Initiatives for Enhancing the Canadian Clinical Research Environment

St. Michael’s Hospital’s initiative towards transparency & unbiased reporting of clinical trial results

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OUTLINE

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ISSUES

• **US study of 51 academic medical centers** *(Chen R, et al. BMJ. 2016 Feb 17;352:i637)*:
  
  o 4347 interventional clinical trials (Oct 2007-Sep 2010).
  
  o As of July 2014, 66% of the trials disseminated results, with 35.9% achieving this within 24 months of study completion.
TrialsTracker

- An online tool that tracks how many trials are updated with results on clinicaltrials.gov OR published in peer reviewed journals (https://trialstracker.ebmdatalab.net/#/).

- TrialsTracker reported that 45% of clinical trial results worldwide were never reported to the clinicaltrials.gov registry or published.
The Tri-Council Policy Statement, Ethical Conduct for Research Involving Humans (i.e., TCPS 2) does not provide explicit rules for trial reporting.

...researchers, research sponsors and institutions have an ethical responsibility to make reasonable efforts to publicly disseminate the findings of clinical trials in a timely manner by publications and by the inclusion of the findings ... , or information about where to access findings (e.g., lists of publications, links to publications or to the trial website) in the publicly accessible registry...
WHY IS IT IMPORTANT TO REPORT

• The public will have access to ongoing clinical trials and basic study results.

• Reduces publication bias and duplication of research efforts.

• The International Committee of Medical Journal Editors (ICMJE) requires trial registration as a condition to publish a clinical trial.

• Section 801 of the FDA Amendments Act (FDAAA 801) requires Responsible Parties to register and submit summary results of certain clinical trials with ClinicalTrials.gov.
US FDA & NIH RULE CHANGES

• Effective January 18, 2017, the FDAAA 801 mandated:
  o all “Applicable Clinical Trials” be registered on clinicaltrials.gov; and
  o have results reported on clinicaltrials.gov no later than 12 months after the last patient has been followed up for the primary outcome.

• NIH applies the rule to all NIH funded interventional trials.

• There may be consequences for non-compliance to the responsible party which is often a sponsoring institution.
We reviewed the list of unpublished trials provided by TrialsTracker.

- **Inclusion:** all interventional trials completed between Jan 2006 and Dec 2014 (except for Phase 0/1 trials).
  - According to TrialsTracker, St. Michael’s completed 43 eligible trials and hasn't published results for 31 trials (72%).

- We followed up with our researchers about the status of their trial.

- We also searched NCT ID in PubMed using advanced search criteria to verify publication.
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**OUR RESULTS**

**Out of 43 eligible trials**

- 12 trials identified by TrialsTracker as published reported NCT ID in the publication abstract.
- Out of 31 trials reported by TrialsTracker as not published:
  - 16 trials were published in peer reviewed journals but they did not report NCT ID in the abstract but mostly in the methods or not at all.
  - 4 trials were in press/under review or revision.
  - 4 trials are being written for publication.
  - 7 trials were not published.
OUR RESPONSE

• Steps to ensure that our clinical trial results are easily accessible and/or published:
  
  o Developed **institutional guidelines** mandating trial registration, timely updates, and summary results reporting.
  
  o Implementing a **system to monitor compliance** and follow up with the investigators who do not follow the guidelines.
GUIDELINES FOR CLINICAL TRIALS REGISTRATION & RESULTS REPORTING (effective September 1, 2017)

• **Be registered** on one of the registries that are accepted by ICMJE and WHO.

• **Ensure that the trial record is updated in a timely manner** as required by the registry.

• **Post summary results** to the respective registry as per the following:
  o Applicable Clinical Trials (ACT): **within 1 year** of the primary completion date. ➔ *This is required by FDA*
  o Any clinical trials funded wholly or partially by NIH: **within 1 year**. ➔ *NIH*
  o Any interventional studies that are not ACTs and are not funded by the NIH: **within 2 years**. ➔ *We are establishing this.*
ENGAGING THE COMMUNITY

- Developed an **info guide** (see [our website](#)) and advice: e.g.,
  - Summary results posted in clinicaltrials.gov will not impact on the ability to publish on peer-reviewed journals.
  - Work with the editor to ensure NCT ID appears in the abstract.

- Involved the **Applied Health Research Centre** (clinical trial coordination centre at SMH) to assist researchers and the **Research Ethics Board (REB)**.
Developing a system to track compliance:

- Clinical trial registration is required for the REB approval.
- Summary results reporting to the registry is required for the REB closure.
- Our new online clinical research & institutional authorization system called “CAPCR” (originally developed by UHN) will include REB approval/closure.
- Trial registration and summary results reporting will be tracked through CAPCR in the future.
• Timely dissemination of trial results is important for the complete and unbiased reporting of all research results (including those that are not publishable).

• Trials Tracker provides a useful tool for audit despite its limitations (Cobey et al., CMAJ 2017; Coens et al., F1000Research 2017, 6:71).

• Other Canadian institutions such as the Ottawa Hospital Research Institute have conducted an internal audit and contacted individual researchers whose trial results were not made public.

• We would like to know what other institutions are doing. Please contact Yunjo Lee (LeeYu@smh.ca).

• For more info, see our website.