

Nuffield Council on Bioethics: Children and clinical research: ethical issues

Response by the Wellcome Trust

October 2013

Key Points

- The Wellcome Trust recognises the importance of funding research related to children and has funded a number of significant projects. More specifically, we will only fund research involving children if their participation is deemed necessary to answer the research question, there is relevant ethics committee approval, and all measures have been taken to safeguard and promote their interests.
- The Trust funds 41 grants amounting to £36M of research involving children. The majority of this funding is for cohort and population studies in low and middle income countries.

Introduction

1. The Wellcome Trust welcomes this consultation, which covers important issues that have received little attention to date.
2. The Wellcome Trust is pleased to provide an overview of our funding of research involving children. The majority of this funding has been for cohort and population studies in low and middle income countries.
3. As much of the call for evidence is directed at seeking the specific views of researchers, parents and children we have limited our response to providing an overview of research we fund and a short summary of our position on the themes of the consultation. We have made our funded researchers aware of this consultation and requested they send their views directly to the Nuffield Council Working Party.

Wellcome Trust funding related to research involving children

4. The Wellcome Trust currently funds 41 grants totalling £36M relating to research involving children (see Annex A for further details)¹. Twelve of these awards were made collaboratively with the Medical Research Council and UK Department for International Development as part of the Global Health Trials initiative². The awards made are mainly cohort or population studies in low and middle income countries. Funding for research involving children has been awarded at all career-stages and for both clinical and basic biomedical science.

¹ This may not be wholly exhaustive if children were a subset of the participant group.

² <http://globalhealthtrials.tghn.org/>

5. Of particular note are the following significant financial commitments and major longitudinal studies involving childhood cohorts:

Current funding over £2.5M

- Prof Betty Kirkwood, *London School of Hygiene and Tropical Medicine*
SPRING (for MDGs): Sustainable Programme Incorporating Nutrition and Games (for maximising child development, growth and survival in disadvantaged populations).
- Dr Michael English, *University of Oxford*
Improving the ability of health systems to delivery essential hospital services – examining strategies targeting seriously ill children and new-borns in Kenya.
- Prof Anthony Costello, *University College London*
Population science of maternal and child survival
- Prof George Davey Smith, *University of Bristol*
The Avon longitudinal study of parents and children (ALSPAC): An international resource for population genomics and life course epidemiology.
- Prof Bongani Mayosi, *New Groote Schuur Hospital*
Genetics of rheumatic heart disease and molecular epidemiology of *Streptococcus pyogenes* pharyngitis (The RHDGen Network).

Significant completed funding

- Professor Christine Power, *Institute of Child Health, University College London*
The National Child Development Study – the 1958 birth Cohort (2001-2006, £2M)
- Professor Timothy Spector, *Kings College London, St Thomas Hospital*
TwinsUK Genetic Epidemiology Resource (2006 – 2011, £1.8M)
- Professor Linda Richter, *Human Sciences Research Council*
Birth to Twenty (BT20) cohort, South Africa (2002-2007, £1.7M)
- Professor Cesar Victora, *Federal University of Pelotas*
Pelotas birth cohorts, Brazil (2003-2008, £1.1M)

Ethical considerations

6. Subject to relevant ethics committee approval, the Trust does fund research involving children, as long as their participation is deemed necessary to answering the research question and all measures have been taken to safeguard and promote their interests. As with all research involving human participants, the first priority for researchers should always be the protection of the rights, interests and safety of research participants. The Trust expects that all research involving human participants should be undertaken in accordance with the appropriate standards.

