Forthcoming practical framework for ethics committees and researchers on post-trial access to the trial intervention and healthcare

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When research concludes, post-trial access (PTA) to the trial intervention or standard healthcare can be crucial for participants who are ill such as those in resource-poor countries with inadequate healthcare, British participants testing 'last-chance drugs' unavailable on the National Health Service (NHS) and underinsured US participants. Yet, many researchers are unclear about their obligations regarding the post-trial period, and many research ethics committees (RECs) do not know what to require of researchers. Consequences include participants who reasonably expect but lack PTA to the trial intervention, unplanned financial liabilities for NHS Trusts forced to fund this, negative press and potential to undermine public trust.[1–3,i]

One reason for the lack of clarity is controversy over whether and when participants should have access, after the study, to the study intervention. At one extreme is the view that continued access should be ensured when the intervention has benefited the participant or when it has proven safe and effective for the participant population, irrespective of the cost and burden of ensuring continued access. At the other extreme is the view that continued access need never be provided so long as non-availability of the study intervention post-trial was adequately disclosed when participants were invited to participate.[6] There is also disagreement about when poststudy access to the study intervention should be considered beneficial for participants. The spectrum ranges from the view that the intervention should be regarded as beneficial for a proposed use only after the intervention has received regulatory approval, to views employing a lower standard of evidence.

Another reason for lack of clarity may be the absence of *practical* guidance. Certainly, there are many international and national legislation and guidance documents on PTA to trial drugs, healthcare and information, but these are inconsistent, ambiguous or silent about many crucial details.[7 8] Many reports with content on PTA that is relevant to research conducted in the UK are unlikely to be read by British RECs due to international focus and length.[9 10] British regulations,[11] which are weaker than international guidelines, merely require each application to a REC to include 'details of the plan for treatment or care of subjects once their participation in the trial has ended' or 'an explanation of why that information is not being provided'; they prepare RECs neither to pre-empt issues about PTA to the study intervention nor to ensure adequate disclosures to participants of what PTA they will or will not have to the study intervention.

The discussion on PTA has focused mostly on research conducted outside resource-rich countries with universal healthcare. However, these issues arise worldwide, including in the UK,[1 2 12] whenever participants want continued access to a study intervention that is unaffordable or otherwise unavailable. They are most pressing when participants are seriously ill and the study intervention has a better clinical profile than the standard treatment or is the only (remaining) option.

The UK Health Research Authority's forthcoming document *Care after research: A framework for NHS RECs*[13] (see online supplementary appendix 1) seeks to address RECs' and researchers' need for practical guidance in the face of various incompatible, yet often individually reasonable views. It prompts RECs to address specific questions about researchers' plans for the post-trial period; ensure there are plans for transitioning sick participants to healthcare; examine any plans to ensure PTA to the study intervention; and verify that documents for participants explain what will (or will not) happen post-trial, and identify any uncertainty. It allows RECs to decide when PTA to the trial intervention may be feasible or appropriate but, to inform their deliberations, summarises important legal, ethical and practical issues, and key legislation and guidance.

Care after research results from a collaboration between two King's College London academics and the Research Ethics Advisor of the Health Research Authority. With funding also from the Wellcome Trust and Brocher Foundation, these authors developed it iteratively via a 3-year international consultation that engaged major pharmaceutical companies, patient advocacy groups, the British Medical Association, Nuffield Council on Bioethics, National Research Ethics Advisors' Panel, European Forum on GCP, Uganda National Council for Science and Technology, World Health Organisation, the Editor of the *Indian Journal of Medical Ethics*, a member and international panellist of the US Presidential Commission for the Study of Bioethical Issues, REC members and Chairs, members of the NIH's Clinical Center Department of Bioethics, two heads of the NIH's Fogarty International Center programmes in Bioethics, as well as prominent research ethicists.

Care after research applies to the 79 British RECs,[ii] and so, indirectly, to the researchers who apply to them for permission to conduct research. Four consultation sessions that piggy-backed on large-scale training events for UK RECs should drive domestic adoption. It is too early to assess its impact on RECs,

[i]There is a dearth of information on types, rates and mechanisms of care after research in the UK. However, limited UK information suggests that some REC-approved documents for recruiting participants lack appropriate plans, some participants expect but lack PTA to the study intervention, and some NHS Trusts have been forced to fund post-trial access to the study intervention (sources include examples of anonymised protocol and informed consent extracts from applications submitted to a North London REC and verbal reports made by many REC members and chairs involved in the consultation process). Wide variations in rates of reporting plans for post-trial access to the study intervention have been reported in informed consent forms and protocols for US-sponsored antiretroviral trials.[4 5]

[ii]These together reviewed 5560 applications between 1 April 2011 and 31 March 2012. Source: personal communication between NS and Health Research Authority staff.

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researchers, and participants: *Care after research* came into force only in December 2012. However, participants should benefit at least from clearer and more complete information on care after research, and NHS Trusts and research sponsors should have fewer unplanned financial liabilities. The international consultation, intended to raise awareness of the consultation's product, revealed support for the document's practical approach and belief in its adaptability outside the UK. It will be important not only to foster and monitor domestic impact, but also to encourage international adaptations.

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