

Determining the Level of Statisticians' Participation in Canadian-based Research Ethics Committees

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1 Background

In many research institutions, local research ethics committees (RECs) (henceforth to be referred to as research ethics boards (REBs)) are trusted to advance or safeguard the research ethics at the institution. These are autonomous bodies whose primary role is to advance the protection or safety of human or animal subjects in medical research and to promote or foster high ethical standards for the conduct of research. As defined by the Group of Medical Advisors (GMA-5) [1] *ethics* are “principles of right conduct, guiding what ought to be done. Although they may reflect enduring moral values, ethics are not static but evolve with time (MR87)”. As attested to by the rigorous guidelines that include the Belmont Report [2], NIH95 [3], the Helsinki Declaration [4], CIOMS93 [5], CIOMS91 [6], CIOMS85 [7] and GMA-5 [1], high ethical conduct for research involving human subjects has appropriately taken centre stage, with some degree of consensus by the international community on what proper ethical conduct for research involving human beings should entail; the Nuremberg code [13] is one such example. For detailed list of bibliographies on ethical issues in research involving human subjects, we refer the reader to the National Library of Medicine website:

(http://www.nlm.nih.gov/pubs/cbm/hum_exp.html)

In addition to abiding by the Nuremberg code, Canadian researchers are also encouraged to abide by the Tri-council Policy Statement [9] and the ICH Harmonized Tripartite Guideline [8]. The Tri-council comprises the Canadian Institutes of Health Research

(CIHR) (formerly called Medical Research Council of Canada (MRCC)), the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Social Sciences and Humanities Research Council of Canada (SSHRC). These guidelines form the basis of the role of REBs. Different guidelines include various ways in which an REB could be formed comprising different members with relevant skills to make fair and effective evaluations of the ethical standards of the projects submitted to the committee. In Canada, according to the Tri-council Policy Statement (Article 1.3), the REB shall consist of at least five members, including both men and women, of whom “at least two members have broad expertise in the methods or in the areas of research that are covered by the REB”. In some REBs, one such member is a (bio)statistician (William et al [10]). The involvement of a statistician in REBs has been advocated by several authors including Vail [31], Alberti [28], Altman ([26], [27]) and Newell [30]. Based on his experiences as a biostatistician on a UK-based REB, Vail [31] describes the workload involved and some of the statistical issues arising in submissions to the REB with emphasis on sample size.

William et al [10] noted that in recent surveys by local RECs and researchers done by Foster and Holley [15] and Holley and Foster [16], there was some consensus on what questions ethical reviews needed to ask, which include (from William et al [10]):

- Will the research project, as designed, answer the question?

As noted by William et al and supported by Foster [14] and the Nuremberg code [13] (paragraph 2), this question clearly indicates the view that the validity of the scientific methods used in the research is to be assessed in the ethics review. This view is also supported by the GMA-5 [1] guidelines with regards to the functions of a Scientific and Ethical Review Committee (SERC) in the review of radiological studies (emphasis is ours):

“...The initial function of the SERC is to review the research protocol and assess its *scientific validity as well as its utility*. The research project would include sufficient scientific information about such factors as the current state of knowledge, *research design, methodology*, risks and benefits, and radiological requirements. The SERC should check accuracy of projected doses, *review of the statistical analysis*, ensure that radiation protection safeguards are in place and that quality assurances principles (including dosage form and safety) have been adequately addressed.”

The issue of validity of research results plays an important role in evidence-based medicine [37]. Jones et al [17] reported “poor study design” as the second most frequent reason for requiring revisions of protocols. The first was “improperly designed consent form”. Other examples that highlight the important role of statistics in medical research include the following questions which are part of the list of questions that members of one of the local REBs are recommended to consider when reviewing all submissions: (i) Are the issues of reliability and validity of the project’s instruments (questionnaires, tests) noted in the proposal? (ii) What is the sample size and how has this been calculated? (iii) Are the methods clear: what is to be done, with whom, when, how, where, and why?

2 The Role of Statistics and Statisticians in Research

As indicated above, statistics is an important tool in any research endeavour and as the title says (Rao [11]; Lecture 3, p.96) “statistics is an inevitable instrument in search of truth”. As defined by V. Barnett (Rao [11])

“...statistics is the study of how information should be employed to reflect on, and give guidance for action in a practical situation involving uncertainty.”

