

## **Funding and independence of research at the Clinical Trial Service Unit & Epidemiological Studies Unit (“CTSU”) of the Nuffield Department of Population Health, University of Oxford**

CTSU is a world leader in the conduct of large-scale randomised controlled trials, and combined analyses (“meta-analyses”) of detailed data from randomised trials, which provide reliable evidence about the safety and efficacy of treatments. Such trials and meta-analyses – which may be of existing or new treatments – are essential to help guide health-care strategies appropriately.

The conduct of trials involving thousands of participants, often in multiple countries around the world, requires a substantial research effort and can be very costly. CTSU has been successful in receiving large research grants from government (e.g. National Institute for Health Research, Medical Research Council) and charitable sources (e.g. British Heart Foundation), as well as from the pharmaceutical industry. Given the costs involved in running large studies, industry funding helps to ensure that the trials are of sufficient size and scope to assess the safety and efficacy of treatments reliably.

**In order to ensure that CTSU’s research is conducted independently of all sources of funding, we have had a number of measures in place for many years:**

### ***CTSU policy on consultancies, honoraria or other financial benefits***

CTSU has had an explicit policy for about 30 years of not accepting any personal payments directly or indirectly from industry. It only seeks reimbursement to the University of Oxford of the costs of travel and accommodation to participate in scientific meetings.<sup>1</sup> This approach ensures that decisions to give lectures or advice are determined by the scientific value of doing so, and not by personal gain.

CTSU staff are also advised that it is generally not appropriate to have shares in tobacco, alcohol, drug or biotechnology companies which might be directly or indirectly affected by CTSU publications or public statements.<sup>1</sup> (Professor Rory Collins holds no shares in any company.)

### ***Obtaining funding for CTSU research***

CTSU decides what trials it wants to do for scientific reasons and then tries to persuade industry and non-industry sources to cover the costs. For example, for our Heart Protection Study, it took several years to obtain the funding, with half coming from the UK Medical Research Council (government) and the British Heart Foundation (charity), one quarter from Merck (supplier of simvastatin) and one quarter from Roche (supplier of vitamins E, C and beta-carotene). This trial showed that statin therapy reduced the risk of heart attacks and strokes safely for a wide range of patients at high-risk of such events, but the vitamins produced no benefit; both results were published alongside each other.<sup>2,3</sup>

In other instances, CTSU has obtained all of the necessary funding from industry for trials intended to address important public health questions that would not otherwise be answered. For example, our most recently completed THRIVE trial (funded by Merck) showed that niacin – which has been used routinely for over 50 years to modify cholesterol – did not reduce the risk of heart attacks and strokes, but did increase the risk of other serious adverse events (such as diabetes, bleeding and infections). As soon as those findings emerged, they were provided to regulatory authorities, presented publicly, and will soon be published prominently with detailed tabulations of adverse events.<sup>4</sup>

All of CTSU’s research that receives industry funding is governed by University of Oxford contracts which protect our independence in the way that we design, conduct, analyse, interpret and report the results of the research. Indeed, in the case of all of our clinical trials, CTSU (not the funders) hold the databases and control all of the analyses, with no restrictions on what is reported.

### ***Cholesterol Treatment Trialists’ (CTT) Collaborative meta-analyses of statin trials***

This collaborative effort was established in the early 1990s.<sup>5</sup> It is coordinated jointly by the CTSU in Oxford and the National Health and Medical Research Council Clinical Trials Centre (CTC) in Sydney, with the database held securely and analysed in both locations. It is not funded by the pharmaceutical industry; instead, funding has been provided by government (Australian National Health and Medical Research Council, UK Medical Research Council, European Community Biomed Programme) and charities (Australian National Heart Foundation, British Heart Foundation, Cancer Research UK).

The aim of the CTT collaboration was to bring together data for each patient in all of the large-scale randomised controlled trials of statin therapy in order to be able to assess – more reliably than was possible with any of the individual trials – the effects of cholesterol-lowering statin therapy on heart attacks, strokes, revascularisation procedures and vascular deaths among different types of patient (for example, men and women; young and old; higher and lower risk).<sup>5</sup> The CTT collaboration also aimed to assess any effects of statins on other types of death and on site-specific cancers.

The academic investigators who ran the statin trials, and the funders of those trials, agreed to provide the required data on major vascular events, cause-specific mortality and site-specific cancer on the understanding that their data would not be released to third parties without their explicit permission. (Note: Data on all other adverse events – including muscle aching or myopathy – were not sought, and so the CTT collaboration does not currently have access to such data for meta-analyses.<sup>5</sup>)

Obtaining these individual patient data from each of the trials, running careful consistency checks of them, conducting extensive analyses of the collective database (involving about 170,000 patients in 27 trials) and reporting the results in a series of papers has been a substantial collaborative effort.<sup>6-8</sup> As a consequence of this effort, the CTT collaboration has provided information that would not have otherwise have emerged about the effects of statins on these outcomes for different types of patient which has contributed considerably to helping doctors to use statins more appropriately.

### ***CTSU patent for statin-related myopathy genetic test***

CTSU's SEARCH trial (funded by Merck and governed by an Oxford University contract, as described above) was set up to determine whether more intensive lowering of cholesterol levels with 80mg daily simvastatin might be better than a standard 20mg daily dose. We found that the higher dose caused more cases of "myopathy" (defined as muscle symptoms plus substantial elevation of blood levels of the muscle enzyme creatine kinase), and also identified a genetic variant which predisposed patients to an increased risk of myopathy. This information was reported prominently.<sup>9,10</sup>

In order to ensure that a test for this genetic variant was made available to patients, the University took out a patent on this finding and licensed it to Boston Heart Diagnostics who provide the test. Consistent with CTSU's approach to personal payments (see above), its staff waived their rights to any income from this discovery, which has instead been made available to support research.

### ***Awards to CTSU for contributions to medical research and public health***

From time to time, CTSU scientists are awarded medals or prizes by scientific societies, charitable foundations or industry. In accordance with CTSU's policy (see above), no money associated with awards from industry is accepted by staff. For example, in 2004, Rory Collins was awarded the Pfizer Medal which came with a £50,000 unrestricted research grant to Oxford University. (Professor Collins has not received other research funding from Pfizer, although he did serve unpaid on the Steering Committee for the ASCOT trial of atorvastatin, which was coordinated by Imperial College, London.)

**CTSU (1 July 2014)**

## References

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