

## Best Brains Exchange – Using Administrative, Electronic Medical Record and Patient Health Record Data in Clinical Trials

March 22/23, 2016, Toronto, ON

### Summary Report May 17<sup>th</sup>, 2016

#### Overview

On March 23rd, 2016, a Best Brains Exchange (BBE) on the topic of “Using Administrative, Electronic Medical Record and Patient Health Record Data in Clinical Trials” was held by the Canadian Institutes of Health Research (CIHR) in collaboration with the Ontario SPOR Support Unit (OSSU) and the Institute for Clinical Evaluative Sciences (ICES), in consultation with the Population Health Research Institute (PHRI) and Clinical Trials Ontario (CTO). The BBE brought together leading Canadian and international data, evaluation, clinical trial, implementation and population health researchers along with provincial policy and decision makers to consider how administrative data and/or electronic medical record (EMR) data and/or patient health record (PHR) data can be leveraged to build and expand the evidence base for new and existing clinical and health system-level interventions, and attract more investment to Canadian clinical trials. Special attention was paid to ethical, confidentiality and privacy issues that may inhibit or facilitate the use of these data in trials.

More specifically, the BBE objectives were designed for participants to:

1. Gain a comprehensive understanding of the quantifiable benefits and challenges in using administrative/EMR/PHR data in trials, with attention given to: timeliness, cost effectiveness, and quality of results from current or previous studies that integrate administrative/EMR/PHR data to capture clinical outcomes in trials
2. Examine trial study designs and novel approaches that integrate administrative/EMR/PHR data for both clinical and health system outcomes which could be used as models/exemplars for future studies. Examples include:
  - a. Pragmatic randomized trials using routine electronic health records with opt-in prior consent
  - b. How administrative and/or EMR data can enable the identification of potentially eligible study participants at suitable research sites
3. Explore innovative strategies that support the integration of administrative/EMR/PHR data into decision making (e.g., by providing relevant prevalence information that helps decision makers estimate the potential impact and cost-effectiveness of interventions for individual sites/regions or on a provincial scale)
4. Based on current context, lessons learned and best practices, begin to consider priorities for reactivation studies or new trials that could potentially integrate administrative/EMR/PHR data.

## Highlights from International Speaker Presentations (Packard, Christiansen)

The term “medical databases” encompasses: administrative data (linked, linkable or stand-alone datasets), registries, electronic medical records (EMRs) and personal health records (PHRs). Canada has exceptional medical databases and researchers who lead world-class clinical trials and health system trials. However, Canada has not yet brought data assets and expertise together to support innovative trials in the way that front-running jurisdictions have done.

Leaders from Scotland and Denmark provided examples of the innovative ways that medical databases can be used to support trials such as:

- E-recruitment: Identifying potential sites for trials and supporting recruitment (e.g., generating “heat maps” that provide principal investigators with guidance on which sites to involve)
- E-feasibility: Conducting feasibility assessments (e.g., providing information about the number of potential participants, helping principal investigators know in advance whether a trial would have sufficient power)
- E-studies: Using information in medical databases to measure trial outcomes and/or to enhance the core datasets for clinical trials, cohorts, tissue sample and image databases
- E-follow up: Conducting long term follow up studies of trial participants

Information from medical databases can complement trial datasets to address the five “S’s” of clinical trials (see text box). As demonstrated by the powerful WOSCOPS Twenty Year Follow-Up Study<sup>1</sup>, a major advantage of using medical databases for follow up is that researchers can identify trajectories, not just events within a fixed time period. Further, the cost for long-term WOSCOPS Follow-Up Study was a small fraction of the cost of the original trial (tens of thousands vs. millions).

<p style="text-align: center;"><u>Five S’s of Clinical Trials</u> (Christiansen, see Appendices)</p> <ul style="list-style-type: none"><li>• Too <b>Small</b> to detect rare side effects</li><li>• Too <b>Short</b> to detect long-term side effects</li><li>• Too <b>Simple</b> to detect (drug) interactions</li><li>• Too <b>Selected</b> to be generalizable to all types of patients</li><li>• Too <b>Specific</b> to assess all relevant outcomes</li></ul>
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In summary, the use of medical databases in trials may:

- Reduce cost and thereby allow larger trials
- Support more complete long-term follow-up
- Allow multiple outcomes to be monitored

However, there are caveats. Use of medical databases requires full understanding of data quality limitations, excellent knowledge of database holding and case validation work. It is also important that the public and trial participants support use of their data in trials.

In Denmark there is a long-standing history of public support for use of public data in research. Danish researchers approach patients about trials directly with little to no involvement of care providers. In Scotland,

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<sup>1</sup> 20-year follow-up of the West of Scotland Coronary Prevention Study (WOSCOPS)  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0075379>

an approach has been adopted where trial participants are always contacted by someone they know, or would reasonably expect to have access to their data. NHS Scotland has also established the [SHARE](#) site through which members of the public can register their interest in being contacted about upcoming trials.