Piantadosi ([12], Chapter 2) provides more details on the connection between medical research in the context of clinical trials and statistical reasoning, and this further highlights the paramount importance of statistics in medical research. As in peer-review of funded projects or manuscripts, proposals going through an REB have to pass the minimum statistical

and ethical standards, and statisticians play a crucial role in this regard. The primary role of a statistician is to provide independent advice to researchers on statistical issues shared by many research projects, with the aim of enhancing or safeguarding scientific integrity. These issues include study design, sample size, randomization of subjects, and data collection instruments, to mention a few.

There has been extensive research on reporting of results of clinical or medical studies by several authors: examples include Bailar and Mosteller [32]; Gehlbach [33]; Walter [24] and, Altman and Bland [25]. Guidelines on reporting have also been disseminated by different working groups such as the International Committee of Medical Journal Editors [34], the Standards of Reporting Trials Group [36], and the Working Group on Recommendations for Reporting Clinical Trials in the Biomedical Literature [35]. For detailed information on the topic of reporting clinical trials, see Piantadosi ([12], Chapter 14) and references therein. Table 1 below summarizes the results of the literature search on the topic using Pubmed. It is clear from the results in Table 1 that research on statistical aspects of trials or assessment of these issues from an REB’s perspective has been one of the least studied aspects of medical research. Based on this background we decided to survey Canadian-based REBs to determine the level of statisticians’ participation on REBs. We hope that the results will highlight the importance of the evaluation of research validity, and hence statistician membership in REBs. Further, we hope this will raise debate on whether statistician REB membership is needed after all and if so how this can be achieved or enhanced.

Table 1: Number of recalls/hits for different search strategies using Pubmed

Search Terms	Number of Hits
Medical research ethics statistical methods	141
Medical research ethics statistical issues	56
Research ethics statistical issues	85
Ethical issues statistical methods	196
Ethical issues statistical issues	106
Research ethics committee statistical issues	5
Research ethics board statistical issues	1

3 Objectives of the paper

The objective of this paper is to report the results of a national survey of Canadian-based REBs. This was a cross-sectional study whose primary purpose was to elicit responses from chairs of REBs on the level of statisticians' participation on such committees. Specifically, we were interested to know how many of these committees have a statistician in their membership. For those that do not have one, we were interested to know (i) why they do not have one (ii) how they deal with statistical issues (iii) whether they consider that their committee needs a statistician

4 Methods

All active REBs in Canada have to register with the National Council on ethics in Human Research and this information is updated continuously on the web (<http://ncehr-cnerh.org>). This registration information includes contact person, physical and email addresses, and location (province and institution) of the REB. At the time of our study, March 2003, there were 224 REBs registered from which a simple random sample of 140 was obtained. This study was approved by the McMaster University Research Ethics Board. A short survey questionnaire, information sheet and consent form were mailed out to the contact person of each selected REB, to be filled by the chair of the REB in March 2003. We adopted the Dilman's [38] approach in order to increase our response rates. Thus, approximately one month after the initial mail-out, a reminder email was sent to all these that had not responded at the time. This was followed up by a telephone call one month later.

5 Results

The data collection is still ongoing, but to-date the response rate is about 60%. Table 2 below shows the cumulative response rate over time after each reminder.

Table 2: Response rate over time

After	Mode	Cumulative Response Rate
Initial contact	Mail Out	38.3%
1st Reminder	Email	58.2%
2nd Reminder	Telephone	60.3%

Overall about 77.6% (95% confidence interval (CI)=0.694, 0.857) of the REBs reported having no statistician in their membership, and 77.1% reported

that they do not feel that they need a statistician. Table 3 below show the distribution of the responses to the question "How do you deal with statistical issues without a statistician in membership?"

Table 3: Frequency distributions of how REBs without a statistician deal with statistical issues

Response (n=59)	Frequency: Count (%)
Approach a statistician if necessary	26 (44%)
Within committee	30 (51%)
Prior review by research and development committee	12 (20%)
Others	8 (14%)

For REBs that did not have a statistician in their membership, we were interested to know why they did not have one. Below are some of the reasons reported by those respondents that do not have a statistician:

Table 4: Some Reasons for not having a statistician in committee

"There would be no disadvantage in having one"
"One is preferred but not always available"
"Occasionally it would be helpful"
"I think it is necessary to have at least a researcher who is an expert within statistical issues"
"By not having a statistician, we acknowledge that our methodological competence is not complete"
"We have tried (and failed) to recruit statisticians"
"Ethical decisions do not depend on such detailed scrutiny"
"We have extensive statistical training"
"Certainly such expertise is important in evaluating methodology in an assessment of cost-benefit analysis. ...With limited resources it is a struggle to simply get people to serve"
"...now that you mention it!"