7. As with all funding requests, candidates must address in their application the ethical issues their research raises and specifically where human participants are involved³. Guidance is specifically given for research involving participants incapable of providing consent, including children.
8. For UK based studies, the Wellcome Trust collects information about ethical practices but cedes responsibility for ethics procedures to the host university's committee. The Trust appreciates that ethical issues may arise throughout the research and has therefore stipulated in the grant conditions that ethical approval must be in place at all relevant times during the award.
9. In low and middle income countries the Wellcome Trust can, and does, feed into the ethical framework of studies directly as appropriate. This can include assisting with the formation of ethical guidelines, advising on consent forms and providing additional funding for community engagement as part of fully informed consent processes. In large scale consortia we have established working groups to address the ethical issues that arise throughout the project.
10. The Trust's position regarding the themes of this consultation is below.
 - **Consent procedures:** Consent procedures should be considered on a case-by-case basis. Considerations include carrying out all necessary discussions with a parent or other legal guardian, as well as the child participant to the extent appropriate. An important issue of consideration is re-consenting procedures when the child reaches the age of 18.
 - **Recruitment:** Recruitment requires a multi-tiered approach tailored to the circumstances of the research. This can include engagement through the Health Ministry (where appropriate), local community, school and family.
 - Potential research participants and their communities should be informed about the risks and benefits of research and a relationship of trust needs to be developed between researchers and participants.
 - The Trust funds engagement activities focused on involving communities in participatory research. This is assessed on a case-by-case basis and activities have been held in both LMICs as well as the UK⁴.
 - **Dissemination:** The Trust expects all the outputs, including negative results, of research funded by the Trust to be published in an appropriate form (usually peer reviewed journals) and made available through open access. Additional forms of dissemination are encouraged and funded researchers are asked to provide a data management and data sharing plan where appropriate. Data sharing is particularly important in the context of studies related to children as there is an onus to ensure that the research is not unnecessarily repeated and findings can be shared. The Trust actively supports the sharing of data collected in research studies. For example, through the Wellcome Trust Sanger Institute, we support

³ <http://www.wellcome.ac.uk/About-us/Policy/Policy-and-position-statements/WTP052064.htm>

⁴ Example Trust funding of UK community engagement in participatory research:
<http://www.southampton.ac.uk/geneticimprinting/informationpatients/transientneonataldiabetes.page>

the DECIPHER Database⁵. This database holds genomic variation data contributed by more than 240 clinical genetics centres from 33 countries. It therefore also has the potential for being used as a powerful recruitment tool, which we encourage researchers and participants to contribute data to.

- **Health Related Findings:** In the course of a study involving human participants, researchers may make a finding that has health or reproductive importance to an individual participant. The Trust considers that the potential for individual feedback of findings should be a consideration at the inception of a study. To facilitate this, the Trust and Medical Research Council are currently developing a framework on health-related findings in research, which we expect to publish by early 2014. This framework is not specific to children in research, however, it includes relevant considerations for researchers in this field.

⁵ <http://decipher.sanger.ac.uk/>

ANNEX A: Current Wellcome Trust funding related to children

Principal Investigator	Administering Organisation	Application Title
Dr Stephen Baker	University of Oxford	The epidemiology, genomics and longitudinal immune response of Shigella infections in Vietnamese children.
Dr Helen J Baker-Henningham	University of the West Indies, Jamaica	Promoting young children's social and emotional competence and preventing conduct problems: Follow up of a cluster randomised controlled trial.
Dr Anna Battersby	Imperial College London	The ontogeny of innate immunity in Gambian infants.
Dr James A Berkley	University of Oxford	Co-trimoxazole prophylaxis among children with severe malnutrition.
Dr Badara Cisse	London School of Hygiene & Tropical Medicine	Randomized trial of spatially targetted control to virtually eliminate malaria
Dr Sian E Clarke	London School of Hygiene & Tropical Medicine	Malaria in school-aged children: Epidemiological risk, disease burden and strategies for control.
Prof Anthony Costello	University College London	Population Science of Maternal and Child Survival.
Prof Nigel A Cunliffe	University of Liverpool	New childhood vaccines for Malawi: Impact of a national pneumococcal and rotavirus vaccine roll-out on child mortality and disease burden, in a region of sub-optimal strain coverage.

Principal Investigator	Administering Organisation	Application Title
Prof George Davey Smith	University of Bristol	The Avon Longitudinal Study of Parents and Children: An international resource for population genomics and lifecourse epidemiology. Core Programme Support 2011-2013.
Dr Delanjathan Devakumar	University College London	The effects of antenatal micronutrient supplementation and current air pollution on growth and lung function in 8 year old children.
Dr Karen M Devries	London School of Hygiene & Tropical Medicine	The Good Schools Study: A cluster randomised controlled trial of an intervention to prevent violence against children in Ugandan primary schools.
Miss Sophiya Dulal	Misc. Nepal	Does daily antenatal multiple micronutrient supplementation, compared to iron and folic acid, lead to a difference in IQ at 10 years of age among children in Nepal?
Dr Pablo Endara	London School of Hygiene & Tropical Medicine	Risk factors associated with non-atopic wheeze among migrant children in urban area of Ecuador. A case-control study.
Dr Michael Charles English	University of Oxford	Improving the ability of health systems to deliver essential, hospital services - Examining strategies targeting seriously ill children and newborns in Kenya.
Dr Rashida Ferrand	London School of Hygiene & Tropical Medicine	Treatment support for older children and adolescents living with HIV: A household-randomised trial linked to evaluation of decentralised HIV testing and care in Harare, Zimbabwe.
Mr Miguel Antonio Garcia Knight	University of Oxford	Analysis of T cell responses to HIV-1 infection in Kenyan infant cohorts.
Prof Diana M Gibb	Medical Research Council	A randomized trial of therapy shortening for minimal tuberculosis with new WHO-recommended doses and FDC drugs in African/Indian HIV+/HIV- children.

