V, Williamson PR, Hickey H *et al.* (2011) Processes in recruitment to randomised controlled trials (RCTs) of medicines for children (RECRUIT): a qualitative study *Health Technology Assessment* **15(15)**: 1-116, at page 57.

[194] See, for example, Shilling V, Williamson PR, Hickey H *et al.* (2011) Processes in recruitment to randomised controlled trials (RCTs) of medicines for children (RECRUIT): a qualitative study *Health Technology Assessment* **15(15)**: 1-116, at page 79, which highlighted that parents experienced difficulties in refusing to take part because of obligations to the hospital and its practitioners, personal commitment, and anticipated regret.

[195] Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83 asked children if they felt free to dissent to study participation, and 14 out of 37 (38 per cent) said they did not. Eight of these children decided to enrol; out of those, three gave the reason that this was due to pressure from parents; one child indicated pressure from doctors; and four as combined pressure from parents and doctors. Shilling V, Williamson PR, Hickey H *et al.* (2011) Processes in recruitment to randomised controlled trials (RCTs) of medicines for children (RECRUIT): a qualitative study *Health Technology Assessment* **15(15)**: 1-116, at page 46, note the response of one young person who had not met the practitioner before the trial began, who stated, "[maybe] it was better, maybe someone separate […] in case they might object to us not, um, taking part in the study".

in some cases, be inaccessible both to parents[196] and to children and young people.[197] It was suggested to the Working Party that much better use of information technology could help reduce communication difficulties, and could also reduce the burden of research participation, for example through the use of appropriate apps to gather information without interfering with children's everyday lives.[198] It was noted, however, that while children and young people may, in general, be very comfortable with using these technologies, professionals and parents might not have the same expertise.

2.29 Children with severe communication difficulties can be particularly overlooked: they may be excluded by doctors from discussions about research because of assumptions that they are unable to understand the protocol (even when they are fully able to do so), or excluded altogether from the pool of potential participants.[199] Language barriers and the associated potential for misunderstandings could also make participation decisions difficult for potential participants and their family members.[200] In response to these difficulties, our stakeholder group argued that parents who do not speak English with confidence need appropriate support to make the right decisions for their child, and that even if an interpreter is available, the process may still feel very intimidating. Instead, the group suggested that participation decisions should be staged over several discussions, including the opportunity for private discussions between parents and the interpreter, and using the interpreter as a mediator between parents and clinicians, as necessary.[201] Techniques such as the use of art and craft, photography, and cartoons have also been used to facilitate the involvement of children with speech or communication difficulties, or those whose first language is not English.[202]

The involvement of children and young people in decision-making

> *"Personally if my parents told me I wasn't allowed to take part in the trial, I think that I would listen to them cos I would kind of trust their judgment on whether they think it is safe or not."*[203]

[196] See, for example, Zupancic JAF, Gillie P, Streiner DL, Watts JL, and Schmidt B (1997) Determinants of parental authorization for involvement of newborn infants in clinical trials *Pediatrics* **99(1)**: e6; Chantler TE, Lees A, Moxon ER *et al.* (2007) The role familiarity with science and medicine plays in parents' decision making about enrolling a child in vaccine research *Qualitative Health Research* **17(3)**: 311-22; Shilling V, Williamson PR, Hickey H *et al.* (2011) Communication about children's clinical trials as observed and experienced: qualitative study of parents and practitioners *PLoS ONE* **6(7)**: e21604.

[197] See, for example, van der Pal S, Sozanska B, Madden D *et al.* (2011) Opinions of children about participation in medical genetic research *Public Health Genomics* **14(4-5)**: 271-8, at page 275, where 42 per cent of participation children, in particular younger children (aged 6-8) said that they would like to receive a special letter with tailored information written specially for them.

[198] Nuffield Council on Bioethics (2013) *Factfinding meeting: setting the research agenda* (London, 9 September: Nuffield Council on Bioethics). One example of this kind of innovation (in the context of care rather than research) is a breathing exercise app for people with cystic fibrosis. See: PC Advisor (2 September 2014) *Cystic fibrosis app takes out top prize at 2014 iAwards*, available at: http://www.pcadvisor.co.uk/news/network-wifi/3542652/cystic-fibrosis-app-takes-out-top-prize-at-2014-iawards/. See also: NHS (2012) *Shared decision making*, available at: http://sdm.rightcare.nhs.uk/.

[199] Nuffield Council on Bioethics (2013) *Stakeholder meeting* (London, 17 July: Nuffield Council on Bioethics). See also: Morris J (2003) Including all children: finding out about the experiences of children with communication and/or cognitive impairments *Children & Society* **17(5)**: 337-48 and Garth B, and Aroni R (2003) 'I value what you have to say'. Seeking the perspective of children with a disability, not just their parents *Disability & Society* **18(5)**: 561-76.

[200] For example, Nabulsi M, Khalil Y, and Makhoul J (2011) Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective *Journal of Medical Ethics* **37(7)**: 420-3 noted that the Arabic translation for the word 'randomisation' is 'ashwa'I' meaning happening in a haphazard way. There is no other Arabic equivalent.

[201] Nuffield Council on Bioethics (2013) *Stakeholder meeting* (London, 17 July: Nuffield Council on Bioethics).

[202] See: Alderson P, and Morrow V (2011) *The ethics of research with children and young people: a practical handbook* (London: SAGE Publications), at pages 53 and 113.

[203] Nuffield Council on Bioethics (2014) *Be a part of it: what young people think of clinical research*, available at: http://www.youtube.com/watch?v=e2k6eA0dn9Q.

> *"I believe that my child has a right to be part of any decisions regarding his treatment and the risks they may be exposing themselves to."*[204]

> *"I think… for example, my parents maybe are not that educated so maybe they won't understand what the research is about while I will have understood but now if you go tell them they'll tell you 'Oh, don't go to do that!' But I'll know the importance of the research. For me, I'll participate. I might not tell them and secretly do it but I know it has importance. If they won't understand, I will have to hide it from them. I won't tell them!"*[205]

> *"The parent has seen the sun earlier so she has… I mean she knows a lot… she has experienced a lot and she has seen a lot… whatever she tells you, you can also think well about it, that parents love you unconditionally, she can never have bad intentions for you."*[206]

2.30 The published literature suggests that children and young people are involved in participation decisions in very different ways.[207] Some have indicated that they did not take part in the decision at all,[208] whereas others indicated that the decision had been taken jointly,[209] or, in some cases, that they were the 'final' decision-maker.[210] Contrary to expectation, these differences do not appear simply to correlate with age.[211] The severity of a child's illness, and the suddenness of either the diagnosis or the opportunity to take part in research, may both be important factors with respect to a child's possible involvement in the decision. Examples have been cited of young people with cancer being excluded from discussions about taking part in research and enrolled in studies with immediate effect; this contrasts with the more active role of young people with diabetes in making decisions about research participation, where

[204] Nuffield Council on Bioethics (2015) *Survey Monkey questionnaire: analysis of parents' responses*, available at: http://nuffieldbioethics.org/project/children-research/evidence-gathering-activities/.

[205] 17 year old student, contributing to Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

[206] Ibid., contribution of an 18 year old student.

[207] See, for example, Coyne I, and Harder M (2011) Children's participation in decision-making: balancing protection with shared decision-making using a situational perspective *Journal of Child Health Care* **15(4)**: 312-9; Coyne I, and Gallagher P (2011) Participation in communication and decision-making: children and young people's experiences in a hospital setting *Journal of Clinical Nursing* **20(15-6)**: 2334-43; Coyne I, Amory A, Kiernan G, and Gibson F (2014) Children's participation in shared decision-making: children, adolescents, parents and healthcare professionals' perspectives and experiences *European Journal of Oncology Nursing* **18(3)**: 273-80.

