Reviewer’s report

Title: Current Problems with Large-scale Clinical Trials Examining Cardiovascular Diseases in Japan: Evidence from a Questionnaire Survey

Version: 1 Date: 25 January 2011

Reviewer: Athina Tatsioni

Reviewer’s report:

The issues raised by Sawata et al. in the present paper are interesting and related to important aspects of funding and infrastructure of large-scale CVD trials conducted in Japan. Their findings may guide recommendations on reporting large-scale trials in Japan in order to improve transparency. Although there is no access to the original data, they look sound. The writing is acceptable. The authors may consider the following suggestions for their manuscript:

Major Compulsory Revisions

Title

1) The authors may consider change the title to “Funding and Infrastructure among Large-scale Clinical Trials Examining Cardiovascular Diseases in Japan: Evidence from a Questionnaire Survey

Background

2) The authors may consider delete: “A large number of non-clinical and clinical investigations are required to obtain adequate evidence to improve medical treatment. Additional evidence could be beneficial for the medical practice of many health care providers. Clinical evidence can be used to inform clinical practice guidelines, and can benefit patients by providing a rationale for determining the most appropriate treatment.”

3) The authors may consider delete: “Clinical trials must be conducted to obtain adequate clinical evidence. Large-scale clinical trials involving thousands of participants are particularly important in interventional clinical trials of cardiovascular diseases to evaluate the risk reductions of cardiac events and/or deaths, because of the need to evaluate the incidence of cardiovascular events with relatively low incidence. Such clinical trials provide evidence regarding the most appropriate treatment regimen for preventing cardiovascular and metabolic diseases.”

4) The authors may consider delete: “This study was a double-blinded randomized parallel-group controlled trial carried out across 48 institutions from 1993 to 2000. The primary end point was a combined measure of cardiac events, defined as cardiac or non-cardiac death, recurrent non-fatal myocardial infarction, coronary revascularization, and hospitalization because of worsening angina or congestive heart failure. In total, 888 of 1,163 participants with acute myocardial infarction (AMI) were eligible for the full analysis set (FAS).
Participants were randomly divided into two groups; 422 participants received angiotensin-converting enzyme (ACE) inhibitors and 466 did not receive ACE inhibitors. The mean follow-up period was 5.8 years.

5) Where does the following paragraph refer? “After the JAMP study, we found a number of issues surrounding large-scale clinical trials. In particular, the funding sources and infrastructure of clinical trials were found to be major issues. Our results indicated that financial and infrastructural resources must be maintained to adequately conduct clinical trials. However, a substantial cost is involved, and obtaining funding is thus essential for clinical trials. The infrastructural environment surrounding clinical trials is currently inadequate, although this situation is improving.” Does it refer to the present or an authors’ previous study? If it refers to the present study, it should be removed from the Introduction and placed in the Results section. If it refers to a previous study, authors should mention a reference.

6) Please change “…Considering the current situation surrounding the medical and pharmaceutical industries as well as the researchers, it is impossible to completely avoid conflicts of interest of researchers…” to “…Considering the current situation surrounding the medical and pharmaceutical industries as well as the researchers, it would be unlikely for researchers not to have conflicts of interest…”

7) The authors may consider avoid using numbers to report the purpose of the study. Instead, authors may consider the following phrase: “In this study, we conducted a survey among trial sponsors to clarify the current funding and infrastructural environment surrounding large-scale clinical trials in cardiovascular and metabolism diseases in Japan”

8) It is unclear how the survey would help “To find ways of improving the environment surrounding clinical trials in Japan more generally”. It may help identify certain issues in research infrastructure. Therefore, the authors may consider clarify or remove the previous phrase.

9) The authors may consider delete: “To this end, we surveyed the current situation using questionnaires. In this article, we report the results of our survey regarding relevant issues surrounding large-scale clinical trials for cardiovascular diseases in Japan.”

10) The authors may consider delete or move the following phrase to Discussion: “These results will contribute to the future improvement of conflict-of-interest management in Japan as well as other countries.”

Methods

11) How “…the individual with the most responsibility…” was defined?

12) Please clarify what “…29 newly identified…” means and how they were identified. Did authors use the same process as for the 90 trials?

13) A brief presentation of the questionnaire content, i.e., number of questions, type /categories /content of questions, time needed to fill in the questionnaire. Did authors pilot any survey before they perform the study?
14) What do authors mean by “true endpoints”? Do they mean “hard outcomes”?

15) The authors may consider compare the results between studies sponsored by industry/private sector vs. studies with a public sponsor.

Results

16) A “Figure 1” to present the questionnaire may be informative.

17) A formal statistical test might be useful to compare number of participants between respondents and non-respondents in Table 1.

16) Table 2 may be redundant. The information may be given only in the Results section text.

18) The authors may consider merge Tables 3 to 7, present results separately for studies sponsored by industry/private sector vs. studies with a public sponsor and formally compare them. For number of participants (Table 3), median with interquartile range (IQR) would suffice.

19) Please clarify “self-funded” in a footnote for Table 2. Please also, clarify what “other” included in a footnote for Tables 3, and 7.

Discussion

20) Discussion should be shortened. The authors should not include arithmetic results in their Discussion section. These results have already been reported previously in the paper. In addition, if the authors compare the results between studies with a private sponsor vs public sponsor, the Discussion should also include comments on these results as well.

21) The following sentence is not related to the present study findings: “This finding indicates that unclear funding sources could potentially bias trial results.”

22) What do authors mean by “true endpoints”? Do they mean “hard outcomes”? 

23) The authors may add one paragraph to comment on the limitations of their study, i.e., high non-response rate, data collected through a survey process, lack of a control group.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.