This response was submitted to the evidence call issued by the Nuffield Council on Bioethics' Working Party on *Children and clinical research: ethical issues*. Responses were gathered from 7 August to 31 October 2013. The views expressed are solely those of the respondent(s) and not those of the Council.

34. AMRC 311013

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RE: Children and research

Key points:

- Research into childhood health and disease brings significant benefits as it not only improves an individual's health as a child but influences their long-term wellbeing into adulthood. This means there are huge economic gains to be made from investment in this research as healthy children become healthy and productive adults.
- There is a risk-averse culture within the medical and academic community and wider society, which acts as a barrier to conducting medical research involving children and young people.
- There is a lack of high-quality paediatric research in the UK; more academic clinical specialists are needed and infrastructure in the NHS could be improved.
- There are many similarities between child and adult research, including shared barriers. Solutions developed for adult research could also be applied to tackle these in the paediatric field. *Our vision for research in the NHS* sets out practical steps that we can all take to embed research throughout the healthcare system.
- The transition from childhood to adulthood is gradual and dynamic; this poses challenges and requires flexibility from carers and researchers. It is vital that research is designed around the participant, and in consultation with them.
- AMRC is working with the Royal College of Paediatrics and Child Health and the Medicines for Children Research Network to bring together funders, patient groups and health professionals to identify challenges, find solutions and promote research to specifically address child health and disease.

The Association of Medical Research Charities is a membership organisation of the leading medical and health charities funding research in the UK. Working with our members, we aim to support the sector's effectiveness and advance medical research by developing best practice, improving public dialogue about research and science, and influencing government to ensure the best research can go ahead and be translated into new treatments.

34. AMRC 311013

Medical research charities exist because the public choose to donate their money to support research to develop new treatments and cures. In 2012, AMRC members invested over £1.2 billion into health research in the UK. Approximately 4% of UK research grants in 2011 funded by AMRC members are directly linked to research in children or young people, with 24 AMRC member charities funding such research.[1] This does not include infrastructure investments which may be focused on paediatric research, such as dedicated centres, and there is likely to be further research funded by our members that would be relevant to child health or may be of a more basic nature not linked to a specific type of research.

Many medical research charities have patient groups closely allied to them and as such are able to provide a unique perspective, representing the needs of both patients and researchers. AMRC recently held a child health research seminar to explore the experiences of our members and identify actions to create a better environment for paediatric research in the UK. This work is now being taken forward and has informed the development of a meeting of the All-Party Parliamentary Group on Medical Research, which will be held on the 6 November. This meeting of parliamentarians, young patients, medical and ethical experts, NHS officials and regulators aims to catalyse action on the issues identified at both meetings. Kate Harvey presented at the seminar and Professor Bobbie Farsides will be on the panel for the 6 November meeting.

We welcome the opportunity to respond to this consultation. Several of our members have also responded individually. Below we address only the questions that we can provide informed answers to based on our experience and that of our members. Where our answer covers two or more questions we have listed all of the questions above our answer.

How should children be recruited to clinical research?

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

   Risk aversion among clinicians, particularly those not personally involved in research, and the general public is felt to be the main obstacle to recruitment. This is true for recruiting sick children and also healthy volunteers to take part in research. For this latter group, where personal risk outweighs personal benefit, there is a particular reticence to encourage child participation across society. A wider discussion about the risks and benefits of taking part in research is needed to understand the reasons behind this and to seek to address them, whether they are legitimate or whether they stem from misunderstanding or lack of information. It may also be valuable to consider tailoring approaches to different research participants.

   Many further obstacles are common between child and adult research, including lack of awareness of opportunities to take part in research and information about what this involves, delays in obtaining NHS R&D permissions holding up research, staff not having the time nor the training to discuss research with their patients; and research not being designed around the participant.

Case study: Time is the biggest barrier for health professionals to engage with research

We surveyed almost 400 GPs, hospital doctors and nurses about their experiences of research over the past two years.[2] Two thirds (62%) told us that not having sufficient time to be involved had acted as a barrier to them taking part in medical research. 50% of hospital doctors had found it difficult to access funding for research and 40% had found it difficult to navigate the regulatory system.