[208] See: Chappuy H, Doz F, Blanche S, Gentet JC, and Tréluyer JM (2008) Children's views on their involvement in clinical research *Pediatric Blood & Cancer* **50(5)**: 1043-6, where 41 per cent of children said that they had not contributed to the participation decision, for reasons including confidence in their parents, having no choice about taking part, or that the decision was too difficult.

[209] Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83.

[210] For example, 85 per cent of adolescents who participated in Miller VA, Baker JN, Leek AC *et al.* (2013) Adolescent perspectives on phase I cancer research *Pediatric Blood & Cancer* **60(5)**: 873-8 indicated that they were the final decision-maker. Fifty per cent of participants also stated that the most important individual to influence their decisions was themselves.

[211] Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83: the children who said they wanted "total involvement" in making decisions ranged between nine and 19, while those who wanted "a little involvement" ranged from seven to 16. Almost none, however, wanted to make decisions solely on their own: 97 per cent wanted to involve parents and 94 per cent physicians. See also: Chappuy H, Doz F, Blanche S, Gentet JC, and Tréluyer JM (2008) Children's views on their involvement in clinical research *Pediatric Blood & Cancer* **50(5)**: 1043-6: only two of the 29 young people (aged 16 and 18) taking part in the study said they made the research decision for themselves.

there is no pressure or urgency about taking part.[212] While one study found that children would have liked to be more involved in the decision than they were, few actually appeared to raise this with their parents or doctors.[213] However, research with children who have long-term conditions suggests that they are able to make informed and "wise" decisions in their own best interests and should be treated as "informed partners".[214] Similarly, children with chronic illnesses may be more knowledgeable about research concepts such as placebos than their healthy counterparts.[215] In contrast, children who suddenly become acutely ill or have just received a frightening diagnosis may, temporarily, be much less capable of taking part in decision-making than they are in their ordinary lives.[216]

2.31 These variations with respect to children's roles in decision-making were also expressed by children and young people who contributed to our evidence-gathering activities, when invited to consider what role in a (hypothetical) research decision they should have. They approached their involvement in participation decisions from three distinct perspectives:

> *"I think I should decide because it's my own risk."*[217]
>
> *"You should talk about it at home as they [parents] might have a good reason why you shouldn't take part in the research."*[218]
>
> *"If mummy and daddy say no I shouldn't do it."*[219]

Again, these differences in children's assumptions about their (hypothetical) decision-making role did not correlate directly with age: while some nine year olds felt strongly that they should decide alone, some sixth formers participating in our Youth REC film made clear they would be guided by their parents,[220] as did 17 and 18 year old students taking part in our school-based consultation in Kilifi, Kenya.[221]

2.32 In many cases, parents and children will both contribute in some way to a participation decision, with family dynamics and relationships determining how the final decision is

---

[212] Broome ME, Richards DJ, and Hall JM (2001) Children in research: the experience of ill children and adolescents *Journal of Family Nursing* **7(1)**: 32-49.

[213] Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83. All of the 37 children interviewed would have liked to have been involved in the decision about taking part in oncology research but 18 had no memory of being involved. Only four participants discussed increased decision-making roles with parents.

[214] See: Alderson P, Sutcliffe K, and Curtis K (2006) Children as partners with adults in their medical care *Archives of Disease in Childhood* **91(4)**: 300-3, which observed that children who have type 1 diabetes can, from around four years of age, begin to understand the principles of controlling diabetes, and can therefore make informed decisions.

[215] Cherrill J, Hudson H, Cocking C *et al.* (2010) Clinical trials: the viewpoint of children with a chronic illness compared with healthy children *Archives of Disease in Childhood* **95(3)**: 229-32.

[216] Nuffield Council on Bioethics (2014) *Factfinding meeting with members of PORT* (London, 18 December: Nuffield Council on Bioethics).

[217] Nuffield Council on Bioethics (25 November 2013) *Blog: what do you mean - ask children?!*, available at: http://blog.nuffieldbioethics.org/?p=907.

[218] Nuffield Council on Bioethics (2013) *Survey Monkey questionnaire: analysis of young people's responses* (London: Nuffield Council on Bioethics).

[219] Ibid.

[220] Nuffield Council on Bioethics (25 November 2013) *Blog: what do you mean - ask children?!*, available at: http://blog.nuffieldbioethics.org/?p=907; Nuffield Council on Bioethics (2014) *Be a part of it: what young people think of clinical research*, available at: http://www.youtube.com/watch?v=e2k6eA0dn9Q.

[221] Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

reached.[222] Practical challenges may arise, however, as to how initial information about the proposed study can best be shared between researchers, parents and children, in order to facilitate this approach. While the obvious approach may be to provide information to parents and children together in joint meetings with the researcher, this may sometimes cause difficulties for parents because they are unprepared for what will be said, and hence may be less able to support their child in absorbing the information. Thus, a *shared* approach to participation decisions might, in practice, actually undermine parents' ability to give emotional care to their children.[223] An alternative approach preferred by some parents is therefore for researchers to give them information about the study first, so that they can share it with their child in a way they feel most appropriate.[224] Some children and young people, on the other hand, have resisted this approach, saying they would prefer researchers to talk to them directly, rather than solely to their parents.[225] Moreover, as well as supporting how participation decisions are made, family relationships can also put pressure for decisions to be made in favour of a particular course of action. For example, for terminally ill children, an agreement to participate in research may stem from a desire to do as their family wishes.[226]

2.33 Even where children are not able to take an active part in the decision at all (for example, for research involving babies, or children who are too ill to communicate), the issue of shared decision-making may still arise with discussions both between parents, and with wider family and friends.[227] Some studies have found that, despite the consultative role of family and friends, final decisions about participation tend to be made by mothers,[228] although this can present particular challenges in more patrilineal societies where decision-making is traditionally seen as the father's role.[229] Some

[222] See, for example, Olechnowicz JQ, Eder M, Simon C, Zyzanski S, and Kodish E (2002) Assent observed: children's involvement in leukemia treatment and research discussions *Pediatrics* **109(5)**: 806-14; Snethen JA, Broome ME, Knafl K, Deatrick JA, and Angst DB (2006) Family patterns of decision-making in pediatric clinical trials *Research in Nursing & Health* **29(3)**: 223-32. While questions of gender did not emerge as an issue in the UK-based respondents to the Working Party's consultation, the consultation with students and community representatives in Kilifi, Kenya, highlighted how protective attitudes to girls increased, rather than decreased, as they matured: Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school students in Kilifi, Kenya* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

[223] Young B, Ward J, Salmon P *et al.* (2011) Parents' experiences of their children's presence in discussions with physicians about leukemia *Pediatrics* **127(5)**: e1230-e8, at e1235.

[224] Snethen JA, Broome ME, Knafl K, Deatrick JA, and Angst DB (2006) Family patterns of decision-making in pediatric clinical trials *Research in Nursing & Health* **29(3)**: 223-32.This view was also expressed by siblings of children enrolled in a clinical trial, for example: "I think it would have been better if the family would have told him what he had to go through and all that. I don't think he would have taken it so hard as he did when the doctors told him. That his parents actually told him, I don't know, you trust them I guess." See: Snethen JA, and Broome ME (2001) Children in research: the experiences of siblings in research is a family affair *Journal of Family Nursing* **7(1)**: 92-110, at page 101.

[225] Unguru Y, Sill AM, and Kamani N (2010) The experiences of children enrolled in pediatric oncology research: implications for assent *Pediatrics* **125(4)**: e876-e83, at e880.

[226] Hinds PS, Drew D, Oakes LL *et al.* (2005) End-of-life care preferences of pediatric patients with cancer *Journal of Clinical Oncology* **23(36)**: 9146-54 observed that two out of seven children with terminal cancer who enrolled in a clinical trial did so because their loved ones wanted them to, and concludes that decisions about end of life care are primarily based on relationships.

