Exploring collaboration between life-sciences industry and young people to improve research

Friday 22nd April, 11-3pm

Hosted by the Nuffield Council on Bioethics
28 Bedford Square, London WC1B 3JS

Note of the meeting

Background

This meeting was hosted by the Nuffield Council on Bioethics, in order to explore the benefits of young people's involvement in the wider research agenda, the challenges to achieving such involvement, and most importantly how to start tackling those challenges. In order to enable those present to express freely any thoughts or concerns, the meeting was held under the 'Chatham House' rule, whereby comments may be reported but not attributed to named individuals. This note takes the same approach, with delegates and their affiliations listed as an appendix.

The meeting took the form of a series of brainstorming workshops, initiated by short presentations from speakers including young people with experience of influencing how research is carried out; those with experience within the National Institute of Health Research (NIHR) of promoting such involvement; and those with expertise from industry (from both practical and policy angles) and in ethics. This note summarises the main points that emerged during the day. While it should not be assumed that all present necessarily agreed with all comments made during the workshop sessions, the final section of this note ('Conclusions and way forward') represents a consensus.

1) Introductory remarks: setting the scene

Historically, the culture in children's research has focused on protection, to the extent that it was felt only to be acceptable to involve children and young people in clinical research where interventions had already been found to be safe in adults. Unfortunately, however well intentioned, such an approach led to children and young people being provided with treatment and care that lacked an adequate evidence base.

Much, however, has changed in recent years:

- The European Paediatric Regulation now mandates research with children and young people unless specific exemption criteria apply: the question is thus how, not whether, to carry out clinical research with children.

- Inspirational 'Young People's Advisory Groups' (YPAGs) have developed through the NIHR's Clinical Research Network: Children, with five active groups based in Liverpool, Nottingham, Birmingham, Bristol, and London, and a national mental health group. The five geographical groups came together to host a national conference in 2013 under the banner of 'GenerationR', leading to the development of a national website, and a 'GenerationR Alliance' of organisations supporting GenerationR's aims. The 'YPAG' model is spreading: to Europe, North America and Australia under the 'ICAN' banner, and also in developing countries with a group recently established in Cambodia, and others under consideration in Malawi and Kenya. However, the previous dedicated support for NIHR YPAGs is no longer available and whilst some have achieved temporary funding support, there is a risk that the internationally-recognised young person's involvement in the UK is in jeopardy.

- The Children's Research Industry Group (CRIG) has been developed with the NIHR Clinical Research Network: Children's Specialty, to improve cross-sector collaboration between researchers working within the NIHR and industry, and to identify common issues arising in clinical research with children.

- The Nuffield Council on Bioethics published a report Children and clinical research: ethical issues in 2015, in which it argued that genuine engagement with children, young people and parents, throughout the research endeavour, was ethically necessary. The report challenged the idea that children and young people were necessarily 'vulnerable' in research, arguing that vulnerability often arises because of the *situation* in which children are placed in research - and that this is often something that researchers can do something about. By involving children, young people and parents in research design, researchers can be much more confident that they are alert to ways in which their studies and the way they are organised might inadvertently create situations in which children feel vulnerable. The report strongly supported the work of the YPAGs, and made the practical recommendation that, given pressures on the public purse, it was only fair that industry should contribute financially to their running costs.

- The Health Research Authority is committed to encouraging the influence of PPI ('patient and public involvement') on the research agenda, seeing this as an important element in promoting the quality and deliverability of research.

As a point of clarification, it was noted that while the term 'children and young people' was often used as a shorthand for those aged 0-18, these boundaries were not absolute. As in health services, there could be a period of transition between children's and adults' services, and 18 should not be seen as a firm cut-off point. Similarly, there can be overlaps between research in pregnancy and research once a child is born.

In what follows, delegates sometimes spoke about 'patient involvement' and sometimes specifically about the involvement of children, young people and parents. While the *means* used for engagement might differ between children/young people and adults, the overarching challenges, ideals and ways forward with respect to fruitful collaboration appeared to be common across the age-range.