[1] AMRC grants database 2011. Data was analysed using a list of search terms (below) in titles and abstracts (for grants with abstracts provided) for all grants active in 2011 calendar year. Search terms: paediatric; child; children; teenage; adolescent; infant; baby; babies; young people; childhood; newborn; juvenile.

[2] http://www.amrc.org.uk/sites/default/files/doc_lib/AMRC_Medical_Research_Topline_FINAL_130408.pdf

Case Study: There is a lack of information about research opportunities for the public

An NIHR Clinical Research Network "mystery shopper" survey[3] of 82 hospital sites across 40 NHS Trusts in England examined the basic points-of-contact for patients (reception desks, patient advice services, patient information centres, noticeboards and hospital websites) and assess whether patients had easy access to information about local clinical research opportunities, and how to get involved.

The survey found that 91% of hospitals did not have any public information about studies they were supporting in basic point-of-contact areas, only 34% of sites had information about clinical research on their websites that was useful to patients and of the 40 Patient Advice and Liaison Services (PALS) only three had any information on research. In response to the survey the NIHR Clinical Research Network produced a We do Clinical Research resource pack that pulled together a selection of best practice, top tips and promotional materials designed to help Trusts increase research awareness and promote the local research opportunities available to their patients. Take-up of the resources provided in the pack has been growing steadily since its publication.

Overcoming these obstacles is essential for the long-term health and wealth of the UK. By addressing the health needs of children we can ensure they grow up healthy and become productive members of society, able to contribute to the UK economy. Figures published recently by the Department of Health in the Chief Medical Officer's Annual Report reveal the true cost of poor childhood health[4]:

- the annual cost to the public sector in England associated with children born preterm until age 18 is around £1.24 billion – total societal costs (including parental costs and lost productivity) are around £2.48 billion in total
- the potential annual long-term cost to UK society of one major kind of injury, severe traumatic brain injuries, is estimated at between £640 million and £2.24 billion in healthcare, social care and social security costs and productivity losses
- the long-term costs of obesity in England are £588– 686 million per annum
- for mental health disorders the annual short-term costs of emotional, conduct and hyperkinetic disorders among children aged 5–15 in the UK are estimated to be £1.58 billion and the long-term costs £2.35 billion.

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

Our members have highlighted specific challenges for research that arise as children transition through adolescence and into adulthood. Consent requirements change, the location of treatment and research may change and the individual's personal life situation progresses. All these factors and others affect a person's willingness to participate in research. Health professionals and researchers should be flexible and understanding about these changing needs, designing research around the individual.

[3] http://www.crncc.nihr.ac.uk/Resources/NIHR%20CRN%20CC/News/Documents/Mystery_shopper_report_complete.pdf
[4] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/252652/33571_2901304_CMO_All.pdf

Case study: Supporting research participation for teenagers

Having arthritis as a teenager is particularly challenging and young people often find their symptoms become worse during adolescence. It is vital that teenagers with healthcare problems are given the best treatment to address their particular needs. However, adolescents often find themselves the 'forgotten' group between paediatric and adult care. Access to clinical trials is more difficult during this period of transition and as a result the lack of research in this area means that young people miss out on potential new treatments.

The Arthritis Research UK Centre for Adolescent Rheumatology, led by Professor Lucy Wedderburn, is the world's first centre for adolescent rheumatology (and is one of the UK's leading centres specifically dedicated to research in adolescents). Understanding how and why arthritis develops and progresses in adolescents will support the development of better treatments for conditions including juvenile idiopathic arthritis (JIA), as well as methods to prevent complications that adolescents with arthritis develop in later life, and tests that may predict how the disease will progress. The Centre is helping to also help raise awareness of the health needs of adolescents with rheumatic disease and to ensure that teenagers have uninterrupted and full access to clinical trials, giving them access to the latest treatments.

More information is available at: http://www.arthritisresearchuk.org/research/grant-tracker-items/2012/arthritis-research-uk-centre-for-adolescent-rheumatology.aspx#sthash.7rnrtP74.dpuf

What research proposals should be regarded as ethically acceptable?

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

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

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

   Like adults, children can see the value of medical research and be altruistic. If a study has received ethical approval and the child has the maturity and information to enable them to make an informed decision to participate we believe they should be allowed to do so. This is true for sick and healthy children, especially for non-interventional research where risks are often lower, for example giving access to personal data.