[227] See: Jollye S (2009) An exploratory study to determine how parents decide whether to enrol their infants into neonatal clinical trials *Journal of Neonatal Nursing* **15(1)**: 18-24, at page 21, which notes that, "apart from discussing the trials amongst themselves most parents discussed the trials with family and/or friends." This will vary depending on parental relationships and decision-making styles: see, for example, Thomas M, and Menon K (2012) Consenting to pediatric critical care research: understanding the perspective of parents *Dynamics* **24(3)**: 18-24, at page 20, which compared a parent's response that "we made the consensus together" to an observation that "even my husband doesn't really know what it [the research protocol] is. I just said it was a study in ICU. He never bothers with papers anyway."

[228] Jollye S (2009) An exploratory study to determine how parents decide whether to enrol their infants into neonatal clinical trials *Journal of Neonatal Nursing* **15(1)**: 18-24, at page 22. See also: McKenna K, Collier J, Hewitt M, and Blake H (2010) Parental involvement in paediatric cancer treatment decisions *European Journal of Cancer Care* **19(5)**: 621-30, at page 624; Miller VA, and Nelson RM (2012) Factors related to voluntary parental decision-making in pediatric oncology *Pediatrics* **129(5)**: 903-9.

[229] Jao I, Mwangome N, Davies A, Molyneux CS and Marsh V (2014) *Nuffield Council on Bioethics Working Party on ethical issues for research involving children: report on consultations with community representatives and secondary school*

parents would much prefer to leave the decision to doctors.[230] Knowing what other parents have, or would, decide in similar circumstances may also be very reassuring for parents faced with difficult participation decisions.[231]

Making decisions: the law and international guidance

The role of regulation

2.34 The first part of this chapter explored the empirical evidence available on how children, young people and parents experience the invitation to take part in clinical research, and the factors influencing their decision-making. The message that emerges strongly from this review is that the main influences on how children, young people and parents make decisions appear to be *situational*, depending heavily on the nature and context of the research, the situation of children or young people and their families, and the relationships they have with the researcher or research team. The question of *who* actually makes the decision, and the role of children and young people in cases where they are not the primary decision-maker, emerges relatively rarely in the published literature.

2.35 We now turn to the regulatory approaches with respect to the recruitment of children and young people into clinical research, which, by contrast, focus very much on the role and status of the decision-maker. A key protection for any research participant, found in both international statements on research ethics and in domestic legal requirements, is that participation should be *voluntary*: the free, informed, choice of the person concerned. For adults, this is usually achieved through a formal, active, process of consent.[232] The same requirement for consent applies when children and young people are being invited to take part in research; however the question then arises as to *who* provides that consent and, if not children or young people themselves, what part they may be expected to play in the decision. Below, we provide an overview of the stipulations of international ethical declarations, European law and guidance, and law and guidance within the UK with respect to:

- who gives consent;
- the role of children and young people in that process; and
- the provision of age-appropriate information for children and young people.

2.36 It is important to note that the notion of children and young people 'participating' in a decision-making process can be understood in very different ways. On the one hand

students in Kilifi, Kenya (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme). See also: Loue S, and Okello D (2000) Research bioethics in the Ugandan context II: procedural and substantive reform *The Journal of Law, Medicine & Ethics* **28(2)**: 165-73, at page 167.

[230] See: Jollye S (2009) An exploratory study to determine how parents decide whether to enrol their infants into neonatal clinical trials *Journal of Neonatal Nursing* **15(1)**: 18-24, at page 22. The role of doctors in participation decisions was also noted in Deatrick JA, Angst DB, and Moore C (2002) Parents' views of their children's participation in phase I oncology clinical trials *Journal of Pediatric Oncology Nursing* **19(4)**: 114-21, at page 118, where one parent noted: "What made it so hard for me is that I'm not a doctor, and he was so well-educated. He usually guides me well with decisions, but he couldn't tell me what to do here".

[231] See, for example, Eder ML, Yamokoski AD, Wittmann PW, and Kodish ED (2007) Improving informed consent: suggestions from parents of children with leukemia *Pediatrics* **119(4)**: e849-e59, at e854: "I think maybe having patients or parents actually talk to other parents who either went with the clinical study or didn't. I mean, it's good to talk to the doctors, but you want, like, a regular person's point of view."

[232] There may be exceptions to this approach where research involves the 'secondary' use of information collected for other purposes, although such uses are tightly regulated. See: General Medical Council (2009) *Confidentiality*, available at: http://www.gmc-uk.org/Confidentiality___English_0914.pdf_48902982.pdf, paragraphs 40-50.

children participating in a decision may be understood to mean that they have some, however small, part in the process: the decision is not simply made on their behalf or without their knowledge. On the other hand, participation may be understood much more actively as requiring that children's views are "taken note of and may be acted upon".[233] A requirement or recommendation that children participate in any decisions about taking part in research thus potentially captures a range of activity; from brief consultation, to giving children authority to make those decisions entirely for themselves. Full authority may not, however, always be desired. Related research in English schools exploring children's understanding of what 'children's rights' should involve, for example, found that most children interviewed conceptualised these as being respected and trusted, or as 'having a say' in decisions that affect them, but not necessarily as making these decisions on their own.[234] Similar views with respect to their roles in decision-making about research were expressed by children and young people who took part in our Youth REC workshops.[235]

International declarations and guidance

2.37 The **Declaration of Helsinki**, first developed by the World Medical Association in 1964 and now in its ninth revision,[236] is probably the best known and most influential international statement on the ethical principles that should be applied in "medical research involving human subjects".[237] On the question of consent to research participation, the Declaration is very clear that "participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees."[238] Where a potential research participant is *not* capable of giving their own consent, the Declaration requires consent instead to be sought from "the legally authorised representative". It further specifies that "when a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorised representative. The potential subject's dissent should be respected."[239]

2.38 No specific reference is made in the Declaration to 'children' or 'minors': the only distinction made is between those capable, or incapable, of giving consent. It is, therefore, silent both on the extent to which children may be considered capable of giving informed consent for themselves, and on the role of parents, though parents' role as the "legally authorised representative" of their children may be implied. The

[233] Boyden J, and Ennew J (1997) *Children in focus: a manual for participatory research with children* (Stockholm: Radda Barnen), at page 33. See also Suzanne Uniacke's distinction between "consideration respect" and "compliance respect": Uniacke S (2013) Respect for autonomy in medical ethics, in *Reading Onora O'Neill*, Archard D, Deveaux M, Manson N, and Weinstock D (Editors) (London: Routledge).

[234] Morrow V (1999) 'We are people too': children's and young people's perspectives on children's rights and decision-making in England *The International Journal of Children's Rights* **7(2)**: 149-70.

[235] Spencer G, Boddy J, and Rees R (2014) *"What we think about what adults think": children and young people's perspectives on ethics review of clinical research with children* (London: Nuffield Council on Bioethics). See also the Introduction for a description of this project.

[236] Including seven substantive revisions and two 'notes of clarification' in 2002 and 2004. The most recent revision dates from October 2013. See: World Medical Association (2013) *WMA Declaration of Helsinki - ethical principles for medical research involving human subjects*, available at: http://www.wma.net/en/30publications/10policies/b3/index.html.

[237] The term 'research subject' is used throughout the Declaration of Helsinki, and also in some other declarations and regulations. For the reasons discussed in Chapter 1, we prefer to use the term 'research participant', other than when directly quoting from other sources.

[238] World Medical Association (2013) *WMA Declaration of Helsinki - ethical principles for medical research involving human subjects*, available at: http://www.wma.net/en/30publications/10policies/b3/index.html, at paragraph 25.