2) The need for change: where engagement can help

The benefits of collaboration between industry and young people were presented from both perspectives:

- YPAGs provide a practical example of how young people can have a direct impact on the conduct of studies - both to the benefit of the research itself, and to the young people taking part.

    - A 'gold standard' project, identified as such by a National Children's Bureau report in 2014, was a study into polycystic ovarian syndrome. Young people were involved as partners across many aspects of the study, including commenting on study design, helping determine outcome measures, influencing the formulation and the design of the packaging, and commenting on the study information sheets. One specific change made as a result of their input was the inclusion of an element of pain relief in the medication – an aspect of the condition that had not been considered before young people's involvement. As a result of the partnership with young people, the final product was much more 'patient-friendly'.

    - The young people involved in this project also gained directly. They gained confidence from being listened to, and from knowing that they had made a useful contribution. It was motivating to work alongside researchers, and to feel that they had helped others. Involvement in a YPAG also brings science to life.

- From the point of view of industry, the appetite for engagement with patients is definitely growing, and the potential value of partnerships with patients is well-recognised: for example in helping ensure that research questions are relevant, and that protocols and formulations are as well adapted to their needs as possible. It is perhaps fair to say that industry is at the start of this journey, and that in some cases they are more comfortable with partnerships with adults than with children and young people. They need help with how to navigate such partnerships.

- The practical benefits to industry are also beginning to be recognised: if studies are not designed with children and families in mind, they will be difficult to recruit to, and that wastes time and money. In one example, a study information sheet was criticised by the Research Ethics Committee, and subsequently re-written with the help of a YPAG - if the YPAG had been involved earlier, much time would have been saved.

- Industry also recognises the importance of nurturing children's curiosity in the life sciences: note for example the schools website of the Association of the British Pharmaceutical Industry (ABPI).

3) The challenges to collaboration between industry and patients

Challenges, however, remain in making such collaborations the norm. These include:

- ***Getting key people to recognise the benefits of engagement with patients*** (children, young people and parents in the case of paediatric research). Contract Research Organisations (CROs) host studies for different companies and hence are well placed to encourage involvement, but not all client companies are responsive. Awareness of PPI also seems to vary by sector *within* companies: those working in rare diseases, for example, are often more familiar with PPI.

    - While the aim is to achieve collaboration across the board, pragmatically it may be best for a company to start developing collaborations in one particular area, which can be seen to be 'piloting' collaboration. A pilot approach would also help develop the evidence base - it is critical to be able to demonstrate impact clearly, and for 'converts' to be able to demonstrate the value to their colleagues. Such evidence also needs to be readily accessible, for example through some kind of online 'hub'.[1]

    - The buy-in of the Chief Executive Officer is transformative: in one company the message has come very clearly from the CEO that patient involvement is a necessary part of study development. If a researcher's presentation on a study proposal does not include a slide explaining the proposed patient engagement, funding will not be agreed.

    - Might it be possible to promote engagement by making it mandatory through regulatory requirements? (eg via Health Research Authority, European Medicines Agency etc.) However, that might run the risk of engagement being seen as a 'compliance', rather than a 'quality' issue, with the result that engagement activities simply become a tickbox exercise.

- ***Who in a company is responsible*** for engagement? Often it is not really anyone's job.

    - One company's 'patient centricity' programme has a remit to introduce the potential opportunity afforded by PPI to its R&D portfolio of projects. The internal website (due to become public in due course) includes examples of good practice in PPI, although to date the team's work has focused primarily on research with adults.

    - The growth in industry-sponsored conferences, and the increasing numbers of staff with different roles in industry (not just 'patient-facing' roles) suggests that 'ownership' of responsibility for PPI is becoming more widespread in companies.

- ***Lack of knowledge and uncertainty about what 'involvement' or 'engagement' is***: even researchers who are positive about partnerships with children and young people may lack

[1] Note that GenerationR has a website that could potentially fulfil this role; as could the NIHR. The 'EUPATI' project includes a collection of case studies of (adult) patient involvement from different companies.

confidence or knowledge about how to go about establishing such partnerships. Different understandings of what 'involvement' or ‘engagement’ entail (in some cases conflated with market research) complicate the picture.

