Clinical Trial Transparency: Update on recent developments

Submission to the Science and Technology Committee’s inquiry into research integrity

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Note: This evidence is being submitted to provide the Committee with an update on recent developments relevant to clinical trial transparency in the UK.

EXECUTIVE SUMMARY

1. The Health Research Authority has set an important precedent by making public clinical trial audit findings in full, line by line. In future, all UK public institutions conducting trial audits should publish their audit findings in full, line by line.
2. In 2017, DFID, MRC and NIHR voluntarily signed up to the WHO Joint Statement, pledging to adopt global best practices in clinical trial transparency within a year. One year later, DFID has not adopted any relevant policies. MRC and NIHR have some strong policies in place, but important gaps remain. DFID, MRC and NIHR should be encouraged to fully deliver on their transparency commitments as rapidly as possible.
3. UK universities and medical research charities have not yet signed up to the WHO Joint Statement. They should be encouraged to do so.
4. These recent developments underline the importance of setting up a National Clinical Trial Audit System, and of phasing in sanctions for the failure to register clinical trials and post their results.

ABOUT THE SUBMITTING PARTY

TranspariMED is a UK-based initiative that develops and promotes policy solutions to the problem of evidence distortion in medical research.

HEALTH RESEARCH AUTHORITY SETS TRANSPARENCY PRECEDENT

In response to a Freedom of Information request filed by TranspariMED, the Health Research Authority (HRA) has released the line-by-line results of its earlier trial registration audit. The data set contains detailed information on the trials that the HRA had found not to be registered at the time. The HRA’s decision to release this information is a significant positive step forwards.

The HRA’s decision sets an important precedent for the publication of line-by-line audit results by other UK public institutions, trial funders and trial sponsors. For example, past trial audits by the MRC and NIHR have only published aggregate data. Line-by-line information makes publicly visible the trial registration and results sharing performance of individuals and institutions, and enables...
third parties to follow up on unregistered trials and those missing results. This is likely to raise improve registration and reporting rates.

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In future, all UK public institutions conducting trial audits should publish their audit findings in full, line by line.

TRANSPARENCY POLICIES OF UK PUBLIC TRIAL FUNDERS

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In 2017, DFID, MRC and NIHR voluntarily signed up to the [WHO Joint Statement](#), thereby making specific time-bound commitments to institute policies and processes that reflect global best practices in clinical trial transparency, research integrity, and curbing research waste. The WHO Joint Statement has been strongly welcomed by major medical research stakeholders and transparency advocates, including the AllTrials campaign and TranspariMED.

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Two separate audits recently published by Dr Ben Goldacre’s team at Oxford University provide new data on the transparency policies of DFID, MRC and NIHR. The first audit was conducted in early 2017, so the underlying data is outdated. The second audit, a “live audit” that tracks signatories’ progress against their WHO Joint Statement commitments, is still ongoing, so the data it has generated is still incomplete and unverified. However, both audits paint a similar picture of DFID, MRC and NIHR policies, as does research independently conducted by TranspariMED in parallel.

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MRC and NIHR policies. All available data indicate that MRC and NIHR perform strongly in international comparison in terms of their clinical trial transparency policies. However, the same data also suggests that both MRC and NIHR still fall significantly short of their WHO Joint Statement commitments and hence of global best practices. The Oxford “live audit” of MRC’s policies indicates that significant gaps remain, especially with regard to the posting of summary results onto trial registries. NIHR’s response to a Freedom of Information request by TranspariMED indicates that its policies have similar gaps. As MRC and NIHR have for many years been transparency front-runners in international comparison (against a very low international baseline), it is unclear to what extent, if any, they have further strengthened their policies since signing up to the WHO Joint Statement.

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DFID policies. DFID [does not have any policies](#) related to clinical trial transparency. This is especially concerning as DFID often supports medical research into disease areas for which funding is generally scarce, which makes it especially important to prevent research waste. In addition, some of DFID’s grantees themselves seem to lack strong safeguards against research waste. While some DFID grantees are themselves signatories to the WHO Joint Statement, preliminary data from the ongoing Oxford “live audit” indicates that this is no guarantee that they have indeed put into place strong policies.

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DFID, MRC and NIHR should be encouraged to fully deliver on their transparency commitments as rapidly as possible.
TRANSPARENCY POLICIES AND PRACTICES OF UNIVERSITIES AND MEDICAL RESEARCH CHARITIES

11 No UK university or medical research charity has yet signed up to the WHO Joint Statement. They should be encouraged to do so. Note that medical research charities spend over £1.6bn a year on research in the UK.

12 While some UK universities have individually begun tackling their backlogs of unreported clinical trials and are putting into place stronger policies and processes, written evidence recently submitted to the Committee by the Russell Group (RES0056) and Sam Gyimah MP (RES0057) contains no indication that universities as a group are willing to take decisive action to ensure that the results of all their clinical trials are posted onto trial registries.

13 The audit benchmarks based on the WHO Joint Statement that have been developed by Dr Ben Goldacre’s team provide useful transparency benchmarks against which the policies of a variety of medical research institutions can be assessed. In addition to funders, this includes universities and medical research charities.

14 In the near term, institutions applying for public funding to conduct clinical trials (such as universities) could be asked to self-assess their own policies against these benchmarks as part of the application process to provide assurance that they have put into place adequate safeguards to support research integrity and curb research waste. In the longer term, eligibility for public research funds could be restricted to institutions that have signed up to the WHO Joint Statement and fully implemented its provisions.

IMPORTANCE OF AUDITING AND SANCTIONS

15 All of the above underlines the importance of setting up a National Clinical Trial Audit System based on REC approval records, which is the only mechanism that could identify all unregistered and unreported clinical trials across the public, academic, charitable and private sectors. Please see the two earlier submissions of written evidence by TranspariMED et al for more details. Note that in a recent FOI response, the HRA noted that it had never followed through on its announcement to audit the registration status of trials that had received ethics approval before September 2013 and chase up those responsible to ensure that all these trials are retrospectively registered. Any funding provided to the HRA for the National Clinical Trial Audit System should include a budget line to cover the auditing of older trials and follow-up measures to ensure that they are all registered and their results reported.

16 All of the above also underlines the importance of phasing in sanctions for the failure to register clinical trials and post their results. Over a decade of experience – from the ICMJE trial registration policy to the 2017 WHO Joint Statement – shows that attempts at self-regulation and voluntary initiatives alone are unlikely to deliver satisfactory results at an acceptable pace.
Any system of auditing and sanctions should be geared towards incentivizing the retrospective posting of summary results for older clinical trials. If trial sponsors do not act soon to secure these missing results and place them onto registries, these trials – which often cost millions to run, and sometimes involved thousands of patients – will become research waste as investigators retire and their data sets get deleted.

[ENDS.]