[239] Ibid., paragraphs 28-9.

Declaration further gives no indication as to the threshold of understanding required for assent to be sought, leaving open how the concept of assent might be understood.

2.39 Guidance issued in 2002 (under revision at the time of writing)[240] by the Council for the International Organizations of Medical Sciences (**CIOMS**) in association with the World Health Organization (WHO), by contrast, includes a separate guideline on children as research participants.[241] Guideline 14 specifies that research with children may only go ahead if "a parent or legal representative of each child has given permission", and if "the agreement (assent) of each child has been obtained to the extent of the child's capabilities". A child's refusal to participate or continue in the research should be respected.

2.40 These headline principles are discussed further in CIOMS' commentary on the guideline, where it is noted that the age at which children become legally competent to give consent differs substantially between jurisdictions, and that many children who have not reached the relevant age for their jurisdiction can still understand the implications of informed consent and "knowingly agree" to take part. The term 'assent' is used to refer to this 'knowing agreement', and hence younger children who are not able to provide such agreement are, by implication, not regarded by CIOMS as capable of giving assent, although the commentary states that "the willing cooperation of the child" should be sought. The 'deliberate objection' of children of any age should always be respected unless they need treatment that is not available outside the context of research. The commentary on the guideline further suggests that, while children over 12 or 13 may usually be capable of understanding what is required for informed consent, their agreement (described as "consent (assent)") should usually be complemented by parental permission, even if local law does not require this.

2.41 In general, the CIOMS guideline thus requires the agreement of both parent and child where older children are being invited to participate in research, while encouraging the willing cooperation of younger children, and recognising their right to object.[242] However, the commentary also highlights that, for some forms of research (such as research among adolescents regarding sexuality or use of illegal drugs, or research concerning domestic violence or child abuse), it may be appropriate for ethics committees to waive the need for parental permission. It also recognises that, in some countries, children may be deemed 'emancipated' before the age at which their domestic law would generally recognise adulthood: for example, because they are married, already parents, or living independently, and may hence be able to consent without the permission, or even knowledge, of their parents.

The law and guidance in Europe

2.42 Within the European Union, for the past decade, the **Clinical Trials Directive** of 2001 has set requirements for the conduct of clinical trials of investigational medicinal products which all member states are required to transpose into their national laws

[240] See: CIOMS (2013) *CIOMS Working Group on the revision of the 2002 CIOMS Ethical Guidelines for Biomedical Research*, available at: http://www.cioms.ch/index.php/12-newsflash/232-cioms-working-group-of-the-revision-of-the-2002-cioms-ethical-guidelines-for-biomedical-research.

[241] CIOMS (2002) *International ethical guidelines for biomedical research involving human subjects*, available at: http://www.cioms.ch/publications/layout_guide2002.pdf, Guideline 14.

[242] By implication the CIOMS guidance would see the threshold between being 'older' or 'younger' as around 12, but measured in terms of understanding rather than necessarily chronological age.

(see paragraph 2.51 on implementation in the UK).[243] While, at the time of writing, the Directive is still in force, it is due to be superseded by the **Clinical Trials Regulation** which was adopted in April 2014 and is likely to become effective in 2016 (see paragraph 2.46). There are no European Union requirements with respect to other forms of clinical research with children and young people, and hence the requirements summarised below apply only to the minority of research studies that relate to 'investigational medicinal products' such as new medicines and vaccines.

2.43 Article 4 of the 2001 Directive specifies that trials involving minors may only be undertaken if the consent of the parents or a legal representative has been obtained. The Directive leaves the definition of 'minor' to national governments to determine, although the EU Paediatric Regulation (see paragraph 3.12) defines the paediatric population as encompassing those under 18. Many European countries, although not the UK, similarly interpret minors as being under 18.[244] The term 'assent' is not used in the Directive, but it is specified that the parent's consent "must represent the minor's presumed will". Minors must also receive information, appropriate to their ability to understand, from staff with paediatric experience regarding the trial, its risks and its benefits. The explicit wish of minors, who are capable of forming an opinion and assessing this information, to refuse participation or to withdraw from the trial must be "considered" by the investigator. Thus the Directive emphasises the importance of children and young people receiving appropriate *information* about the trial, but is silent with respect to the role they could or should play in the actual decision about research participation.

2.44 The European Commission has published additional **guidance**, produced by an *ad hoc* working group, on the ethical considerations that should be taken into account with respect to the Directive.[245] This guidance notes that the Directive itself does not use the term 'assent', but that the term does appear in the Declaration of Helsinki. The guidance attempts to provide a bridge between the Directive and the Declaration by specifying that it will use the term 'assent' to mean "the expression of the minor's will to participate", thus referring back to the requirement in the Directive that a parent's consent should "represent the minor's presumed will". It goes on to emphasise the importance of children participating in the consent process with their parents wherever appropriate, and specifies that researchers should provide age appropriate information, and give families enough time to make their decision.

2.45 The guidance further notes how "some authors"[246] use the term "knowing agreement" to "reflect the outcome of the process of providing age appropriate information, obtaining assent, and whenever possible obtaining written confirmation from the child".[247] However, it goes on to use the term 'assent' in a very different sense from the CIOMS guidance. CIOMS uses the terms 'assent' and 'knowing agreement' with reference to young people who are legally minors within their own jurisdiction but nevertheless able to understand the implications of informed consent (see paragraph 2.40). However, the European Commission guidance suggests that, in some cases,

[243] Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
[244] European Commission (2008) European Union ethical considerations for clinical trials on medicinal products conducted with the paediatric population *European Journal of Health Law* **15(2)**: 223-50, at paragraph 5.4.
[245] European Commission (2008) *Ethical considerations for clinical trials on medicinal products conducted with the paediatric population*, available at: ftp://ftp.cordis.europa.eu/pub/fp7/docs/ethical-considerations-paediatrics_en.pdf.
[246] The document does not specify which authors are being referred to here, but it seems likely that this is a reference back to the CIOMS guidance.
[247] European Commission (2008) *Ethical considerations for clinical trials on medicinal products conducted with the paediatric population*, available at: ftp://ftp.cordis.europa.eu/pub/fp7/docs/ethical-considerations-paediatrics_en.pdf, at paragraph 5.7.

assent may be obtained from children as young as three who have "the emergent capacity to agree".[248] The guidance further firmly recommends that assent should be obtained in writing as soon as children have reached school age and are able to read and write. We summarise these very different understandings of what assent might involve in Box 2.3 below on pages 60-1 after our discussion of the law in the UK.

2.46 The **Clinical Trials Regulation**, which repeals and replaces the Clinical Trials Directive, was adopted on 16 April 2014, and is due to become effective at some point after 28 May 2016, once the necessary new systems have been put into place.[249] Unlike Directives (which member states transpose into their own legal systems), Regulations have 'direct effect', and so the text of the Clinical Trials Regulation will automatically become law in all EU countries as soon as it comes into force, without further interpretation. However, the regulatory structure established by the Clinical Trials Regulation falls into two parts: Part I of an application to carry out a clinical trial will be handled by any one member state on behalf of all member states (and the assessment by this 'receiving' member state will be binding on all others); while Part II of the application must be submitted to each individual member state where the research will be taking place (see paragraphs 3.53 and 3.61 for other requirements set out in the Regulation). Detailed requirements for consent fall within this second category, and hence may differ between EU countries, although the Regulation itself sets out various minimum requirements.

