Summary of a joint workshop to explore the ICMJE proposal on *'Sharing clinical trial data'*

Summary

Key conclusions from a workshop of clinical trialists held to discuss the new proposal on *'Sharing clinical trial data'* underlying published studies from the International Committee of Medical Journal Editors (ICMJE) included:

- The overarching **importance of encouraging data sharing** in clinical trials, recognising the **value of sharing** these data.
- A strong preference for establishing a **bottom-up collaborative model** for data sharing with appropriate incentives and safeguards for trialists, rather than one mandated by publishers.
- The need to ensure **informed and responsible re-use of data** for secondary analysis and validation, and **protection of patient privacy.**
- The need to implement **data standardisation** across disciplines to **ensure quality and utility of shared data**, particularly when comparing and combining data from different trials.
- The importance of giving due consideration to the **resource implications** and wider opportunity cost of different mechanisms for sharing data from clinical trials, and possible ways to overcome this such as adopting a proportional approach to sharing data or tabulation of underlying data.
- The need for **clarification about the aims** of the ICMJE data sharing proposal, in order to determine how best to achieve these aims and establish a fit-for-purpose framework.
- Who should 'own' the data sharing framework and the subsequent role of journal editors in implementing this framework.

Introduction

On 8 September 2016, the Academy of Medical Sciences and Wellcome held a workshop to discuss the new proposal on *'Sharing clinical trial data'* underlying published studies from the International Committee of Medical Journal Editors (ICMJE).[1] The workshop, chaired by Professor Sir Michael Rawlins FMedSci, Chair of the Medicines and Healthcare products Regulatory Agency, brought together clinical trialists primarily working in the academic sector. Delegates were introduced to the proposal by Professor Jeff Drazen, Editor-in-Chief of the New England Journal of Medicine, before participating in a discussion on the current proposal.

The ICMJE published its proposal on *'Sharing clinical trial data'* in early 2016. It outlines intentions to request authors to share de-identified individual patient data underlying an article no later than six months after publication and includes proposals to request a plan for data sharing, amongst other suggested requirements. At the workshop there was strong support for sharing data and emphasis on the value of doing so, but questions were raised about whether the ICMJE proposal offered the best mechanism for doing this.

[1] Taichman, D *et al.* (2016). *Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors*, Ann Intern Med, 164**(7)**, p505-506

The discussion points outlined below reflect the views of the attendees expressed at the meeting, and do not necessarily represent the views of all participants, their organisations, the Academy of Medical Sciences or Wellcome.

Building a data sharing framework

There was a wide ranging discussion on the challenges that need to be overcome to enable a successful framework for sharing of the clinical trial data underlying published studies in journals.

Validation and re-use of data

Some concerns were voiced about the validation and re-use of clinical trial data by secondary analysts. Delegates stressed that contextual knowledge of the original clinical trial is critical, and that sharing data with researchers who lack this knowledge may result in incorrect interpretations and misleading secondary analyses. There was concern that the ICMJE proposal may encourage 'data dredging' (misuse of data mining to examine multiple hypotheses in the same dataset), thus increasing the risk of false positive results. There was also apprehension that incorrect secondary analyses could be used maliciously to allege falsification of study results, potentially undermining public trust in clinical trials. When legitimate errors in an original trial *are* identified, these must be reported and managed appropriately according to the type, and impact, of the error. Further to this, delegates questioned whether secondary analysts are accountable for informing the data custodian of serious, incidental findings affecting a patient.

Delegates described the more general challenges posed with information security, for instance when releasing data from long-term clinical trials or a restricted patient cohort. Therefore it is important to ensure that patient privacy is protected.

When to share data following publication

There was limited discussion around the precise timelines for data sharing, however, delegates did note that early data sharing could present an issue for junior researchers who tend to derive publications from subsequent analyses of clinical trial datasets generated by their team. It was observed that the proposed publication plans and embargoes on data may help to overcome this issue. In addition, one delegate noted that some of the responses received to the consultation on the ICMJE proposal highlighted potential difficulties for junior researchers in low- and middle-income countries, in particular, who may find it increasingly difficult to conduct secondary research within pressured timelines when compared with junior researchers in areas with more resource. Rapid data sharing following publication may have the potential to compromise the work of these researchers.

