

NUFFIELD COUNCIL ON BIOETHICS

Children and clinical research: ethical issues

Report developments

July 2016



Introduction

- 1 The Nuffield Council's report [Children and clinical research: ethical issues](#) was published on 14 May 2015. This paper notes key developments and evidence of impact in the period since the report's publication.

Reaction

Key stakeholders' responses

- 2 The Royal College of Nursing (RCN) and Royal College of Paediatrics and Child Health (RCPCH) both issued responses to the report to journalists under embargo before the report was published. Several other organisations published responses on their blogs and websites, including Simon Denegri at Involve / NIHR, the Institute of Cancer Research, Association of Medical Research Charities, US Presidential Commission for the Study of Bioethical Issues, and the Global Health Network. In addition, several charities and patient information websites have promoted the resources internally and online.
- 3 The HRA published a [response to the report](#) in which it stated:

"The Health Research Authority welcomes this Nuffield Council on Bioethics' report; indeed, the HRA's National Research Ethics Advisors' Panel (NREAP) commented that that it was "one of the best reports produced by the Nuffield Council on Bioethics". We have disseminated the report to our research ethics committees for information and we will be taking it to our autumn regional Chairs' Network Meetings for further discussion."

General media coverage

- 4 The report was covered in a number of national and regional online and print media in the week following the launch, including BBC News Online, the Daily Mail, the BMJ and Research Fortnight. The Lancet published a full page editorial on the report, which also featured on the front cover. Assistant Director Katharine Wright was interviewed on BBC Breakfast TV on 16 May alongside Georgia Semple, a member of the Liverpool Young Persons' Advisory Group, and her father Calum.

Dissemination, presentations and events

- 5 From the date of its launch until 1 July 2016, the report was downloaded 1,959 times, the magazine downloaded 939 times and viewed over 600 times on issuu (an online publishing platform), and the one-page summary accessed 530 times from the Council's website. The project webpage was the third most visited on the Council's website in this period, with over 10,530 views.
- 6 Copies of the report, short guide and one-page briefing have been sent to key stakeholders including research funders, the Health Research Authority (HRA) and National Research Ethics Service (NRES), the Department of Health, relevant Royal Colleges, and approximately 350 MPs and peers. Further dissemination has been initiated at conferences, presentations, and other meetings.

7 Members of the Working Party and Secretariat have been invited to present the report's conclusions at a number of events, including:

- Helen Sammons presented about the report at the University of Nottingham Postgraduate Children and Childhood Network Annual Conference on 'Child Participation and Academic Research: ethical and practical issues' (15 May 2015)
- Susan Tansey discussed the report at an EnprEMA workshop (2 June 2015)
- Kate Harvey ran a workshop during the International Children's Advisory Network (iCAN) launch and Research Summit in Washington DC (26 June 2015)
- Katharine Wright presented at the UK Children's Research Collaborative meeting (22 June 2015)
- Hugh Whittall presented at a Bioethics Advisory Committee of Singapore public forum on children and research (4 July 2015)
- Katharine Wright held a workshop for young people organised by the NIHR/Wellcome Trust Cambridge Clinical Research Facility (19 September 2015)
- Katharine Wright and Vicki Marsh presented on the report in two sessions at the Oxford Global Health and Bioethics International Conference (28-29 September 2015)
- Joe Brierley was invited to attend and submit a question about children and research at a meeting of the All Party Parliamentary Group (APPG) on Medical Research (28 October 2015)
- Katharine Wright presented at the NIHR 4th Annual Health Research Management Workshop (23 November 2015)
- Katharine Wright presented about the report at a Ministry of Defence Research Ethics Committee (MODREC) training day in Whitehall, London (6 January 2016)
- Kate Harvey gave the Adam Hay Lecture at the Children's Cancer and Leukaemia Group Winter meeting in Leicester, UK (25 January 2016)
- Kate Harvey managed a stand at the AWARE for All - London 2016 event, run by the Center for Information & Study on Clinical Research Participation (CISCRP) (7 March 2016)
- Hugh Whittall held a stall presenting the report and other materials at the Global Summit of National Ethics Committees in Berlin, Germany (16-18 March 2016)
- Katharine Wright gave a presentation at an Intensive European Bioethics Course on 'Ethics of Paediatric Research' organised by The University of Padova, Italy (24 May 2016)
- Kate Harvey and Isla-Kate Morris (University of Southampton) gave a workshop at the annual the Association of Research Managers and Administrators (ARMA) Annual Conference at the Birmingham NEC (8 June 2016)
- Kate Harvey and Mark Sheehan ran a workshop with secondary school students as part of the Oxford Science Festival, alongside Ilina Singh, Professor of Neuroscience and Society at the University of Oxford (23 June 2016)