2.47 The Regulation follows the example of the Directive in deferring to individual member states to define 'minors', thus leaving intact the present scope for difference across the EU as to the age at which young people are treated as legally competent to make their own decisions about research.[250] The requirement for informed consent from research participants should, in the case of minors, be understood as "an authorisation or agreement from their legally designated representative" (presumably usually a parent).[251] The Regulation also sets requirements regarding the information that both children and their legally designated representatives should be given about the proposed research, notwithstanding the provision for more specific requirements by individual member states. Thus:

- information for the participant or for the legally designated representative must "be kept comprehensive, concise, clear, relevant and understandable to a lay person";[252] and

[248] Ibid., at paragraph 7.1.2.

[249] European Parliament and Council of the European Union (2014) *Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*, available at: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN, Articles 83 and 99. See also: Lexology (11 August 2014) *Clinical trials - greater transparency and uniformity across Europe*, available at: http://www.lexology.com/library/detail.aspx?g=0902d376-0c4e-443f-8100-527099b69ff3 for a useful summary of the provisions of the Regulation.

[250] European Parliament and Council of the European Union (2014) *Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*, available at: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN, Article 2(18): "'Minor' means a subject who is, according to the law of the Member State concerned, under the age of legal competence to give informed consent."

[251] Ibid., Article 2(21) (in definitions) and Article 32(1)(a) (requirement for such consent). No direct reference to parents is made in the Regulation.

[252] Ibid., Article 29(2)(b). The requirement that the information should be 'comprehensive' was added in as a later amendment to the Article.

- minors must receive information about the study "in a way adapted to their age and mental maturity and from investigators or members of the investigating team who are trained or experienced in working with children".[253]

2.48 Similarly, the Regulation sets out minimum requirements with respect to the way in which minors should be involved in a decision to take part (or not take part) in research, while also leaving scope for variation in approach between member states:

- a minor should "take part in the informed consent procedure in a way adapted to his or her age and mental maturity";[254]
- it is open for national laws to specify that "a minor who is capable of forming an opinion and assessing the information given to him or her, shall also assent in order to participate in a clinical trial";[255] and
- "the explicit wish of a minor who is capable of forming an opinion and assessing the information" provided to refuse participation in, or to withdraw from, the clinical trial at any time, should be "respected" by the investigator.[256]

2.49 As the summary above indicates, there are a number of significant differences between the 2001 Directive and the 2014 Regulation, even without considering the scope for individual member states to make their own (additional) requirements with respect to both consent and assent processes (see Table 2.1 below). The Regulation specifically requires that children and young people should "take part" in the consent process, as well as retaining the earlier requirement to ensure that age-appropriate information is provided by professionals with the necessary skills. The opaque reference in the 2001 Directive to parental consent reflecting their child's "presumed will" has disappeared. Parents (or other legal representatives) are described as providing "authorisation" or "agreement" rather than 'informed consent', drawing attention to the significant difference between a person consenting to a procedure for themselves, and authorising that procedure on another person. Finally, the role of the child (albeit restricted to one "capable of forming an opinion and assessing the information") in determining their involvement in research is significantly strengthened: the wish of such a child should be "respected" rather than simply "considered".

Table 2.1: Comparing the Clinical Trials Directive and Clinical Trials Regulation

	2001 Directive	**2014 Regulation**
Definition of minor?	Depends on member state	Depends on member state
Information for minors?	Yes, appropriate to age of child, from skilled professional	Yes, appropriate to age of child, from skilled professional
Minors take part in consent process?	Not specified	Yes, in a way adapted to their age and maturity
Reference to assent	None	Member state may require
Dissent of minors able to form an opinion	To be 'considered' by investigator	To be 'respected' by investigator

[253] Ibid., Article 32(1)(b).
[254] Ibid., Article 32(2).
[255] Ibid., Article 29(8).
[256] Ibid., Article 32(1)(c).

2.50 Finally, many European states (both members and non-members of the EU) are signatories to the Council of Europe's Convention on Human Rights and Biomedicine, generally known as the **Oviedo Convention**.[257] Many European researchers are thus also bound by the provisions of the Convention and its additional protocol concerning biomedical research.[258] The Convention follows the example of the Declaration of Helsinki in that it implicitly includes children and young people within a general category of "persons not able to consent to research", without reference to the threshold at which children might be regarded as able to consent for themselves. Consent should be sought from a "legal representative" or from "an authority, person or body provided for by law".[259] However, the Convention differs from the Declaration of Helsinki in making specific reference to 'minors' when specifying how those deemed unable to consent should be involved in the decision about taking part in research. Recognising the developmental nature of childhood, it requires that "the opinion of a minor shall be taken into consideration as an increasingly determining factor in proportion to age and degree of maturity".[260]

The law in the UK

Clinical trials

2.51 The law relating to the role of children in making decisions about research involvement in the UK differs, depending on whether the research in question is a "clinical trial of an investigational medicinal product", and hence subject to the EU rules described above. Where the research falls into this category, it is currently governed by the 2004 *Clinical Trial Regulations* which apply across the UK, and age is the deciding factor.[261] **Young people aged 16 or above** are regarded as adults and are entitled to give or withhold consent for themselves. Their parents are not given any special role: if 16 or 17 year olds lack capacity to make the decision for themselves, they are treated on the same basis as adults without capacity, and consent must be sought from a legal representative (who may be, but need not be, their parent). Where **children aged under 16** are invited to take part in a clinical trial governed by the Regulations, consent must be sought from a parent, and children's own consent will not be legally valid, regardless of how capable they are of understanding and weighing the issues at stake. While these 2004 Regulations will require revision once the 2014 EU Clinical Trials Regulation comes into force, individual EU member states will retain their entitlement to define the age of majority and to specify the manner in which children should be involved in the decision to participate in research (see paragraphs 2.46 to 2.48).

[257] Council of Europe (1997) *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, available at: http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm. The UK, however, is not a signatory.

[258] Council of Europe (2005) *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, available at: http://conventions.coe.int/Treaty/en/Treaties/Html/195.htm. The UK, however, is not a signatory to the Convention.

[259] Ibid., Article 15(1)(iv).

[260] Council of Europe (1997) *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, available at: http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm, Article 6(2).

[261] The Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1031, as amended. Note that these Regulations implement the provisions of the 2001 Clinical Trials Directive (in addition to other functions relating to medicines safety), and that therefore some of the provisions will be superseded once the Clinical Trials Regulation comes into force.

Research other than clinical trials: England and Wales

2.52 For research that does not constitute a clinical trial of an investigational medicinal product (and in practice, most clinical research comes into this second category[262]), the legal position in the UK is much less clear. In England and Wales, under the Mental Capacity Act 2005, **young people aged 16 and 17** are treated as adults and presumed to have capacity to make their own decisions unless the opposite is demonstrated.[263] This would include the decision to participate in clinical research. Similarly, the Family Law Reform Act 1969 makes clear that 16 and 17 year olds with capacity can provide their own, legally valid, consent to their own medical *treatment*, although the Act is silent on the (distinct) question of consent to clinical research.[264] However, under the common law in England and Wales, parents do not lose their power to give consent to treatment on behalf of their children until the latter reach the age of 18: parents' and children's powers to consent thus coexist up to that point. If a 16 or 17 year old refused to consent to treatment, a valid consent could potentially still be obtained from their parents, or from a court, if treatment was held to be in their best interests.[265] When considering such a case, courts would take account of the welfare principle and statutory 'welfare checklist' set out in the Children Act 1989[266] and the provisions of the Human Rights Act 1998.

2.53 Returning to the question of consent to research, then, while the provisions of the Mental Capacity Act offer assurance to young people and health professionals that consent from a 16 or 17 year old to take part in clinical research is legally valid, it remains unclear whether a young person's *refusal* to participate in research could be overridden by their parents or by a court. In practice, however, it seems highly unlikely that a 16 or 17 year old would be compelled to take part in research against their will, unless the research in question represented the only way of accessing a particular experimental treatment that was strongly believed to be the best option for the young person's condition, and a court agreed. In such a case, the decision would effectively relate to the young person's treatment, with the research element being viewed as peripheral.[267]

---

[262] 17 per cent (820 out of 4,832) of applications to RECs in England from April 2013 to March 2014 were for clinical trials of investigational medicinal products.See: Health Research Authority (2014) *Health Research Authority annual reports and accounts for the year to 31 March 2014*, available at: http://www.hra.nhs.uk/documents/2014/07/annual-report-2013-2014.pdf, at page 89.

