

CTT Collaboration Independent Oversight Panel

Minutes of teleconference on Wednesday 11th October 2017

Attendees

Oversight Panel: Emily Banks, Michael Blastland, Stephen Evans, Robert Temple, Peter Weissberg, Janet Wittes; *CTT, Oxford:* Jane Armitage, Colin Baigent, Rory Collins, Christina Reith

Apologies

CTT, Oxford: Jonathan Emberson

Members of the panel were thanked for agreeing to join the Oversight Panel. The panel members introduced themselves and outlined their backgrounds. The following topics were discussed:

Background to CTT Collaboration and current adverse event (AE) project

The reasons for the foundation of the Cholesterol Treatment Trialists' (CTT) Collaboration and its previous work (as detailed in the briefing document) were summarised. The existing CTT dataset includes individual participant data (IPD) from large-scale (≥ 1000 participants), long-term (≥ 2 years scheduled treatment duration) randomized controlled trials of statin therapy, and includes information of major vascular events, cancers and deaths.

In response to ongoing concerns about statin therapy, which has affected statin uptake and hence has become a major public health issue, the CTT Secretariat at the Clinical Trial Service Unit (CTSU) in Oxford has initiated a new programme of work to collect and analyse individual participant data on all types of adverse event (as well as laboratory and co-medication data) that were recorded in the statin trials eligible for the CTT meta-analyses in order that comprehensive analyses of all possible effects (either adverse or beneficial) of statin therapy in these trials can be conducted.

The CTT AE project is progressing well. The protocol was published in 2016 and ethics approval obtained. The project has been presented to members of CTSU's Departmental 'Participant Panel' (consisting of people who have previously participated in one or more of its clinical trials) who indicated that they are strongly supportive of the project and would want their trial data to be used maximally (even if their original trial consent form had not explicitly mentioned use of data meta-analyses). It is expected that data will be available from 27 of 28 eligible published trials, with 21 such trials having already provided this data at the time of the TC (16 via pharmaceutical company data sharing platforms and 5 via direct data transfer).

Major challenges of the CTT project are: (i) the scale of the project (the data received from 21 trials to date include ~ 15 million records); (ii) the heterogeneity of the types of data received (which is being addressed by converting the data into a common format based on CDISC SDTM and MedDRA methodology); and (iii) the different forms of access to data from several different portals in most cases, rather than the data actually being provided to the Secretariat.

The plan is to construct extensive tabulations of results from analyses (eg, webtables based on MedDRA format as has previously been done for several CTSU trials) and to make these publicly available so that their findings can be explored in detail.

Data sharing

The topic of data sharing was discussed; in particular it was noted that:

- The original datasets of major vascular events, deaths and cancers were provided to the CTT Secretariat on the understanding that the Secretariat would not be share the data with third parties.
- For this new CTT AE project, legal data sharing agreements (DSAs) prohibit sharing with third parties and the data would not have been provided in the absence of such DSAs.

The CTT Collaboration seemed likely to be the only group that was both willing to put in the considerable effort to bring together these AE data and had the expertise to harmonise the data and conduct the analyses. Consequently, the CTT Collaboration decided to establish the Independent Oversight Panel to help ensure that there was appropriate transparency and independent oversight of the process.

Composition and remit of Independent Oversight Panel

The question of whether the Panel should include a wider range of people (including, for example, those who have been critical of statin therapy or of the previous work of the CTT) was discussed. However, the Panel agreed that:

- The aim of the Panel should be to include individuals who can be objective and impartial about the issues rather than trying to achieve ‘balance’ by including a range of views.
- The current Panel includes people who have not previously had a particular ‘stance’ or made public statements in relation to statin therapy (Michael Blastland, Robert Temple and Janet Wittes), and also a member (Stephen Evans) of the BMJ Editor’s review panel that was established to consider, and declined, a request for retraction of articles by Abramson et al and Malhotra.

The panelists therefore felt that the current Panel membership is sufficiently balanced, but further people could be invited to join the Panel in the future if that was considered warranted.

Oversight Panel Terms of Reference

The proposed terms of reference of the Oversight Panel considered by the Panel were:

1. Monitor progress with pre-specified and exploratory analyses of the updated CTT database.
2. Advise on the interpretation of analyses that are specified in the published protocol and, as the Panel considers appropriate, to recommend additional exploratory analyses.
3. Scrutinise requests from both CTT Collaborators and external parties for particular analyses, and advise on appropriate ways to address and interpret them.
4. Seek an external statistical audit of particular analyses if required to address concerns.
5. Report publicly on the governance arrangements of the project, in particular (but not limited to) the approach to requests for data-sharing and additional analyses.
6. Ensure that the findings are presented in a balanced way so that doctors, patients and the public can make informed decisions.

Members of the Panel suggested the 5th point be modified to “Advise on the governance arrangements...”

The Panel members felt that questioning by external parties should be welcomed, but responses be intended to address the wider public, clinicians and policy makers.

Posting of Oversight Panel details on CTT website

Panel members agreed that it would be helpful to post the following information on the CTT website (www.cttcollaboration.org) in relation to the Oversight Panel:

- Member names and brief background/profile;
- Declaration of interests for Panel members; and
- Panel Terms of Reference

Action Points and next meeting

- Oxford to circulate Revised Terms of Reference to the Panel for review and approval
- Oxford to provide Panel with: draft profiles for review and revision; draft Declaration of Interests text for review; relevant external comments on the planned AE project.
- Agreed that the next meeting should take place in approximately 6 months’ time. A Doodle poll to this effect will be sent to Panel members.