Data standardisation

Data standardisation is central to enabling re-use of shared data and delegates highlighted the importance of universally recognised data standards for the utility of shared data. Data standardisation, whilst essential, can be resource intensive but wider implementation of data sharing could lead to standardisation becoming part of routine practice. One delegate suggested that the work by the COMET (Core Outcome Measures in Effectiveness Trials) initiative could be used as a starting point for establishing wider data standardisation across all clinical trials.[2] It was

[2] The COMET initiative is working to standardise reported outcomes of trials in different clinical disciplines to facilitate better data sharing practices: http://www.comet-initiative.org/

emphasised that data standardisation will require a fit-for-purpose governance framework and high quality protocols.

Resource implications

With thousands of clinical trials published annually, many delegates cautioned of the need to consider the opportunity cost of making all underlying patient data from all clinical trials available in a usable form. There were two alternative options proposed by delegates to address these resource implications, with the first suggestion being that a proportionate approach could be taken to sharing clinical trial data. For instance, only trials likely to cause significant changes to clinical care could be prospectively selected for data sharing. Delegates also proposed another option where investigators could provide detailed tabulations of underlying data for each clinical trial, which would also address concerns around access to adverse event data that are not published. These tabulations would act as an alternative to sharing all data and in circumstances where further data are required, a collaborative approach could then be taken.

The role of medical journals

There was general consensus on the overarching need to encourage data sharing in clinical trials, as well as the significant value of sharing such data. In addition, there was wider agreement that this should be a bottom-up, collaborative approach modelled on current exemplary data sharing practices. Delegates emphasised that currently, collaborative data sharing models are often used successfully between academic clinical trialists. One delegate also observed that mandatory pooling of data through formal mechanisms – as proposed – may not engender a collaborative environment but rather an adversarial one.

It was noted that the new European Clinical Trial Regulation will come into effect in 2018. This will mandate measures to introduce greater transparency, including submission of a full clinical study report for trials which have led to a request for marketing authorisation. Delegates noted that any data sharing framework proposed by ICMJE should not duplicate, nor be more unnecessarily prescriptive than, these regulatory and other existing requirements.

There was a strong call amongst delegates for the ICMJE to further clarify the aims of its data sharing proposal, in order to determine how best to achieve them. Delegates questioned whether journals should do more work to ensure that prospective clinical trial registration is fully effective before implementing a data sharing framework. Whilst recognising that journals play an important role in enhancing transparency and maximising the benefits of clinical trials – by promoting the knowledge gained and ensuring that the outcomes are clearly communicated – some delegates queried whether journals were the appropriate body to establish a data sharing framework.

Conclusions

In general, delegates agreed on the importance of data sharing and that this, if properly done in a way that both protects patient privacy and rewards the contribution of clinical trialists, is welcome. They emphasised that some academic clinical trialists already share data and collaborate with fellow researchers, and that most publicly funded research in the UK mandates data to be made available if a reasonable request is made. Many delegates indicated a preference for continuing with this collaborative approach. It was recognised, however, that a formal mechanism and vehicle

to manage data sharing in an independent and transparent manner could be helpful, and currently does not exist, but should be balanced against the opportunity cost of such an approach. It was also acknowledged that lessons on data sharing could be learnt from other disciplines such as genomics where this is already established as part of common practice.

This document reflects the views of the attendees expressed at the meeting and does not necessarily represent the views of all participants, their organisations, the Academy of Medical Sciences or Wellcome For further information, please contact Liberty Dixon, Policy Officer, Academy of Medical Sciences (Liberty.Dixon@acmedsci.ac.uk; +44(0)20 3141 3222) or Jennifer O'Callaghan, Clinical Data Sharing Manager, Wellcome (J.O'Callaghan@wellcome.ac.uk; +44(0)20 7611 7323).

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