- Kate Harvey gave a presentation about the report at the 2016 iCAN Research and Advocacy Summit in Barcelona (1 July 2016).

Academic publications

- 8 Secretariat staff and Working Party members have also published several articles in academic journals drawing on the report:
- Wright K (2015) [Are children vulnerable in research?](#) *Asian Bioethics Review* **7(2)**: 201-13
 - Wright K (2015) [Need for clinical research in children and young people](#) *BMJ* **351**: h6902
 - Wright K, Collins S, and Farsides B (2015) [Why young people participate in clinical trials and the implications for research governance](#) *The American Journal of Bioethics* **15(11)**: 22-3
 - Wright K, and Farsides B (2016) [Children and clinical research: a response to Chwang](#) *Bioethics* **30(1)**: 56-7
 - Sammons HM, Wright K, Young B, and Farsides B (2016) [Research with children and young people: not on them](#) *Archives of Disease in Childhood*
Published online first: 4 May 2016

Animation

- 9 The Council's animation [Health research: making the right decision for me](#) has been watched over 5,600 times on YouTube. Comments on the video include:

"A really great video. Resonates with my own experience of working with children and young people and their concerns about research AND their altruism."

Bernie Carter, Professor of Children's Nursing, University of Central Lancashire

"I will use the video with my students."

Leonardo Reynoso-Erazo, Coordinador de la Residencia en Medicina Conductua, Universidad Nacional Autónoma de México

"The animated video is excellent and captures everything that is important from a child / adolescent's perspective in taking part in research."

Lord Colwyn

- 10 Several translations of the animation have also been produced since the project's launch (see '[International](#)' section below).

Other organisations' guidance and publications

- 11 The Council's report has been cited in subsequent publications released by other organisations, including:
- INVOLVE / NIHR briefing note for researchers: ['Involving children and young people in research: top tips and essential key issues for researchers'](#)

- INVOLVE/HRA joint briefing: [‘Impact of public involvement on the ethical aspects of research’](#)
- INVOLVE/HRA joint statement: [‘Public involvement in research and research ethics committee review’](#) lists chapter 3 of the report under ‘Supporting reading’
- [RCPCH ‘Infants’, Children’s and Young People’s Child Health Research Charter](#)

12 The Council also responded to the HRA’s consultation on the draft UK Policy Framework for Health and Social Care Research, the final version of which is intended to be published in Summer 2016.

Journal citations

13 Since its launch, the report has also been cited in a number of academic journals, including:

- van Delden JJM, and Ho CWL (2015) [Vulnerability in healthcare and research involving children](#) *Asian Bioethics Review* **7(2)**: 115-25
- Ho CWL, Reis A, and Saxena A (2015) [Vulnerability in international policy discussion on research involving children](#) *Asian Bioethics Review* **7(2)**: 230-49
- Thompson H, Frederico N, Smith SR *et al.* (2015) [iCAN: providing a voice for children and families in paediatric research](#) *Therapeutic Innovation & Regulatory Science* **49(5)**: 673-9
- Dar A (2015) [Decision-making about child participation in medical research: a relational approach](#) *Child & Family Law Quarterly* **27(2)**: 109-28
- Morrow BM, Argent AC, and Kling S (2015) [Informed consent in paediatric critical care research – a South African perspective](#) *BMC Medical Ethics* **16(1)**: 1-13
- Woolfall K, Frith L, Dawson A *et al.* (2015) [15 minute consultation: an evidence-based approach to research without prior consent \(deferred consent\) in neonatal and paediatric critical care trials](#) *Archives of disease in childhood - Education & practice edition* **Published online first**: 13 October 2015
- Humphreys SJ (2016) [Ethical research practice and journal publication](#) *Ethics and Social Welfare* **10(1)**: 71-4
- Sibley A, Pollard AJ, Fitzpatrick R, and Sheehan M (2016) [Developing a new justification for assent](#) *BMC Medical Ethics* **17(1)**: 1-9
- Bluebond-Langner M, Chambers L, Lapwood S, and Noyes J (2016) [Promoting high quality research with life-limited children and their families: establishment of a joint research group between Together for Short Lives and the Association for Paediatric Palliative Medicine](#) *Journal of Advanced Nursing* **Published online first**: 6 January 2016