Although, as already described in the introduction, most guidelines on ethical reviews clearly indicate that scientific validity of research projects needs to be evaluated, clearly the implementation would vary from REB to REB. We also requested REBs to send us their checklist in order to assess if they ever

request that statistical issues be addressed in the review. We received 21 checklists. Below is the distribution of some statistical issues that were stated in some of the checklists

Table 5: Distribution of Statistical Issues in REB checklists

Statistical Issue: n= 21	Frequency: count
Study design and methodology	13
Study population/Sample size	6
Randomization	5
Data analysis plan	3
Statistical justification for study design	2
Methods of Data Collection	2

6 Discussion

There are several statistical issues that can arise in reviews of research projects submitted to REBs. These issues will include sample size issues, study design, randomization issues in clinical trials, sampling issues in surveys, and data collection instruments in terms of their reliability and validity. Table 5 above gives a glimpse about some of these. It is important to note that from an REB's perspective the objective is not to critique the statistical methods of the research proposals in terms of what should be the best approach or design for the study. Rather, the goal is to assess the validity of the methods or study design in terms of whether it will allow the investigators to answer the research problem leading to valid results. The goal is to protect the potential research subjects from participating in a study that may not be worthwhile.

Even with a single one of the above issues, there are multiple facets to it: we will use the sample size as an example. In determination of sample sizes in clinical trials, there are several important aspects that need to be taken into consideration (see Appendix A). All these are important questions which form crucial elements of the main question: *How much data should I collect to answer the question of interest and have faith that the answers are correct?* While one would hope or expect these issues to be addressed by a statistician, either as a consultant or co-investigator, at the planning stages of the research protocol, the reality is that very rarely is this ever the case. As such, most projects are submitted to REBs with several statistical deficiencies. One would hope that all research institutions will make efforts to en-

hance statisticians' participation in REBs and put the resources in place to encourage their involvement.

7 Concluding Remarks

The level of statisticians' participation in Canadian research institutions as judged by REB membership in Canada-based REBs seem to be very low. As reported by some REBs, lack of resources to recruit and maintain people with this type of expertise may partially explain the situation. However, as indicated by some of the responses received, there also seems to be a lack of recognition or knowledge of the complexity and importance of some of the statistical issues that need to be dealt with, and hence the importance of statisticians' involvement in these committees. This is despite the fact that the need for statisticians' involvement has been pointed out by many authors. We hope that the results of this study will help to generate some debate on the importance of the role of REBs in save-guarding scientific integrity and the need to include a statistician on the committee to properly deal with statistical issues. At the same time we hope to make statisticians aware of the desire of many REBs to have a statistician on their committees, and the current lack of such membership on these committees, so that they will be aware of the need to get more involved in REBs.

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4. What is the unit of randomization? Is it individual subjects, family practices, hospital wards, communities, families, etc?
 5. What is the research design: independent, paired or multiple groups?
 6. Research subjects: what is the inclusion and exclusion criteria? These are important in assessing patient compliance, risk (poor or good prognosis), chances of treatment response, potential drop-out rate, etc.
 7. How long is the duration of the follow-up? Is it long enough to be of any clinical relevance?
 8. What is the desired level of significance?
 9. What is the desired power?
 10. What type of summary or test statistic will be used for analysis? Will it be a one- or two-tailed test?
 11. The smallest difference (see Spiegelhalter and Freedman [19] and Spiegelhalter et al [18]): Is it stated as
 - (a) the smallest clinically important difference? (Lachin [20])
 - (b) the difference that investigators think is worth detecting? (Fleiss [21])
 - (c) the difference that investigators think is likely to be detected? (Halperin et al [22]).
 12. Justification: Most importantly, is the justification provided on how the various prior estimates used in the calculations were obtained and their usefulness in the context of the study? This also deals with the clinical relevance of the estimates depending on the source (ie published data, previous work, review of records, expert opinions, etc).

APPENDIX A

Important Issues in Determining Sample Sizes in Clinical Trials

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1. The objective of the research: Is the research dealing with an estimation, hypothesis or equivalence testing problem?
 2. The outcome(s) of the research:
 - (a) Is/Are the outcome(s) categorical or continuous?
 - (b) Is it a multiple or single outcome study?
 - (c) What is(are) the primary outcome(s)?
 - (d) What is(are) the secondary outcome(s)?
 3. Are there any covariates or factors for which to control?