Notwithstanding the many benefits noted above, “only a handful” of trials in Denmark and Scotland make use of medical databases. There is great opportunity to grow the practice of using medical databases in trials.

### Highlights from Canadian Speaker Presentations (Avina, Tu, Tamblyn)

The speakers presented examples of powerful, local (within province) trials that made use of administrative and/or EMR data. However, in each case, significant and disproportionate effort was required to get to the point that the researchers could begin working with data. The requirements to seek approval from multiple data holders and/or research ethics boards (often at multiple sites) served as barriers. Issues include:

- Application to access data is too long
  - Process to complete the application is lengthy
  - Some databases require justification for EACH requested variable
- Too many approvals are needed from too many different people/groups
  - In one case this meant submission to and feedback from ~7 different governing bodies
  - The same (lengthy) process must be followed to submit a study amendment data
- Too long to get approvals
- Too long to do data extraction
  - Data from different databases are not received together as one extraction
- Lack of coordinated process to import and link external databases

Canada has a unique opportunity to be a leader in the use of medical databases in trials. Expert knowledge of data holdings will be required. The agreement rate with administrative data is likely to vary significantly depending on the outcome being studied; but it isn't as though other data are perfect. Randomized control trial “gold-standard” clinical data may miss events (e.g., telephone follow-up) or be misclassified (e.g., due to reviewer-dependent judgments). Ultimately, a minimally acceptable agreement rate (e.g., 80%?, 90%?, 99%?) will need to be determined between variables from medical databases and outcomes as measured in study-specific trial datasets.

Becoming a leader in the use of medical databased in trials will require significant changes such as:

- A fast-track standardized process for linking trials to administrative data to measure outcomes (consent standardized)
- The assembly of registries of important study populations through clinical and administrative data registries
- Fully integrating EMR/ PHR and administrative data for clinical care and research

## Highlights from Breakout Groups

### 1) *Ethics, consent and public engagement (facilitated by Paprica)*

This is a complex topic without a simple answer. There is no silver bullet. Public support for use of medical databases in trials is very important and tied to trust in research generally. Clinical Trials Ontario is leading work to improve the efficiency of trials while maintaining public support/trust and can be a resource. Notwithstanding the fact that there is no “quick fix”, there are short term actions that can be taken including:

- Identify additional opportunities where consent for research might be obtained (e.g., if someone comes to hospital for surgery or for any reason, they are asked if they provide consent to be approached to be in trials, asking participants of large cohort studies if they consent to linkage for long-term follow up and secondary uses of linked data)
- Develop standard language to include in consent forms that allows linkage and secondary uses <sup>2</sup>
- Create a publication that researchers can cite in their Research Ethics Board (REB) submissions to support the validity and appropriateness of the consent process they are proposing (the publication will not just be a document that describes what has been done, it will present best practice information including the key decision point(s) in terms of one approach to consent vs. another)
- Public engagement and primary care provider engagement – several activities were proposed including focus groups to determine how to stakeholders want to be involved, integrating professional public relations advice in engagement planning (as PHRI and SHARE in the UK have done) , educational materials in various formats etc.

### 2) *Timely access to high-quality data-within and across provinces (facilitated by Victor)*

Delays to accessing data and lack of transparency around the process to access data are major issues. There is also room for improvement with respect to how current the data are that are made available (i.e., minimizing the lag time between the date that data are collected and when they are available for use). Provinces are in ‘different places’ with respect to access; they should learn from each other and also be open to distributed data network approaches (e.g., the approach proposed by the Pan-Canadian Real-world Health Data Network, [www.prhdn.ca](http://www.prhdn.ca)). Top recommendations were to:

1. Determine the baseline for data access and develop/spread best practices based on current examples from Canadian organizations
2. Engage funders, government and data providers by developing a business case and value proposition for access to data (keeping this patient-focused, also highlighting how much time and research dollars are currently wasted due to inefficient and duplicative processes)
  - a. Bring specific examples of improvements in quality/cost due to data availability and analyses

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<sup>2</sup> Post-meeting notes: based on knowledge gained through the BBE, Dr. Nav Persaud has added a new consent form for the study [CLEAN Meds](#) to seek patient consent for long-term follow up using administrative data. During and after the BBE examples of text related to linkage were identified including from PHRI. Don Willison and Ray Saginur offered to provide support on standardized text for consent forms that would allow linkage for long-term follow up and/or secondary use of linked trial data.