   Children with a health condition should be given the opportunity to take part in research where the risks are "minimised" and where the research offers a prospect of direct benefit to children with the same or similar condition. Though they may not benefit in terms of their personal medical condition, knowing that they are helping others can have a huge positive effect on their mental wellbeing. For healthy children taking part in research it is also possible that they themselves, or someone they love, may become ill and the findings of the research benefit them in the future. If the child is sufficiently well informed and considered able to make a decision based on that information and their personal beliefs, then it is right that they should be able to choose to take part in research where they do not stand to personally benefit.

Case study: Information about research must be tailored for young people

The Medicines for Children Research Network's Young Persons' Advisory Group has been advising the National Research Ethics Service (NRES) on the materials that it produces for the public. They have found that the NRES materials failed to meet their needs. Holly Lamden is 18 years old, and a member of the Liverpool Young Persons' Advisory Group:

> "A lot of the materials we see are highly formulaic. They are clearly designed to tick legal and governmental boxes, but they produce assent forms that are 15 pages long. An eight year old is not going to read this. Researchers need to make a distinction between child and adult studies. Paediatric studies need to stand alone."[5]

For the above benefits to be realised it is essential that the findings of research, whether positive or negative, are disseminated and, where appropriate, translated into clinical practice. This is part of the moral contract between researcher and participant. For this reason we support the registration and reporting of clinical trials.[6]

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

Patients, the general public and clinicians can have different perceptions of risk. People with first-hand experience of a condition, and especially those with terminal conditions, often view the benefits of research participation as outweighing the risks. Children and parents in these circumstances are also likely to take this view. But it is crucial that the research team communicate fully all of the risks and benefits so that they can make an informed decision. Where risks have been fully explained to participants and their parents, and accepted by them, it could even be considered unethical not to allow participation in trials where they stand to gain life-enhancing benefit.

New adaptive licensing approaches, which are sensitive to where patients' perceptions of risk may be different to those of an ethics committee, could be an important means of accelerating the testing and possible adoption of new treatments, offering some hope to patients where few viable therapies exist.

It is important for research ethics committees to contain paediatric specialists or experts in research involving children to help them consider the different viewpoints that parents and children may have.

Case study: People with serious conditions consider risks and benefits differently

The Welsh Institute for Health and Social Care, University of Glamorgan, supported by Genetic Alliance UK, convened a group of patients with serious and/or rare conditions and family members of someone with a serious and/or rare condition.[7] They explored the risks and benefits of hypothetical case studies and heard from a number of expert and advocate witnesses about how the regulatory system currently works, its strengths, and its potential weaknesses. The findings demonstrated that people with serious conditions are willing to take great risks for the potential cure or improvement of their condition.

At the end of the study the group made a number of recommendations:

- Regulators should include psychosocial factors in their decision making.
- Regulators should be more permissive for those treatments for people with rare and/or serious conditions.

[5] http://www.crncc.nihr.ac.uk/Resources/NIHR%20CRN%20CC/Documents/Newsletters/NFTN_EMAG_issue9.pdf
[6] http://www.alltrials.net/supporters/
[7] http://www.geneticalliance.org.uk/docs/citizens-jury-report.pdf

- Patients should be more involved in all stages of the process, from setting the research agenda, to post-marketing authorisation decisions.
- Patients should be better supported to make their own decisions.

How should research in children be encouraged?

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

The public, which includes patients, should be involved in the setting of research priorities. The James Lind Alliance Priority Setting Partnerships[8] and the UK Database of Uncertainties about the Effects of Treatments (UK DUETs)[9] provide valuable information about treatment uncertainties collected from patients, carers, clinicians, and from published research recommendations. These cover a wide variety of health problems and help identify areas of unmet need, allowing research funders to target limited resources to where they can have the greatest impact.

All AMRC members produce research strategies that assess the current state of scientific knowledge in their area of interest (usually a specific condition) and patient experience. Patients, carers, clinicians, researchers and the charity's supporters are consulted in the process of developing a research strategy. Through this wide stakeholder engagement, unmet need is linked to feasibility assessments of any research that could be part of the solution. Using this information charities set targets that they wish to achieve through their research funding activity, identifying gaps in knowledge and capacity and finding the most appropriate way to address them.

It is crucial that the setting of priorities by research funders is transparent. This helps researchers know to whom to apply for funding and ensures the public is fully aware of how research funds are being spent. Both parties may then also have the opportunity to engage with the funder.

