Research integrity and clinical trials transparency

Thank you for your letter dated 11 December 2017. Since 2013, we have been actively developing and number of varied initiatives to promote research transparency and integrity, particularly in respect of clinical trials, and we are therefore grateful for this opportunity to update the Committee on this work.

The MRC currently spends around £20 million per year on early phase (I and II) clinical trials, clinical intervention studies, public health or behavioural interventions, and global health trials (non-UK and non-EU). Since 2006 when responsibility for funding Phase III trials in the UK was transferred to the NIHR, most studies funded by the MRC have been early phase trials funded through the Developmental Clinical Studies scheme. Some late-phase clinical trials continue to be supported through research fellowships and research grants, particularly within the Joint Global Health Trials programme. In addition, the MRC provides underpinning funding to the Methodology Research Programme, MRC Hubs for Trials Methodology Research, the MRC Clinical Trials Unit at UCL and the MRC Population Health Research Unit at the University of Oxford.

Trials administered by the NIHR Efficacy and Mechanism Evaluation (EME) programme, which is co-funded by the MRC and NIHR, are subject to the NIHR research transparency requirements with regard to registration and timely publication of results.

1. Actions taken since the 2013 review

1.1. MRC requirements for trial registration, publication and data-sharing have been clarified and published in the MRC Policy on Open Research Data: clinical trials and public health interventions (October 2016). This policy applies to public health and all clinical intervention studies. All award holders should prospectively register intervention studies, make the study design and methods public, and ensure findings are publicly available within 12 months of completion.

1.2. MRC requirements stipulate registration in the ISRCTN registry, which meets specific quality criteria to be recognised as a World Health Organization (WHO) primary registry.

1.3. Registration of clinical trials was made a requirement in the MRC Terms and Conditions in December 2015 and the requirement to register is included in award letters for relevant funding schemes.

1.4. In 2017, the MRC was a co-signatory to the WHO Joint Statement on the Public Disclosure of Results from Clinical Trials.

1.5. The MRC actively monitors trial registration and publication:

1.5.1. Award holders are required to provide details to the MRC within one year of registration. In 2017, researchers were contacted about unregistered trials live during the previous five-year period; in most cases the trial had either not yet commenced, or had been registered but the information not provided to the MRC. Within an ongoing annual monitoring programme, we are contacting researchers who have not reported registration details to confirm (or require) registration.

1.5.2. Through this exercise we identified three award holders who had not published findings from trials commenced before 2012. Discussions with award holders have resulted in one submission for publication and further details are awaited for the remaining studies.

1 https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/open-research-data-clinical-trials-and-public-health-interventions/
2 https://www.mrc.ac.uk/documents/pdf/mrc-policy-on-open-research-data/
3 http://www.who.int/ictrp/results/jointstatement/en/
Researchers are being contacted individually about unpublished trials identified within the most recent five-year review.

1.6. **Guidance for applicants** is being updated to emphasise the *MRC Policy on Open Research Data: clinical trials and public health interventions* and to highlight requirements for registration, timely publication, and sharing of data from all types of clinical trials, clinical and public health intervention studies.

1.7. Specific guidance is being developed for the **UK Prevention Research Programme** and public health intervention studies.

1.8. The **post-award monitoring** system is being reviewed to improve the completeness and timeliness of annual collection of registration and publication data. The value of additional data sources, such as ISRCTN registry data, to improve automated monitoring of publications is being assessed.

1.9. The invitation to researchers to provide **annual data on outcomes, outputs and impact** (via Researchfish®) is being updated to highlight requirements to provide details of registration, publications and data-sharing for all types of clinical trials, clinical and public health intervention studies.

2. **Update of the 2013 review of Phase III trials**

2.1. In 2013, evaluation of the MRC portfolio of clinical trials supported between 2009 and 2012 found that 94% were registered in a public trials registry, and 89% of trials completed by 2012 had published results. In an update of this review in 2017, trial registration had increased to 98%, and results had been published from 98% of trials.

2.2. In 2017, using data from the MRC Clinical Trials Directory (maintained manually up to 2007) and portfolio (established since 2006), MRC awards for Phase III trials in the UK between 2000 and 2006 were reviewed. Of 122 completed awards, 97% were registered in a trials registry, and over 99% had published results (one trial was reported in a thesis only). Results from 20% of trials had taken over two years to publish; however, all of these had been published by four years after completion.

2.3. Further details of these reviews are provided on the MRC website[^4].


3.1. In 2017, the MRC undertook a five-year retrospective review of registration, publication and data-sharing from clinical trials that had been supported by directly-funded MRC awards made between February 2011 and February 2016.

3.2. Of 107 trials, 94% were publicly registered in a trials registry. Six trials remained unregistered; the investigators were contacted, provided with the MRC policy and asked to register retrospectively. Further follow-up will be undertaken.

3.3. Of the 40 completed trials, 82% reported at least one publication however only half of these appeared to include the main trial results. Around 8% of trials had been complete for over two years without publishing results.

3.4. Over one-fifth (22%) of trials had produced a dataset for sharing with other researchers.

[^4]: [https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/review-of-clinical-trials/](https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/review-of-clinical-trials/)
3.5. Despite overall positive findings, the review highlighted a lack of awareness among a minority of researchers about MRC’s requirements to register clinical trials and intervention studies that are not subject to the EU Clinical Trials Directive (i.e. not involving investigational medical products [IMPs]). Furthermore, many researchers were not registering their studies in the ISRCTN registry despite this being specified by MRC.

3.6. A report of the review and subsequent recommendations have been published on the MRC website\(^5\).

3.7. The review will be repeated in 2018 to evaluate progress, focusing particularly on awards made since the publication of the *MRC Policy on Open Research Data: clinical trials and public health interventions (October 2016)*

---

4. **Further initiatives to increase clinical trials transparency and data-sharing**

4.1. The MRC is keen to promote access to existing clinical trials datasets for further research and recognises that researchers may need new services to support effective data-sharing. A preliminary survey of MRC researchers interested in sharing clinical trials data indicated that over 70% would value access to a data repository (archive) and/or searchable catalogue to enable them to list datasets available to share.

4.2. During 2017, the MRC has developed a new collaborative partnership with Wellcome, the Gates Foundation and Cancer Research UK and this launched as an academic funder consortium on Clinical Study Data Request (CSDR) in January 2018\(^6\). Recipients of MRC clinical trials funding now have access to CSDR services, including a searchable catalogue into which they can enter details of datasets that they would like to share, a data access committee to adjudicate data requests, and support to de-identify data and draw up data-sharing agreements.

4.3. The MRC is also working with the UK Data Service (UKDS) to promote the established UKDS Re-Share facility as a permanent repository that is available to MRC-funded researchers wishing to deposit clinical trials datasets for sharing.

I trust that this response provides the committee with a clear update on the actions being taken by the MRC to address not only the issue of clinical trials transparency, but also to promote the sharing of data from clinical trials in order to maximise the value from our funded research.

*January 2018*

---

\(^5\) https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/review-of-clinical-trials/

\(^6\) http://www.researchresearch.com/news/article/?articleId=1372345