3. Identify requirements for different data use cases and create a standard minimum dataset
  - a. Research
  - b. Evaluation
4. Work to harmonize data access protocols across provinces
  - a. New and clearer legislation may be required

### *3) New and better data sources and innovative uses of them in trials (facilitated by Tamblyn)*

Foremost, we need a vision to make the most of the opportunity for Canada. There are also practical things that we need to do, many of which will require up-front investment. Main recommendations are:

1. A vision/position paper with a clearly defined vision regarding use of EMR and PHR (and mobile health data) – ICES has offered to coordinate efforts to prepare the paper
2. Re-creation of the wheel for complex data – major change is required, we need to build on existing platforms and create a consolidated platform for access to EMR data so that all customers can access the data in a uniform way
3. Engage the public, clinicians and policy makers – we require a consolidated infrastructure and must engage with stakeholders to make this happen. The time to do this is once the vision/position paper has been drafted. It is essential to have buy-in from the individuals/organizations who will be putting forth the resources and legislative changes (where required)

## Conclusions

Canada is well positioned to be a leader in the use of medical databases in trials. There are short-term well-defined activities that would contribute to this goal, such as developing standardized text related to consent for linkage and long-term follow up. To make the most of the opportunity to use administrative data, EMRs and PHRs in trials, a common vision is needed, alongside investment and broad stakeholder engagement.

## List and Order of Appendices

1. References and Resources (enclosed)
2. [Materials and Presentations from March 23, 2016 Meeting](#)
  - a) Agenda
  - b) Objectives
  - c) Biographies of Speakers and Presenters
  - d) BBE Introductory Presentation
  - e) Christiansen Presentation
  - f) Packard Presentation
  - g) Avina Presentation
  - h) Tu Presentation
  - i) Tamblyn Presentation
3. List of Registrants (provided only to registered attendees of the BBE)

## References and Resources

### *Recommended Readings*

Aviña-Zubieta, J. A., Man, A., Yurkovich, M., Huang, K., Sayre, E. C., & Choi, H. K. (2015). Early Cardiovascular Disease After the Diagnosis of Systemic Sclerosis. *The American journal of medicine*.

[Abstract](#)

Dreischulte, T., Donnan, P., Grant, A., Hapca, A., McCowan, C., & Guthrie, B. (2016). Safer Prescribing—A Trial of Education, Informatics, and Financial Incentives. *New England Journal of Medicine*, 374(11), 1053-1064.

[Abstract](#)

Kaczorowski, J., Chambers, L. W., Dolovich, L., Paterson, J. M., Karwalajtys, T., Gierman, T., ... & Zagorski, B. (2011). Improving cardiovascular health at population level: 39 community cluster randomised trial of Cardiovascular Health Awareness Program (CHAP). *BMj*, 342, d442.

[Full-text](#)

McConnachie, A., Walker, A., Robertson, M., Marchbank, L., Peacock, J., Packard, C. J., ... & Ford, I. (2014). Long-term impact on healthcare resource utilization of statin treatment, and its cost effectiveness in the primary prevention of cardiovascular disease: a record linkage study. *European heart journal*, 35(5), 290-298.

[Full-text](#)

Schmidt, M., Pedersen, L., & Sørensen, H. T. (2014). The Danish Civil Registration System as a tool in epidemiology. *European journal of epidemiology*, 29(8), 541-549.

[Abstract](#)

Scottish Government, Charter for Safe Havens in Scotland: Handling Unconsented Data from National Health Service Patient Records to Support Research and Statistics. November 2015.

[www.gov.scot/Publications/2015/11/4783/4](http://www.gov.scot/Publications/2015/11/4783/4)

Thuesen, L., Jensen, L. O., Tilsted, H. H., Mæng, M., Terkelsen, C., Thayssen, P., & Lassen, J. F. (2013). Event detection using population-based health care databases in randomized clinical trials: a novel research tool in interventional cardiology. *Clin Epidemiol*, 5, 357-61.

[Full-text](#)

Tu, J. V., Donovan, L. R., Lee, D. S., Wang, J. T., Austin, P. C., Alter, D. A., & Ko, D. T. (2009). Effectiveness of public report cards for improving the quality of cardiac care: the EFFECT study: a randomized trial. *Jama*, 302(21), 2330-2337.

[Abstract](#)

### *Additional Danish Resources from Christian Christiansen*

DATABASES: Some years ago, our department wrote a book about many of the databases in Denmark (<https://www.prhdn.ca/SiteAssets/Registerbog%20ed.pdf>). There are many databases using different systems to capture data. Unfortunately, most of the other available information is in Danish. However, several clinical databases still use web-based data collection from companies like OPUS Consult (<http://www.opusconsult.dk/>) and Tieto.

STRATEGY: A few years ago, the ministry of health in Denmark established a strategic alliance for register- and health data, including several stakeholders. They discuss data access issues at their regular meetings. <http://www.sum.dk/Sundhedsprofessionelle/Forskning/STARS-Strategisk-alliance-for-register-og-sundhedsdata.aspx>. We also have coordinating organization for registry research: <http://www.registerforskning.dk/>

INFORMATION TO RESEARCHERS: Some years ago, the ministry of health published a guideline for researchers summarizing legal issues: <http://www.sum.dk/~media/Filer%20-%20Publikationer%20i%20pdf/2014/Kom-god-igang-med-klinisk-forskning-sept-2014/Klinisk-forskning-sept-2014.ashx>