Case study: Children and young people should be involved in setting research priorities

Dr Enitan Carrol is a Reader in Child Health and Consultant in Paediatric Infectious Diseases at the University of Liverpool Institute of Child Health. She recently used a workshop with the Young Persons' Advisory Group to determine whether the research question she was proposing was valid. She feels that, in an increasingly competitive environment, this input can prove vital:

> "It's powerful that the people experiencing a diagnostic device have helped to shape it. Their involvement makes a study more competitive because it provides us with perspectives that we can't find anywhere else. It makes the product more likely to succeed and helps us avoid the development of expensive products that children do not want to use."

Case study: Charities take a strategic approach to tackling disease through research, guided by patients, clinicians and researchers

Breast Cancer Campaign has facilitated research to identify the gaps in breast cancer research to achieve its ambition of overcoming breast cancer by 2050. The recently-published Gap Analysis 2013 brought together over 100 internationally recognised specialist breast cancer scientists, clinicians and healthcare professionals and identified around 100 gaps that exist in breast cancer

[8] http://www.lindalliance.org/
[9] http://www.library.nhs.uk/duets/

research and the strategic solutions to address these.[10] Based on this research, the charity's accompanying action plan *Help us find the cures,* provides a clear strategy for how these gaps could be addressed through its research funding and policy activity.[11] In the coming decades, the charity will commission research to address the critical gaps identified, as well as respond to new developments in the field, and will work with policymakers to improve the environment for medical research, build research capacity, and promote public understanding of the importance of breast cancer research.

Research should only be funded if it is judged to be of high enough quality using peer review. Many charities use lay reviewers in this process as a well as research and medical experts. When assessing proposals reviewers should look at the ability of the research team and their facilities to conduct the research effectively, whether the right questions are being addressed and how the findings will be used.

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

Collaboration is essential in research. As described above, public, private and charitable research funders, researchers and stakeholder groups (patients, parents and carers) work together to coordinate research. A continuous feedback loop between these ensures that research addresses need and is taken up into clinical practice.

AMRC is working with the Royal College of Paediatrics and Child Health and the Medicines for Children Research Network to bring together funders, patient groups and health professionals to identify challenges, find solutions and promote child research. These challenges include those that have been identified so far in this response:

- Identifying health areas that are currently under-represented in medical research
- Raising public awareness and understanding
- Ensuring research is designed around the participant
- Increasing high-quality research capacity: training paediatric research specialists and building infrastructure
- Addressing the lack of time and training among health professionals preventing them from engaging in research
- Opening up the NHS to research

In May this year AMRC launched *Our vision for research in the NHS,*[12] which set out practical steps that we can all take to embed research throughout the NHS. This included three core aims:

1. Every patient is offered opportunities to be involved in research.
2. All NHS staff see the importance of research.
3. The NHS conducts high-quality research and adopts new treatments.

This document is intended to help the NHS and those working with it to embed research in the service so that people of all ages can benefit from involvement in research and the innovative products of research.

What should happen when the research is over?

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

[10] http://www.breastcancercampaign.org/documents/ga-2013/help-us-find-the-cures.pdf
[11] http://www.breastcancercampaign.org/documents/ga-2013/help-us-find-the-cures.pdf
[12] http://www.amrc.org.uk/sites/default/files/doc_lib/Our%20vision%20for%20research%20in%20the%20NHS.pdf

The contribution of young participants in research deserves recognition. And as discussed above, researchers have a moral duty to ensure research is disseminated and benefits others by being taken up into clinical practice. Maintaining a connection with research participants after a project is complete can also be hugely useful if follow-up is ever needed in the future.

Research also takes a long time and advances in healthcare and medicine rarely come from a single study. It is important to consider what will happen after the study, not just dissemination as already discussed, but also building on the knowledge gained. Researchers and funders should consider whether the research has the potential to be taken up and developed further, perhaps by a larger funder or commercial partner.

Where research projects are ended early, the reasons should be clearly communicated to all participants and stakeholders, for example patient groups.

Thank you for the opportunity to feed into this important work by the Nuffield Council on Bioethics. We would be happy to engage further with the Working Party as AMRC develops its own thinking on this subject.

Yours sincerely,

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