  - Some kind of hub or central point providing information about the sources of advice and support available, and how to contact groups such as YPAGs, would be very valuable (as noted above in the context of evidence on impact/value).

  - The rationale for engaging with children and young people is no different from that for engaging with patients of any age: however, the *techniques* used (for example, communication appropriate to stage of development, and the involvement of parents) do differ, highlighting the importance of skilled facilitators.

  - The terms 'involvement' and 'engagement' are used for a variety of activities: a key question is whether the relationship involves a genuine sense of dialogue and a 'feedback loop', as opposed to a one-off market-research-type encounter. If, for example, researchers are not able to take particular ideas on board, there should be mechanisms for feeding back to explain why not.

- ***Perceived conflicts of interest*** can be very problematic: everyone approaches research from a different perspective (whether commercially driven, or concerned with patient advocacy) and these interests need to be acknowledged and recognised. The ABPI's Code of Practice is widely *perceived* as a potential bar to engagement with patients/public of any age, although it was generally agreed that this was a matter of perception/fear rather than an actual barrier. The Code is concerned with the promotion of medicines to health care professionals and other relevant decision-makers, not research per se (although it does not preclude it either), and specifically permits the legitimate exchange of scientific information. Moreover, the ABPI/Involve document Working Together, Delivering for Patients actively supports collaboration between industry and patient charities, although it does not refer directly to research. Nevertheless, anxiety about the Code, particularly on the part of corporate lawyers, can make it very difficult for researchers to engage directly with patients, even at the level of laboratory visits.

  - Transparency is crucial; for example some kind of 'consent form' or commonly-agreed understanding, setting out the nature of each particular partnership between industry and young people, could help. 'Role descriptions' for young people (used in the YPAGs) are also very useful.

  - 'Honest brokers' could play an important role facilitating contact between industry and young people, and in ensuring common understandings of how the partnership will work. YPAG facilitators take on this role, ensuring that both 'sides' are alert to the needs of others. A third party 'broker' would be particularly important where researchers are seeking to contact individuals, rather than approaching an established group.

- A non-binding document produced with the ABPI, on the lines of the *Working Together* document, could play a very valuable role both in setting out good practice and in providing reassurance that such engagement activities are regarded as compatible with the Code of Practice.

- ***How, and from whom, should input be sought?*** - for example from healthy children or from children with the relevant condition? How should global studies be managed: should there be multiple input from the equivalent of YPAGs in a number of countries? What language would it be conducted in? How can confidentiality concerns be handled? How representative is the feedback?

    - There is a need to be flexible in how input is sought: what is right for one study is not necessarily right for another, and the nature of patient involvement will vary.

    - Similarly, what is appropriate in one country might be less appropriate in another, and companies cannot run completely different versions of what is supposed to be one study across a number of countries (thus limiting how they can take on board very different feedback). However, researchers do need to be alert to how such differences may in fact also be very important in study design, and engagement will help identify such factors at an early stage, thus potentially reducing delays in recruitment later.

    - The use of social media offers a valuable way of reaching many people quickly, especially when seeking input on factors that are not commercially sensitive. Websites and direct email offer people less public ways of sharing insights without the need for face-to-face meetings or travel.

    - In face-to-face meetings, it is straightforward to be clear about confidentiality: this is a routine feature of YPAG meetings.

    - In order to avoid single strong voices skewing the debate, it is important to seek multiple views, providing opportunities to comment via different routes (eg online as well as face-to-face), and ideally with some degree of time flexibility to fit around other commitments and/or coping with ongoing illness. It is also important to explain the issues in ways that do not rely on existing knowledge: the input of children who are not familiar with research is just as important as the input of 'expert' children. YPAG facilitators can manage these issues.

- ***Risks of loss of trust***: for example if a study doesn't work in the end, or if a new medicine is approved but not funded.

    - Again, good communication and good systems for feedback are critical.
    - Early engagement with health technology assessment processes and agencies, such as those used by NICE is also important.

- ***Timelines can be very challenging***: for example CROs may be expected to develop firm proposals for study sponsors within two weeks.