- Bate J, Ranasinghe N, Ling R *et al.* (2016) [Public and patient involvement in paediatric research](#) *Archives of disease in childhood - Education & practice edition* **Published online first:** 22 January 2016
- Joseph PD, Caldwell PHY, Tong A, Hanson CS, and Craig JC (2016) [Stakeholder views of clinical trials in low- and middle-income countries: a systematic review](#) *Pediatrics* **Published online:** January 2016
- Errington J, Malik G, Evans J *et al.* (2016) [Investigating the experiences of childhood cancer patients and parents participating in optional nontherapeutic clinical research studies in the UK](#) *Pediatric Blood & Cancer* **63(7)**: 1193-7
- Larcher V, and Brierley J (2016) [Developing guidance for pregnancy testing of adolescents participating in research: ethical, legal and practical considerations](#) *Archives of Disease in Childhood* **Published online first:** 22 April 2016
- Madden L, Shilling V, Woolfall K *et al.* (2016) [Questioning assent: how are children's views included as families make decisions about clinical trials?](#) *Child: Care, Health and Development* **Published online first:** 2 May 2016
- Dupont J-CK, Pritchard-Jones K, and Doz F (2016) [Ethical issues of clinical trials in paediatric oncology from 2003 to 2013: a systematic review](#) *The Lancet Oncology* **17(5)**: e187-e97
- Kelley MC, Brazg T, Wilfond BS *et al.* (2016) [Ethical challenges in research with orphans and vulnerable children: a qualitative study of researcher experiences](#) *International Health* **8(3)**: 187-96
- Parsons S, Dack K, Starling B, Thomson W, and McDonagh JE (2016) [Study protocol: determining what young people with rheumatic disease consider important to research \(the Young People's Opinions Underpinning Rheumatology Research - YOURR project\)](#) *Research Involvement and Engagement* **2(1)**: 1-14
- Oulton K, Gibson F, Sell D *et al.* (2016) [Assent for children's participation in research: why it matters and making it meaningful](#) *Child: Care, Health and Development* **42(4)**: 588-97

Developments relating to specific recommendations

14 Recommendations in the report were targeted at organisations including INVOLVE, NIHR, MHRA, NRES, UK Departments of Health, NHS Employers, Universities UK, the Health Research Authority (HRA), relevant Royal Colleges and the European Medicines Agency, as well as research funders, research ethics committees.

Recommendation 1

We recommend that the Clinical Research Network: Children and the Scottish Children's Research Network should initiate discussions with their industry

partners on ways in which industry could contribute to the costs of young persons' groups in the UK, without compromising their independence.

- 15 The Council hosted a meeting with the National Institute of Health Research (NIHR) to explore collaboration between life-sciences industry and young people to improve research on 22 April 2016. The meeting brought together young people with those involved in promoting involvement from the National Institute of Health Research (NIHR), those with expertise in ethics and representatives of key players in industry including [Proveca](#), [GSK](#), [Roche](#), [Ethical Medicines Industry Group](#), [Quintiles](#), [ABPI](#), [AstraZeneca](#) and [UCB Biopharma SPRL](#). Following the initial meeting, Dr Jacintha Sivarajah, Head of Medical Affairs at ABPI, wrote a blog post titled '[The future of research lies with today's young people](#)'
- 16 A number of suggestions for future action were put forward at the meeting, including the development of a 'statement of aspiration', to which individuals or organisations could sign up, which could then inform the development of a position paper setting out guidance on good practice and showcasing what young people can contribute to clinical research endeavour. The statement was published on the [Council's website](#) on Monday 27 June and signatories included:
- The Association of the British Pharmaceutical Industry (ABPI)
 - AstraZeneca
 - The Ethical Medicines Industry Group (EMIG)
 - GenerationR
 - GSK
 - The Health Research Authority (HRA)
 - NIHR
 - Proveca
 - Quintiles
 - Roche
 - UCB
- 17 A news story on the statement was published on the [HRA website](#) and responsive blog posts were published by [Simon Denegri](#), Chair of INVOLVE and [Bella Starling](#), Wellcome Trust Engagement Fellow and Director of Public Programmes at Central Manchester University Hospitals NHS.