[263] The Mental Capacity Act (MCA) 2005 applies to those over 16 (section 2(5)), and capacity is presumed unless there is evidence otherwise (s 1(2)). Under the Act, a person is held to have capacity if they can understand, retain, and use or weigh information relevant to the decision, and communicate that decision (sections 2(1) and 3(1)). If a 16 or 17 year old is deemed to lack capacity under the MCA 2005 then other provisions of the Act must be met in order for them to be involved in 'intrusive research', including that the research is approved by the appropriate body and their carers are 'consulted' (section 30). For young people under 18, this may include those with parental responsibility for them. The MCA covers England and Wales.

[264] Family Law Reform Act (FLRA) 1969, section 8(1).

[265] Re W (a minor) (medical treatment: court's jurisdiction) [1993] 1 FLR 1; Re R (a minor) (wardship: medical treatment) [1992] 1 FLR 190. These cases have been the subject of considerable academic debate: see, for example, Gilmore S, and Herring J (2011) No is the hardest word: consent and children's autonomy *Child & Family Law Quarterly* **23(1)**: 3-25; Cave E, and Wallbank J (2012) Minors' capacity to refuse treatment: a reply to Gilmore and Herring *Medical Law Review* **20(3)**: 423-49; Gilmore S, and Herring J (2012) Children's refusal of treatment: the debate continues *Family Law* **42(8)**: 973-8. For a recent defence of the 'asymmetry' between entitlement to consent and refuse, see: Manson N (2014) Transitional paternalism: how shared normative powers give rise to the asymmetry of adolescent consent and refusal *Bioethics* **29(2)**: 66-73.

[266] The welfare principle is set out in section 1(1), and the checklist in section 1(3) of the Children Act 1989. These must be applied when making an order under section 8 of the Act, one way in which courts could get involved in decisions about medical treatment or research with children. In deciding whether to make an order, a number of considerations must be taken into account, including "the ascertainable wishes and feelings of the child concerned" (section 1(3)(a)).

[267] See, for example, Simms v. Simms and another; PA v. JA and another [2002] EWHC 2734, where the English High Court granted a declaration that it was lawful and in their best interests for two young people (16 and 18 years old) suffering from probable variant Creutzfeld-Jakob disease to receive a 'treatment' (Pentosan Polysulphate (PPS)) which had not yet been clinically tested, and where its effects on CJD were unknown. In the judgment, PPS was viewed as 'pioneering treatment',

2.54 For **children under the age of 16** who lack the capacity to decide for themselves whether or not to take part in a particular research study, the law is clear: consent can be given, or withheld, by those with parental responsibility for them. In general, consent is only required from one person with parental responsibility, and researchers would not ordinarily be required to obtain consent from both parents.[268] However, the courts have defined a "small group of important decisions" that should not be taken by one parent against the wishes of another, including immunisation and non-therapeutic male circumcision.[269] If a child's parents actively disagreed with each other with respect to their child's involvement in research, researchers might hesitate to proceed on the basis of the consent of just one parent unless authorised by a court to do so.

2.55 Where children are under 16 but *do* have the capacity to decide for themselves whether they wish to take part in a particular research project, a further degree of uncertainty exists. Case law has established that children who have "sufficient understanding and intelligence to enable them to understand fully what is proposed" (often described as 'Gillick competent' children) may provide a legally-valid consent for their own *treatment*.[270] However, there is no case law on whether or not the concept of Gillick competence should also be applied to research decisions. Hence, in practice, researchers are likely to request parental consent in addition to the consent of children under 16, however capable they may appear to be of making their own decision about whether to take part in the research.[271] Guidance issued by the UK's Royal College of Paediatrics and Child Health (RCPCH) in 2014 reiterated this position as follows: "As there is no direct case or statute law in the UK covering non-clinical trial research, it has been presumed that the test of Gillick competence applies. In most instances, the child's assent or consent should be underpinned by parent consent, but this can be problematic where sensitive subjects, such as sexual health, contraception, and adolescent behavioural studies are involved, and there is a duty to preserve confidentiality. In such cases, the need for parental assent or consent should be carefully considered."[272]

---

rather than as an offer to be involved in clinical research. However, the judgment included reference to the fact that the young people concerned were not competent to consent. It is unclear what approach the court would have taken if the young people had been competent and had withheld their consent. For discussion of this decision, see: Fovargue S (2013) The (ab)use of those with no other hope? *Cambridge Quarterly of Healthcare Ethics* **22(2)**: 181-91.

[268] Department of Health (2009) *Reference guide to consent for examination or treatment: second edition*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/138296/dh_103653__1_.pdf, chapter 3, paragraphs 23 and 28.

[269] Re J (child's religious upbringing and circumcision) [1999] 2 FLR 678 and Re B (a child) [2003] EWCA Civ 1148.

[270] Gillick v. West Norfolk and Wisbech Area Health Authority [1986] 1 AC 112 (House of Lords decision). As in the case of 16 and 17 year olds, parents retain concurrent powers to consent until their child reaches the age of 18, and so may potentially override the refusal of a Gillick-competent child, based on their perception of their child's 'best interests': see Re R (A Minor: Wardship Consent to Treatment) [1991] 3 WLR 592. It is, however, emphasised in *Gillick* that practitioners should do their best to persuade children to inform and involve their parents, implying that such involvement is the optimum approach.

[271] See, for example, guidance from the British Medical Association that "parental consent may also be required, even if the child is competent": British Medical Association (2010) *Children and young people tool kit*, available at: http://bma.org.uk/-/media/files/pdfs/practical%20advice%20at%20work/ethics/children%20and%20young%20people%20toolkit/childrenyoungpeopletoolkit_full.pdf, at page 53. The Medical Research Council similarly encourages "parental involvement" in the decision: Medical Research Council (2004) *MRC ethics guide: medical research involving children*, available at: http://www.mrc.ac.uk/documents/pdf/medical-research-involving-children/, at page 23. The General Medical Council takes a more tentative approach, suggesting "if they are able to consent for themselves, you should still consider involving their parents, depending on the nature of the research": General Medical Council (2007) *0-18 years guidance*, available at: http://www.gmc-uk.org/static/documents/content/0-18_0510.pdf, at paragraph 38.

[272] Modi N, Vohra J, Preston J *et al.* (2014) Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees *Archives of Disease in Childhood* **99(10)**: 887-91. The question of the confidentiality owed to minors who do not wish to involve their parents in aspects of their healthcare has been further considered in the case of R (on the application of Axon) v. Secretary for State for Health and Another [2006] EWHC 37.

Research other than clinical trials: Scotland

2.56 In Scotland, young people are formally treated as adults from the age of 16, and parental rights and responsibilities cease at this point.[273] The law is therefore clear that when young people aged 16 or 17 are invited to take part in research, consent must be sought from them, and not from their parents. Children and young people under the age of 16 who are judged to have the capacity to make their own decisions about *treatment* may also provide a legally valid consent for themselves.[274] However, as in England and Wales, the law is silent on whether this provision also applies to decisions about *research*, and as the RCPCH guidance cited above suggests, it is therefore usual practice additionally to obtain parental consent.