    - Building in sufficient time for a genuine partnership to emerge is crucial: this cannot be done in two days, and approaches in this context are at best tokenistic.
    - Given that involvement is usually best as early as possible, perhaps the sponsor companies, rather than the CRO, should initiate partnerships with young people?

- **Finding a secure funding mechanism for collaboration**: the existing YPAGs are run on a shoestring, and security of funding is a real issue. The Chief Medical Officer suggested at the 2013 GenerationR conference that a means needed to be found whereby industry could contribute openly and transparently to the running costs.

    - Most companies would expect to pay: the challenge is to find an appropriate means to do so that retains the genuine independence of the YPAGs, and also allows for other models of collaboration to exist alongside. Transparency would be particularly important. While contributions to a central fund to help support the YPAGs might be problematic, there was a need to ensure that ongoing infrastructure, including the important role of facilitators and other running costs, were supported. Other possibilities include contributions linked with specific collaborations, whether on a 'fee per meeting' basis, or calculated with respect to the likely workload involved in collaborating on a particular study.

It was noted that, in fact, with the exception of the concerns about the interpretation of the ABPI Code of Practice, many of these challenges also arise in non-commercial research: they are not unique to industry.

4) Setting the Ideal: what can we aspire to and what's the opportunity in the UK?

Ideals put forward by delegates included the following:

- YPAGs can and should do more: and in particular be engaged earlier in the process so that they can really influence the design of research. Young people think and see things differently, and researchers need to collaborate with young people in order to ensure that those perspectives are embedded in the design of research, in the operation of research, and in the development of outcome measures that are relevant to patients.

- Researchers need to stop being scared of the word 'vulnerable': children and young people *may* be vulnerable in research, but the way to tackle that risk of vulnerability is by a respectful partnership *with* young people to ensure that studies are designed in ways that best meet their needs. The concept of 'vulnerability' should act as a prompt to design better research, with the assistance of children, young people and parents, and not as an automatic brake on research.

- Partnership with children and young people needs to be both genuine and sustainable. Genuine partnership is about attitudes, respecting the role that children and young people can play in improving research. Such a partnership cannot be sustainable without a secure funding model.

- Flexibility is crucial, so that, as appropriate, researchers can approach either an established generalist group (such as the excellent YPAG model) or young people with specific health conditions (for example reaching young people and parents via relevant charities). Any funding model must be flexible enough to support a range of models of engagement, and should be devised with the input of young people.

- The importance of flexibility arises in many other domains as well: input may appropriately be sought for many different kinds of study (early stage to Phase IV); at different time points in the study; using different methods, and with reference to different aspects of the study. Moreover, input should only be sought when *relevant* and not for its own sake.

- Good facilitation and support for young people is crucial. The balance of workload also has to be right: collaboration with patients/public should not mean expecting them to do all the work, but rather to comment, critique and revise.

- Clear rules of engagement are required, for example in the form of good practice guidance supported by the ABPI, GenR, the Health Research Authority and others, so that researchers and companies can be confident that they are acting appropriately in seeking partnerships with children, young people and parents.

- The positive impact of collaboration needs to be clearly demonstrated, and then built into business and ethics frameworks. Might the European Union 'Horizon 20/20' programme be a possible source of funding to build the evidence base? And might more formal relationships between YPAGs and RECs be one way of 'normalising' YPAG involvement?

- The lesson from the NIHR is that requiring researchers to seek patient/public involvement does make a huge difference in shifting attitudes. Might a similar mandate come from industry itself, given the examples of good practice described during the meeting?

- Industry should aspire to be worldleading in terms both of the *understanding* that the general public has of research into new treatments, and of the *involvement* of both patients and the public in that research. That starts with a conversation - and with the building of trust.

5) Step by step: moving towards an ideal partnership

The following ideas for future action were put forward in the final brainstorming session:

- Write a joint statement, drawn from the discussion at this meeting, covering both the values underpinning collaboration between industry and patients/public (such as partnership and respect), and what is required for collaboration to be effective.

- Explore the possibility of incorporating reference to collaboration with patients in the forthcoming guidance on the new EU Clinical Trials Regulation.