Principal Investigator	Administering Organisation	Application Title
Prof Diana M Gibb	Medical Research Council	Reduction of Early mortality in HIV-infected African adults and children starting antiretroviral therapy: REALITY trial.
Prof Stephen B Gordon	Liverpool School of Tropical Medicine	An advanced cookstove intervention to prevent pneumonia in children under 5 years old in Malawi: a cluster randomised controlled trial.
Dr Diane Gray	University of Cape Town	Early life determinants of infant lung function and chronic respiratory illness in children.
Prof Sir Brian M Greenwood	London School of Hygiene & Tropical Medicine	A trial of the benefit of including azithromycin in the drug combination used for seasonal malaria chemoprevention in African children
Prof Simon P Harding	University of Liverpool	The Retinal Microvasculature in Cerebral Malaria in African Children.
Dr Mark Hatherill	University of Cape Town	MVA85A Tuberculosis Vaccine Prime and Selective Delayed BCG Boost in Infants of HIV Infected Mothers.
Dr Kelsey David Joel Jones	Imperial College London	Pathogen sensing and response in childhood malnutrition.
Dr Julia Kenny	University College London	The impact of HIV and antiretroviral therapy on the cardiovascular system in HIV-infected children.
Prof Betty R Kirkwood	London School of Hygiene & Tropical Medicine	SPRING (for MDGs): Sustainable Programme Incorporating Nutrition & Games (for Maximising child Development, Growth & Survival in disadvantaged populations).

Principal Investigator	Administering Organisation	Application Title
Dr Ghattu Krishnaveni	University of Southampton	Developmental programming of stress responses in Indian children and their association with cardiovascular risk and cognitive function.
Professor Kathryn Maitland	Imperial College London	MICA: Children's Oxygen Administration Strategies Trial.
Dr George Mtove	London School of Hygiene & Tropical Medicine	Association between malaria and non-typhoidal salmonella bacteraemia among African children. A proposal for a case-controlled study.
Dr Eunice W Nduati	Kenya Medical Research Institute (Kemri)	B cell responses in infants at risk of maternal HIV transmission.
Dr Kiran Nistala	University College London	Regulatory and effector B cell function in childhood rheumatic disease.
Ms Dorothy Oluoch	Kemri-Wellcome Trust Research Programme	Who cares about continuity of care? Exploration of community and health worker perceptions and experiences of continuity of care for maternal and child health in Kenya
Dr David Osrin	University College London	Community resource centres to improve the health of women and children in Mumbai slums: a cluster randomized controlled trial of a complex intervention.
Dr Helen A Payne	University College London	The influence of human immunodeficiency virus and antiretroviral therapy on thymic output in infants and children.
Dr Penelope A Phillips-Howard	Liverpool John Moores University	The effectiveness of Mooncups to reduce school absenteeism, and sexual and reproductive harms in Kenyan schoolgirls

Principal Investigator	Administering Organisation	Application Title
Dr Andrew Prendergast	Queen Mary, University of London	The impact of microbial translocation and immune activation on the health of Zimbabwean children.
Professor Martin J Prince	King's College London	The C-MaMiE birth cohort: evaluating the impact of free healthcare on child and family outcomes in Ethiopia .
Dr Audrey Prost	University College London	Community intervention to improve growth among children under 2 in rural India
Dr Sarah G Staedke	London School of Hygiene & Tropical Medicine	School-based Treatment with ACT to Reduce Transmission; Evaluation of the community impact of intermittent preventive treatment for malaria in Uganda.
Dr Laila Jal Tata	University of Nottingham	Assessment of drug safety and the impact of illness in pregnancy: Establishing a routinely updated maternal-child linkage system in The Health Improvement Network database.
Dr Alison M Ward	University of Oxford	Pathways to care for critically ill children.
Dr Elizabeth Whittaker	Imperial College London	The role of IL-17 in childhood tuberculosis.
Dr Anita Zaidi	Aga Khan University	A double blind randomised community-based trial of amoxicillin versus placebo for non-severe pneumonia in children aged 2-59mths in Pakistan.