



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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St. Michael's

Inspired Care. Inspiring Science.

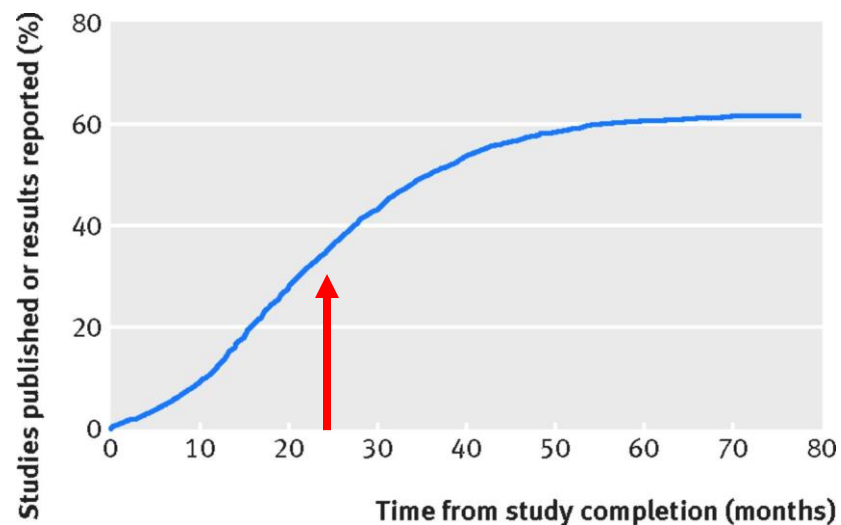
OUTLINE

- **Background**
 - Issues
 - Why is it important to report trial results
 - US FDA & NIH rule changes
- **St. Michael's Hospital's Initiatives**
 - Our review
 - Our results
 - Our response
- **Summary**



ISSUES

- **US study of 51 academic medical centers** (*Chen R, et al. BMJ. 2016 Feb 17;352:i637*):
 - 4347 interventional clinical trials (Oct 2007-Sep 2010).
 - 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.



'We've been deceived': Many clinical trial results are never published

Canadian universities and research hospitals are among the worst offenders, according to new online tool

By Darryl Hol, CBC News | Posted: Nov 24, 2016 5:00 PM ET | Last Updated: Nov 24, 2016 5:35 PM ET



ISSUES

- 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:
 - all “Applicable Clinical Trials” be registered on clinicaltrials.gov; and
 - 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.





OUR REVIEW

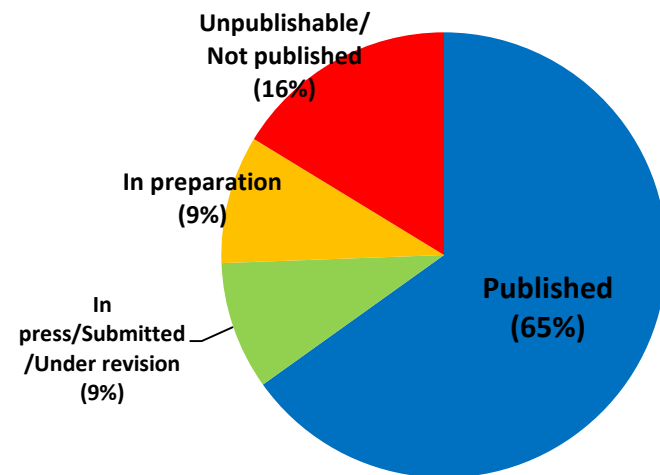
- We reviewed the list of unpublished trials provided by TrialsTracker.
 - Inclusion: all interventional trials completed between Jan 2006 and Dec 2014 (except for Phase 0/1 trials).
 - According to TrialsTracker, St. Michael's completed **43 eligible trials** and hasn't published results for 31 trials (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.



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:
 - Developed **institutional guidelines** mandating trial registration, timely updates, and summary results reporting.
 - 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:
 - Applicable Clinical Trials (ACT): **within 1 year** of the primary completion date. → *This is required by FDA*
 - Any clinical trials funded wholly or partially by NIH: **within 1 year.** → *NIH*
 - 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)**.



TRACKING & MONITORING COMPLIANCE



- 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.



SUMMARY

- 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](#).