- Engage in dialogue with the European Federation of Pharmaceutical Industries and Associations (EFPIA - ABPI is a member) to encourage them to 'scale up' their current engagement with adults to include children/young people/parents. Such an approach might include both emphasising the importance of 'not leaving children out' - and the specific benefits of involving children and young people who in many cases lead the way.

- Gather, share and publicise good practice case studies and evidence of impact.

- Identify whose behaviour most needs to change: seek to influence the scientists and physicians for whom at present PPI is not the norm.

- Establish a group to look at funding models, in order to ensure a better-funded infrastructure.

- Identify regulators to influence (while stepping back at this stage from suggesting PPI should be mandatory): the European Medicines Agency and its Paediatric Committee; the Medicines and Healthcare products Regulatory Authority; and the National Institute for Health and Care Excellence (whose PPI committee no longer exists).

- Explore amending the ABPI Code of Practice to clarify that the rules with respect to promotion should not be applied inappropriately to engagement with patients and the public in connection with research. (Note that the Code of Practice for the Pharmaceutical Industry is administered by the Prescription Medicines Code of Practice Authority (the Authority). The Authority is appointed by and reports to the Board of Management of the ABPI. Amendments to the Code of Practice may be made by a simple majority of those present and voting at a General Meeting of the ABPI. The views of the Authority and the Appeal Board must be sought on any proposal to amend the Code. The views of the MHRA, the Competition and Markets Authority, the Serious Fraud Office, the BMA, the Royal Pharmaceutical Society and the Royal College of Nursing must also be invited.)

- Develop a position paper or guidance document with the ABPI, setting out good practice when working with children and young people, and providing a clear indication that such collaboration is not only acceptable but desirable.

Conclusions and way forward

It was agreed that, as a starting point:

- A note of the meeting would be circulated, and when agreed, published on the Nuffield Council website.

- A 'statement of aspiration' would be developed, based on this meeting, to which individuals or organisations could sign up. This could then lead, with the involvement of young people, to the development of some form of position paper providing good practice guidance, showcasing what young people can contribute.

- The possibility of having input into the guidance around the Clinical Trials Regulation would be explored.

Appendix: Delegate list

- **Simon Bryson,** Director, Proveca
- **Robyn Challinor**, member of Liverpool YPAG
- **Katharine Cheng,** Physician, Maternal and Neonatal Health, GSK
- **Hugh Davies**, former Research Ethics Advisor, HRA
- **Simon Denegri**, National Director for Patients and the Public in Research, NIHR
- **Mark Edwards**, R&D Director, Ethical Medicines Industry Group
- **Carly Greene**, facilitator of West Midlands YPAG
- **Dominik Kraus,** Clinical Scientist Specialist Rare Diseases, Roche
- **Orlane Doumbe**, member of London YPAG
- **Vivienne McDonald**, Director, Integrated Site Strategies, Quintiles
- **Jonathan Montgomery**, Chair of Nuffield Council on Bioethics and the Health Research Authority
- **Achenyo Ochuma***,* Clinical and Regulatory Policy Officer, ABPI
- **Jenny Preston**, Patient and Public Involvement Priority Lead, NIHR CRN Coordinating Centre
- **Mark Robertson**, Director Global Public Policy, Corporate Affairs, Astra Zeneca
- **Sangeeta Jethwa Schnetzler,** Patient Partnership Director, Rare Diseases, Roche
- **David Sciberras**, Director Global Exploratory Development, UCB SPRL
- **Jacintha Sivarajah**, Head of Medical Affairs Research, Medical and Innovation Department, ABPI
- **Richard Staines**, journalist Pharmaphorum
- **Bella Starling**, Wellcome Trust Engagement Fellow, Director of Public Programmes at Central Manchester NHS Trust
- **Susan Tansey**, Vice President & Global Head, Medical Strategy & Science, Quintiles

- **William van't Hoff**, NIHR CRN: Clinical Director for NHS Engagement
- **Erin Walker**, facilitator of London YPAG
- **Sarah Walker-Robson**, Communications Manager, Nuffield Council on Bioethics
- **Katharine Wright**, Assistant Director, Nuffield Council on Bioethics