CTT Collaboration Independent Oversight Panel
Minutes of teleconference held on Monday 17th September 2018

Attendees
Oversight Panel: Emily Banks, Michael Blastland, Stephen Evans, Peter Weissberg, Janet Wittes
CTT, (CTSU, NDPH) University of Oxford: Colin Baigent, Kate Bird, Lisa Blackwell, Rory Collins, Kelly Davies, Heather Halls, Charlie Harper, Lisa Holland, David Preiss, Christina Reith, Enti Spata, Anne Whitehouse
Apologies
Oversight Panel: Robert Temple
CTT, Oxford: Colin Baigent, Boby Mihaylova

Agenda
1. Review and approval of minutes from last TC
2. Panel Declaration of Interests forms
3. Update on project progress/recent CTT Collaborator meeting
4. Funding update
5. Public engagement
6. AOB

1. Welcome and review and approval of last minutes from last TC

The Panel was welcomed, and the recently appointed Director of Communications and Public Engagement (Anne Whitehouse) at the Nuffield Department of Population Health (NDPH, of which the Clinical Trial Service Unit & Epidemiological Studies Unit [CTSU] is a part) introduced.
The minutes from the last Oversight Panel TC (which took place on Wednesday 28th February 2018) have been agreed, and are publically available via the CTT website:
https://www.cttcollaboration.org/independent-oversight.

2. Declaration of Interests Forms

All Independent Oversight Panel members have completed a Declaration of Interests form, and such forms have been posted on the CTT website: https://www.cttcollaboration.org/independent-oversight. The signed electronic copies are held on file in Oxford to protect against identity fraud.

3. Update on project progress

The CTT individual participant data (IPD) meta-analysis project (protocol: *American Heart Journal* 2016; 176: 63-9) to analyse all adverse events (AEs) in eligible large randomized trials of statin therapy is progressing well. The data for each participating trial is being processed so as to be ready for meta-analysis in 3 sequential phases with resolution of queries (or making of appropriate assumptions) at each stage as follows:

- **Phase 1**: Review of **documentation** including detailed review of trial protocols and case report forms (CRFs) to ascertain what was collected
- **Phase 2**: Review of available **tabular data** (to identify potentially key missing/additional CRFs)
- **Phase 3**: **Individual participant data** (most labour-intensive phase)
    - ***Stage 1: Selection of relevant datasets***
        - Number of participants checked to ensure number matches original CTT dataset; IDs also checked to see if correspond to those used in original CTT dataset; if not, matching exercise carried out.
        - Datasets checked against variables in CRFs to identify pertinent missing data.
        - If more datasets received than expected, assessed for pertinence.

- ***Stage 2: Mapping of events and production of tabular summaries***
  - Conversion of trial IPD into a common domain-based format based upon the methodology used by the Clinical Data Interchange Standards Consortium Study Data Tabulation Model (CDISC SDTM).
  - All AEs mapped to a common CTT dictionary based on MedDRA v 20.0 via an automated, self-learning, custom-built process
  - IPD tabular summaries produced, and then checked against previous publications/tabular data.

When the protocol was finalised in March 2016, this yielded 28 published trials, 27 of which were able to provide data. At the time of the last TC in February 2018, data from 24 of these 27 trials had been received. The project remains one of high scale and complexity, but major progress has been made since the last TC in February including:

- IPD now received for 27 trials, with PROSPER being the most recently received data.
- Formal agreement has now also been secured from the HOPE-3 trial (*N Engl J Med* 2016; 374:2021-2031) Collaborators for this dataset to contribute to the CTT analyses.
- Further testing of the CTT MedDRA-based coding system.
- For those trials for which data has been received to date, many have undergone substantial 'Stage 1' processing, and mapping of trial data to CDISC SDTM format is underway.
- Review of available multiple hypothesis testing methods.

This progress was presented at a CTT Collaborator meeting held in tandem with the European Society of Cardiology (ESC) Annual Congress in Munich on Monday 27th August. The feedback from the Collaborators attending this meeting was that substantial progress had been made with this huge task, and that the methodology is appropriate and novel. The Panel reiterated these sentiments.

The predicted papers from the project will be a comprehensive series of topic-specific publications (with an over-arching methodology paper) which will reflect the outcomes outlined in the 2016 CTT protocol. All such publications will present their findings in terms of the balance of overall benefits versus risks.

4. Funding

A British Heart Foundation (BHF) project grant was awarded to the project in April 2018.

5. Public engagement

Patient and public engagement remains a key focus on this project and methods to enable this were discussed, such as creating a series of short videos/animations.

6. AOB

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.