Recommendation 7

We recommend that the UK Departments of Health, NHS Employers, Universities UK and the Health Research Authority should jointly consider what steps they can take to protect the professional time needed for research ethics committees to work effectively.

Recommendation 8

We further recommend that the Royal Colleges and professional bodies concerned with children's and young people's health should make their commitment to evidence-based care clear by reinforcing the professional responsibilities of their members to contribute to the ethical review of research over their professional lifetime. For example, involvement of some form in a research ethics committee (including in an *ad hoc* advisory role) could be encouraged as part of continuing professional development schemes. A number of rotational posts for trainees working in different areas of children's and young people's healthcare could be linked with their local research ethics committees.

18 The Council held a meeting with representatives of the Royal College of Paediatricians and Child Health (RCPCH) and NHS Employers on 5 May 2016. The meeting resulted in a joint statement (due to be published imminently) by the Council and RCPCH which called for NHS workforce planning bodies to acknowledge the importance of building capacity within the workforce to support more high quality research into child health.

19 These recommendations were also highlighted in the Council's response to the [HRA's call for comments on a draft UK policy framework for health and social care research](#), submitted in May 2016.

Recommendation 10

We recommend that the European Medicines Agency's Paediatric Committee should complete its review of the class waiver system as a matter of urgency and ensure that where the mechanism of action of a medicine is potentially relevant for children and young people, research with children and young people goes ahead.

Recommendation 11

We recommend that where research sponsors are eligible for a waiver under the current class waiver system, they consider the evidence on the possible relevance of the mechanism of action of their product for other conditions occurring in children and young people. Wherever appropriate, they should undertake research with these age groups on a voluntary basis.

20 On 23 July 2015, the [EMA reported](#) that it had revised its list of class waivers for medicines that are not required to submit a paediatric investigation plan (PIP) in order to stimulate the development of medicines for children. The EMA's Paediatric Committee (PDCO) assessed the available information on the disease area for all waivers, and any available evidence on their potential use in children. As a result, it revoked eight class waivers, updated a further 15, and confirmed nine waivers on its waiver list at the time of its review. The EMA also noted that PDCO would

continue to revise its class waiver list as more information on diseases and the medicines used to treat them becomes available.

- 21 The EMA's announcement represented a degree of progress with respect to recommendations 10 and 11, as expressed in a [statement](#) released by the Nuffield Council in response to the EMA's revisions, and in a subsequent [blog post](#) by Katharine Wright. This blog highlights that changes to the Paediatric Regulation will also need to be undertaken in order to give PDCO more powers, and that the Regulation is still "a work in progress".

Vulnerability

- 22 The Working Party's conclusions on the concept of vulnerability have been influential beyond the particular issue of research with children and young people. For example, the WHO's forthcoming Ethical Guidance for Managing Epidemic Outbreaks was amended following input from the Council which emphasised that individuals or particular groups are not necessarily inherently vulnerable, but rather that particular *situations* can make these individuals or groups vulnerable.

International

Training course

Building on the relationship with the Global Health Network developed during the Working Party's evidence gathering period, an [e-learning course](#) based on the report was developed for the Network's Global Health Training Centre. Published in November 2016, the course aims to give researchers, and members of ethics committees globally, confidence in considering and deliberating over the challenges of carrying out research with children and young people. As at June 2016, the course had been completed over 1,600 times by users in more than 20 countries. Most views of the course were from UK online users (1,305), and the spread of views across the rest of the world include: 396 from the US; 369 from Kenya; 302 from India; 268 from South Africa; 263 from Germany; 257 from Brazil; 184 from Uganda; 166 from Pakistan; and 153 from Nigeria.