Research other than clinical trials: Northern Ireland

2.57 In Northern Ireland, pending the enactment of mental capacity legislation (under consultation at the time of writing), the Age of Majority Act 1969 specifically enables 16 and 17 year olds to provide valid consent to their own treatment, but is silent on the question of research. However, guidance issued by the Department of Health, Social Services and Public Safety suggests that the standard of Gillick competence may be used to permit young people aged 16 and 17 to consent for themselves to research. The same standard should be used to enable children under 16 to consent to research for themselves where they have the capacity to do so, although parental involvement should always be encouraged.[275] As in England and Wales, parental powers to provide consent continue until their children reach the age of 18, and may coexist with their children's powers (see paragraphs 2.52-2.53).

Examples from other jurisdictions

2.58 Given the extent of cultural diversity with respect to perceptions of childhood (see paragraph 1.15), it is unsurprising that there is considerable variation between jurisdictions, both with respect to the general age of majority, and to specific legislative provisions enabling minors to provide consent in particular circumstances. Examples in Box 2.2 provide an indication of that diversity.

Box 2.2: Diverse approaches to consent for children and young people

In **Finland**, young people aged 15 and over can provide consent for research themselves, as long as the research is likely to be of direct benefit to their health. If no direct benefit is expected, then parental consent is required up to the age of 18.[276] In **Norway**, parental consent is required for young people up to the age of 18 for research that involves bodily intervention or medicinal products. However, the Norwegian Ministry of Health has the power to pass regulations to enable children to consent for themselves

[273] Age of Legal Capacity (Scotland) Act 1991, section 1; Children (Scotland) Act 1995, sections 1 and 2.
[274] Age of Legal Capacity (Scotland) Act 1991, section 2(4).
[275] Department of Health, Social Services and Public Safety (2003) *Reference guide to consent for examination, treatment or care*, available at: http://www.dhsspsni.gov.uk/consent-referenceguide.pdf, Chapter 3, paragraphs 2.2 and 3.1.
[276] Finnish Medical Research Act 1999, section 8. See also: European Forum for Good Clinical Practice (2012) *The EFGCP report on the procedure for ethical review of protocols for clinical research projects in Europe and beyond: question 33 - how is informed consent obtained from vulnerable subjects who are potentially to be involved in a clinical trial?*, available at: http://www.efgcp.eu/Downloads/EFGCPReportFiles/EFGCP%20ECs%20Report%202012%20-%20Question%2033%20Updated.pdf.

from the age of 12 for research involving their personal health data.[277] In **Sweden**, if young people "realise what the research entails" they may consent for themselves to any form of research from the age of 15.[278]

In **Singapore**, by contrast, consent to participate in a clinical trial must be obtained from a parent or guardian until a young person reaches the age of 21, unless they are already married. Consent must also be sought from children and young people themselves if they have sufficient understanding.[279] Draft legislation covering all forms of biomedical research will, if enacted, require consent to be given by both a young person (where they have sufficient understanding of what is involved) and at least one parent, until young people reach the age of 21. However institutional review boards will be authorised, in limited circumstances, to waive the consent of parents, where young people have the understanding to consent for themselves.[280]

In **Kenya**, the KEMRI Ethics Review Committee currently advises that children and young people up to the age of 18 years (the age of legal majority) should only be involved in research with consent from at least one parent. There are, however, exceptions. A category of young people described as mature minors (understood as individuals under the age of 18 who are "married, pregnant, a mother or a household head") may give consent for themselves and for their children, but not for their siblings. For research involving greater than minimal risk and where there is no direct benefit to the individual, it is advised that both parents consent.[281]

Regulatory approach to the role of children and young people

2.59 The sections above summarise a number of regulatory requirements (whether international or domestic, legally-binding or professional good practice advice) with respect to the recruitment of children and young people into clinical research. As will be clear, the general underpinning assumption is that, until the young person reaches the age specified by law[282] in their own country, consent to participate in research will be required from a parent or other legally designated representative. However, there may be added complexities, as found, for example, in the law of England and Wales which recognises the age of 16 for young people to consent for themselves in many matters, while retaining coexisting parental entitlements in some circumstances to make decisions on behalf of their children up to the age of 18. English case law has also

[277] Norwegian Act on Medical and Health Research (the Health Research Act), section 17. See: University of Oslo Library (2008) *Act 2008-06-20 no. 44: Act on Medical and Health Research (the Health Research Act)* available at: http://www.ub.uio.no/ujur/ulovdata/lov-20080620-044-eng.pdf.

[278] Nordforsk (2014) *Legislation on biotechnology in the Nordic countries: an overview*, available at: http://www.nordforsk.org/en/publications/publications_container/legislation-on-biotechnology-in-the-nordic-countries-2013-an-overview-2014; section 18 of The Act Concerning the Ethical Review of Research Involving Humans (2003) (Sweden) (see: Central Ethical Review Board (Sweden) (2003) *The Act Concerning the Ethical Review of Research Involving Humans*, available at: http://www.epn.se/media/75686/the_ethical_review_act.pdf).

[279] Singaporean Medicines (Clinical Trials) Regulations, section 11. See: Singapore Statutes Online (2000) *Singaporean Medicines (Clinical Trials) Regulations*, available at: http://statutes.agc.gov.sg/aol/search/display/view.w3p;page=0;query=DocId%3A%2230491174-f2a3-49ef-9fee-d989473cabac%22%20Status%3Ainforce%20Depth%3A0;rec=0.

[280] Human Biomedical Research Bill (2014), section 8. See: Ministry of Health Singapore (2014) *Human Biomedical Research Bill*, available at: https://www.moh.gov.sg/content/dam/moh_web/PressRoom/Press%20releases/Press%20Release%20Annex%20A%20-%20Human%20Biomedical%20Research%20Bill%20-%20Draft%20for%20Public%20Consultation%20-%20November%202014.pdf.

[281] KEMRI Wellcome Trust Research Programme (2009) *SOP 7: review of the informed consent process and document* (Kilifi, Kenya: KEMRI Wellcome Trust Research Programme).

[282] This may either be a general age of majority, or a lower age specifically designated with respect for consent.

developed the concept of competence to consent to treatment (and arguably also to research) based on children's maturity and ability to understand what is required, even where they have not yet reached the age of 16. Such an approach is, by definition, decision-specific, since decisions about different forms of research, in different circumstances, may make very different demands on a child's intellectual abilities or emotional maturity.

2.60 As we note in paragraph 2.36, however, the question of 'who decides' whether children and young people take part in research clearly extends well beyond the question of who is legally entitled to *authorise* participation. Each of the regulatory instruments described above makes some reference to the extent to which children and young people should themselves be involved in that decision. Most cite the need for age-appropriate information to be provided by skilled professionals so that children can be helped to understand what the research entails. In some cases it is clearly spelled out that children and young people should be involved, to the extent appropriate to their age and level of understanding, in making the decision about taking part in research. However, despite this broad consensus on the value to be placed on including children and young people in the decision-making process, there is considerable variation in interpretation, in particular with respect to the use of the term 'assent'. As Box 2.3 demonstrates, the term is used to mean anything from the "emergent capacity to agree" of a three year old, to the "knowing agreement" of a young person able to understand what the research is entitled, and only prevented by age from providing a legally-valid consent.

