Reviewer's report

**Title:** Modified versus standard intention-to-treat reporting: Are there differences in methodological quality, sponsorship, and findings in randomized controlled trials? A cross-sectional study.

**Version:** 1 **Date:** 24 November 2010

**Reviewer:** Jocelyn Gravel

**Reviewer's report:**

General evaluation:
Is the question posed by the authors new and well defined?
As mentioned in the introduction, the mITT analysis is growing in the medical literature. This was a study to compare methodological quality of mITT in comparison to regular ITT. There are many objectives in the study. It would be important to mention that the objectives of the study were decided before analysis because when I read the abstract published in 2007 (ref #6), there is no mention of the evaluation of the association between mITT and sponsorship or the role of industry. In this abstract, the main objective was: “The aim of this study is to highlight the methodological quality of randomised controlled trials using mITT with respect to trials using a true ITT analysis. Specific focus will be given to the handling of post-randomisation exclusions. “ Was the study registered somewhere to insure that the objective of the study did not change during the process of analysis.

Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
The methods are excellent. This is the strength of the manuscript.

Are the data sound and well controlled?
The result section is clear and concise. It would be very informative for the readers to know what were the major “modifications”.

Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes

Are the discussion and conclusions well balanced and adequately supported by the data?
This is the main weakness of the manuscript. While the primary objective of the study was to: “investigated whether the reporting of mITT in RCTs was associated with industry sponsorship, the presence of authors’ conflicts of interest, and favourable findings”, the discussion mainly discuss about the relationship between industry and publication. I would recommend that the author
focus on their findings and limit their extrapolation regarding the relationship between industry and research. They may be right but their data do not support affirmation such as: “Therefore, while on one hand they try to adhere to some principles of quality trial design (e.g. allocation concealment, blinding), on the other hand generating deviation from the influence the intention-to-treat that results in multiple and unpredictable descriptions of the mITT” (page 13 second para) or: “industry sponsorship of studies may influence the study design of RCTs by aiming to favour the sponsored drug.” (page 14 para 5).

Also, the authors should put their results in the context of other studies that evaluated the use of ITT in the medical literature:

Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ. 1999;319:670-4


Ruiz-Canela M, Martínez-González MA, de Irala-Estévez J. Intention to treat analysis is related to methodological quality. BMJ. 2000;320:1007-8

Do the title and abstract accurately convey what has been found?

Title is correct

The data do not support the last sentence of the abstract. I would retrieve it.

Is the writing acceptable?

Yes but English is not my first language.

Major Compulsory Revisions

1. In the methodology section (page 5 last para), the classification of the ITT and mITT is well described. It would be important to report what were the main “modifications” in the result section. I bet that it will be related to the exclusion of patients that did not receive at least one dose of medication. If this is the case, it is not surprising to find an association between mITT and exclusion of patients post randomisation.

2. The data do not support the conclusion of the abstract: “The use of mITT should be abandoned.” The data show that there was no association between the use of mITT and:
   - Quality of reporting
   - Methodological quality
   - Reporting of a favourable results

However, there was an important association between the use of mITT and:
   - Private sponsorship
- Presence of authors’ conflict of interest
- Exclusion of patient post randomization*

*The exclusion of patient is not a surprise. This is probably why the author named their analysis as “modified ITT”.

I would recommend the following conclusion for the abstract: “We found that the mITT trials were significantly more likely to perform postrandomization exclusions and were strongly associated with industry funding and authors’ conflicts of interest.”

3. It would be important to mention that the objectives of the study were decided before analysis because when I read the abstract published in 2007 (ref #6), there is no mention of the evaluation of the association between mITT and sponsorship or the role of industry. In this abstract, the main objective was: “The aim of this study is to highlight the methodological quality of randomised controlled trials using mITT with respect to trials using a true ITT analysis. Specific focus will be given to the handling of post-randomisation exclusions.” Was the study registered somewhere to insure that the objective of the study did not change during the process of analysis?

4. As mentioned, the author should report what were the major “modifications”.

5. Most of the discussion section is dedicated to the relationship between industry and research. The authors should limit the discussion section about industry and comment about previous studies that evaluated mITT. Also they should put their study in the context of previous study evaluating mITT.

6. The author should modify the conclusion of the manuscript to report what their data support: The mITT trials are more likely to have post randomization exclusions and be associated to industry funding. However, their study, there was no association between the use of a mITT and quality of reporting, methodological reporting and reporting of a favourable result.

Minor Essential Revisions

7. Page 5 second para, the # of the figure is not written.

Discretionary Revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I declare that I have no competing interests'