- 23 The translation of the course into [Spanish](#) was carried out by the Head of the Research Administration Program at the US Naval Medical Research Unit in Peru, who previously initiated and helped to organise distribution of a Spanish language version of the Council's call for evidence in Latin America. Comments submitted on the use of this course includes:

"We have been relying on these online courses for the past 2 years, they fill a key gap. The Children in Clinical Research course has been very important for our research programme".

Director, FiO Cruz, Brazil

- 24 On 24 May 2016, Katharine Wright also contributed to an intensive short course on the ethics of paediatric research hosted by the University of Padova, Italy. The course formed part of the Erasmus Mundus Master of Bioethics course, but was also open to additional participants with a particular interest in paediatric research ethics.

International symposium

- 25 In March 2016, the Council hosted an [international symposium](#) on children and clinical research with the [Global Health Bioethics Network](#) at the Ethox Centre, University of Oxford and the [Wellcome Trust Brighton and Sussex Centre for Global Health Research](#).
- 26 Participants included researchers from the UK, Thailand, Singapore, Kenya, Peru, Malawi, India, South Africa, Ghana, Cambodia, and representatives from the World Health Organisation (WHO), the Pan American Health Organization (PAHO), the Council for International Organizations of Medical Sciences (CIOMS), the London Young People's Advisory Group, the Wellcome Trust, and the Medical Research Council.
- 27 The symposium explored how the Council's conceptual recommendations might apply in a wide range of international contexts, and aimed to help develop practical recommendations for those concerned with research and research governance in order to help facilitate and improve research with children worldwide. The meeting concluded with participants identifying practical next steps and making 'pledges' as to what they what they as individuals or their institutions might be able to do. A [report of the symposium](#) was subsequently published on the Council's website.

Translations

- 28 In June 2015, the Council co-organised a workshop on the ethical issues of involving children in clinical trials with the [V́ctor Grífols i Lucas Foundation](#), a bioethics organisation in Spain. The workshop took place in Barcelona and brought together experts from Spain and the UK to discuss issues raised in the Council's report. A [report](#) of the meeting was subsequently published by the V́ctor Grífols i Lucas Foundation.
- 29 To coincide with the meeting, V́ctor Grífols i Lucas Foundation translated the Council's illustrated [magazine](#) and the [summary and conclusions](#) section of the full report into Spanish. The translated materials have been shared with colleagues in Spain and Latin America, and are being used by the National Institute of Health in Peru who are working to revise national regulations, with special emphasis on the issue of research with children, with the support of PAHO.
- 30 After the meeting, the V́ctor Grífols i Lucas Foundation also translated the Council's animation into [Spanish](#). Subsequently, the Salim El-Hoss Bioethics and Professionalism Program at the American University of Beirut Faculty of Medicine at the American University in Beirut translated the animation into [Arabic](#), and the National Clinical Trials Institute at the Children's Hospital and Zhejiang University School of Medicine in Hangzhou, China, also translated the animation into [Mandarin](#). The Spanish version was published in December 2015 and has had over 920 views to date; the Arabic, published in May 2016, has had over 180 views; and the Mandarin version, published in June 2016, has had over 250 views.

Advisory roles

- 31 The Council has been invited to be an advisory partner on a Wellcome Trust funded programme on public engagement led by [Dr Phaik Yeong Cheah](#), a Bangkok-based Research Lecturer in Tropical Medicine and Global Health at the University of Oxford. Katharine Wright and Kate Harvey have also been invited to advise on the content of a series of programmes on FunKids radio (involving both audio and animation), exploring medical research and how / why people might be involved in it.
- 32 Katharine Wright is a member of the Steering Committee for the GenerationR Alliance, a group formed to support and promote [GenerationR](#), the UK Young Persons' Advisory Group network, and taking forward [recommendations](#) arising out of the 2013 GenerationR conference in order to ensure the greater involvement of young people in clinical research.

Next steps

- 33 The Nuffield Council will continue to monitor policy and practice developments relating to this project. As we have now reached the end of the first year's active follow-up of the report's conceptual and concrete recommendations, the Working Party is encouraged to consider and advise on how best to prioritise and target any future activity.