Box 2.3: Requirements for 'assent'

The term 'assent' is used widely within both international statements on research ethics, and in domestic legislation. However, there is no consensus on how the term should be used:

- The **Declaration of Helsinki** requires researchers to obtain assent from potential research participants who are deemed "incapable of giving informed consent" but "able to give assent". No further detail is given as to what 'giving assent' might mean, or the capacities required to give it.
- The **CIOMS/WHO guidelines** use the term assent to refer to the "knowing agreement" of children "who have not yet reached the legally established age of consent" but who "can understand the implications of informed consent and go through the necessary procedures." By implication, the capacities required for giving assent are the same as those for consent: the only difference is that in the case of assent, domestic law does not recognise the child as legally competent, regardless of the level of their understanding. It is suggested that children over the age of 12 or 13 years of age will usually fall into this category.
- The **EU Commission guidance on the 2001 Clinical Trials Directive** defines assent as "the expression of the minor's will to participate", and suggests that assent may be obtained from children as young as three who have "the emergent capacity to agree". The guidance further firmly recommends that assent should be obtained in writing as soon as children reach school age and are able to read and write.
- The 2014 EU **Clinical Trials Regulation** makes no binding requirements with respect to assent, but leaves it open for national laws to specify that "a minor who is capable of forming an opinion and assessing the information given to him or her, shall also assent in order to participate in a clinical trial". No further detail is given as to how assent should be understood.

- The 2014 guidance issued by the UK **Royal College of Paediatrics and Child Health** defines assent as "the child's active affirmative agreement", and states that it should be sought from the age of seven.
- The 2001 EU **Clinical Trials Directive**, the Council of Europe's **Oviedo Convention** and the 2004 **UK Clinical Trials Regulations** do not use the term 'assent' at all.

2.61 There is further variation in approach with respect to the relevance of children's dissent or "explicit wish... to refuse participation".[283] The 2001 EU Clinical Trials Directive requires only that such a wish be "considered", while the replacement 2014 EU Regulation takes a stronger line in specifying that it should be "respected". In both cases, however, this requirement only appears to apply to "a minor who is capable of forming an opinion and assessing the information provided", thus implying an older child. The CIOMS guidance, in comparison, takes the view that the "deliberate objection" of young children to take part in research should be respected, unless this would be detrimental to their own health. The RCPCH guidance notes that, while in the UK it might be lawful to go ahead on the basis of parental consent against the wishes of a child, researchers should not do so.[284]

Box 2.4: Dissent

- The 2001 EU Clinical Trials Directive requires that the explicit wish of a minor who is capable of forming an opinion and assessing this information to refuse participation should be 'considered'.
- The 2014 EU Regulation specifies that the explicit wish of a minor who is capable of forming an opinion and assessing the relevant information to refuse participation should be 'respected'.
- The CIOMS guidance states that the 'deliberate objection' of young children to take part in research should be respected, unless this would be detrimental to their own health.
- The RCPCH guidance notes that, while in the UK it might be lawful to go ahead on the basis of parental consent against the wishes of a child, researchers should not do so.

2.62 Finally, there is a general lack of clarity as to what professionals should do if children neither assent nor dissent: some instruments, for example, require professionals to 'seek' assent (implicitly focusing on the process rather than the outcome), while others specify that assent should be 'obtained'. The RCPCH guidance is firm in stating that assent should be understood as "active affirmative agreement", and that "lack of objection should not be construed as assent".[285] It is far from clear, however, how a "lack of objection" should be handled by researchers. There would appear to be a significant distinction between such lack of objection and the "explicit wish not to participate" described above. We return in Chapter 6 (see paragraphs 6.4–6.13) to our

[283] The European Parliament and the Council of the European Union (2001) *Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use*, available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF, Article 4(c).
[284] Modi N, Vohra J, Preston J *et al.* (2014) Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees *Archives of Disease in Childhood* **99(10)**: 887-91, at page 888.
[285] Ibid., at page 888.

own view on how the concepts of assent and dissent should be understood, and the practical implications for children's involvement in decisions about taking part in research.

Comparisons from policy areas outside healthcare

2.63 We commented in Chapter 1 that many of the assumptions underlying the way children's participation in research is regulated seem at odds with approaches to children's lives *outside* the research setting (see paragraph 1.25). We have noted, for example, that in many countries, children who are thought too young to make decisions about being involved in research for themselves, are nonetheless expected to take on potentially much more onerous responsibilities: for example, with respect to caring for younger siblings (see paragraph 1.15) or by working to help support their family.[286] The age of criminal responsibility also provides an interesting point of comparison: in England and Wales, for example, it is currently set at age ten and in Scotland at age eight.[287] Young children in the UK are thus deemed capable, in the context of criminal behaviour, of assuming a level of responsibility with respect to their own actions at a time when it is implicitly assumed they cannot take responsibility for even very minor decisions about research that may have few if any long-term consequences for them.

2.64 Where the regulation and guidance cited above make explicit reference to children's age as an approximation for ability to understand what is involved in research, there is a broad consensus that, for most children, this threshold is reached by around the age of 12 to 14.[288] However, the fact that, in many jurisdictions, children are not deemed *legally* competent to consent until they are 18 suggests that there are seen to be concerns at stake other than the intellectual ability required to make a decision. One factor that is likely to be relevant in this reluctance to permit children to authorise research participation themselves is the risk of harm that research may potentially pose. Yet examples from outside healthcare again suggest a lack of consistency in this respect. In the UK, young people cannot buy alcohol or tobacco, or gamble, for example, until the age of 18, but may elect to join the army at 16 with their parents' consent.[289] The high risk that young drivers may present both to themselves and others is reflected in higher insurance premiums up to the age of 25 or beyond,[290] but nevertheless, young people are allowed to start learning to drive on public roads from the age of 17. Children are also encouraged, even required, to take part from a relatively young age in contact sports, such as rugby, where risk of injury is certainly not negligible.[291] While for many children and young people the risks of such sports may be offset by the benefits such as enjoyment that participation offers, this will not always be the case, particularly in the case of compulsory school sports. We return to

[286] Cheah PY, and Parker M (2014) Consent and assent in paediatric research in low-income settings *BMC Medical Ethics* **15(1)**: 22. High numbers of orphans in many countries also lead to 'child-led families' where a child as young as 12 may head a household of younger siblings. In Kenya, for example, the number of orphans in 2013 was estimated at 2.5 million, and in Malawi at over 1.2 million: UNICEF (2015) *State of the world's children 2015: country statistical information*, available at: http://www.data.unicef.org/corecode/uploads/document6/uploaded_pdfs/corecode/SOWC_2015_all-countries-update_214.xlsx.

[287] Section 50 of the Children and Young Persons Act 1933, as amended, and section 41 of the Criminal Procedure (Scotland) Act 1995. See also discussion of 'responsibility' in James A, and James A (2012) *Key concepts in childhood studies*, Second Edition (London: Sage), pp102-4.

[288] See, for example, CIOMS (2002) *International ethical guidelines for biomedical research involving human subjects*, available at: http://www.cioms.ch/publications/layout_guide2002.pdf, at page 68; Modi N, Vohra J, Preston J *et al.* (2014) Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees *Archives of Disease in Childhood* **99(10)**: 887-91, at page 888.

[289] Ministry of Defence: Army (2015) *How to join*, available at: http://www.army.mod.uk/join/How-to-join.aspx.

[290] See: Brake (2014) *Young drivers*, available at: http://www.brake.org.uk/too-young-to-die/15-facts-a-resources/facts/488-young-drivers-the-hard-facts; Young Driver Factbase (2014) *Homepage*, available at: http://www.youngdriverfactbase.com/.

[291] Carter M (2015) The unknown risks of youth rugby *BMJ* **350**: h26.

this point when considering the challenges that those responsible for reviewing the ethical acceptability of research proposals face in determining what is an 'acceptable' degree of risk posed by a research study (see paragraphs 5.19–5.21).

2.65 In this chapter, we have focussed on what is known about the individual interactions between researchers, potential participants, and their families; and on what is required by law or guidance with respect to those interactions. As the references above to risk indicate, however, the role of regulation is not limited to requirements relating to decision-making and consent, but is also concerned with the wider question of the circumstances in which research with children and young people is permitted at all. We turn in the next chapter to this bigger picture: to the influences and requirements that determine which research studies receive both the funding and the approvals necessary to proceed.