The Methods Clusters

In 2016, the BC SUPPORT Unit funded a five-year initiative to study the methods of patient-oriented research: the **"Methods Clusters".**

We started our work by **listening to stakeholders**—including patients, researchers, policy makers, and practitioners. Together, we identified **6 areas** where more methods research was most important. These became the **6 Clusters:**

Knowledge Translation and Implementation Science

Patient-Centered Measurement

Data Science and Health Informatics

Patient Engagement

Health Economics and Simulation Modelling

Real-World Clinical Trials

Each Cluster consulted stakeholders to discuss their **priorities** for patient-oriented research. **35 priorities** surfaced.

To address these priorities, the Clusters funded **42 different projects.** All of these projects were **patient-oriented:** we **studied** patient-oriented research by **doing** patient-oriented research.

This PDF provides a snapshot of the **Real-World Clinical Trials** Methods Cluster as of March 2022.

Real-World Clinical Trials

Overview

A **clinical trial** is a research study that prospectively assigns humans to one or more intervention(s) to evaluate the effects on health outcomes (World Health Organization, 2020). Traditionally, a trial is conducted in an idealized setting to give an intervention its best chance to demonstrate a beneficial effect and often involves the following: narrow patient populations, well-controlled settings, interventions delivered by experts, close monitoring during study follow-up, and emphasis on one primary outcome (often clinical efficiency).

A **real-world clinical trial** (also called a pragmatic trial) is a trial intended to answer how well interventions work beyond the traditional clinical trial setting. It seeks to include broad patient populations, deliver interventions in usual care settings using minimal extra resources, and evaluate multiple outcomes that are important to patients.

Read a blog post by Cluster lead Dr. Hubert Wong: Why are Pragmatic Clinical Trials important for our health system?

Consulting with researchers, policy makers, and practitioners, this Cluster:

- *Identified **3 priorities** to focus on*
- *Funded **7 projects** to address them*

This Cluster was led by **Hubert Wong.**

***Dr. Wong** was seconded to the Unit from the University of British Columbia (UBC), where he is an Associate Professor at the School of Population and Public Health, Program Head of Biostatistics at the Centre for Health Evaluation and Outcome Sciences (CHÉOS), and Associate Head of Methodology and Statistics at the Canadian Institutes of Health Research (CIHR) Canadian HIV Trials Network (CTN).*

Real-World Clinical Trials

Navigation

Real-World Clinical Trials

Projects: Overview

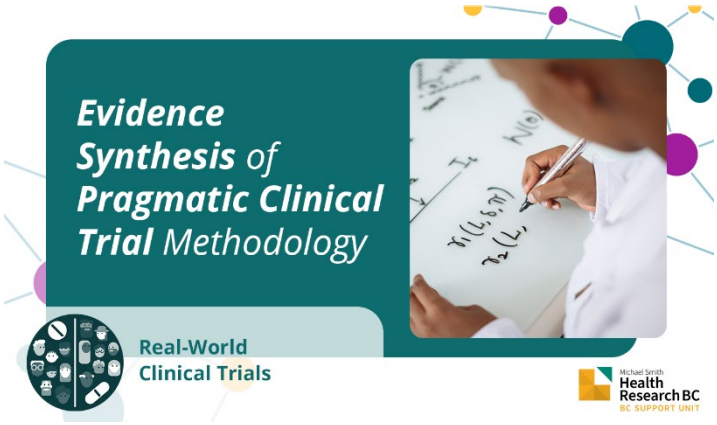
This project explored the question: How do we ensure that composite outcomes in clinical trials are patient-oriented?

Pragmatic clinical trials can mean more complicated data—patients vary, some may not complete the trial. This study explored ways to analyze this more complicated data, so we can determine if a drug will work for a patient as prescribed.

How can we better design and analyze real-world trials to require fewer patients and resources?
This project developed two different methods of increasing efficiency.

Measuring interventions can be difficult due to limited sample sizes, low compliance rates, small to moderate effect sizes. More complicated interventions are also difficult to measure. This project studied these issues.

Who should be required to provide consent for cluster randomized controlled trials? Clinic or hospital administrators? Doctors and other care team members involved? Patients?



What statistical methods are available for designing and analyzing pragmatic trials?
This team performed a review of existing methods, and developed a new one.

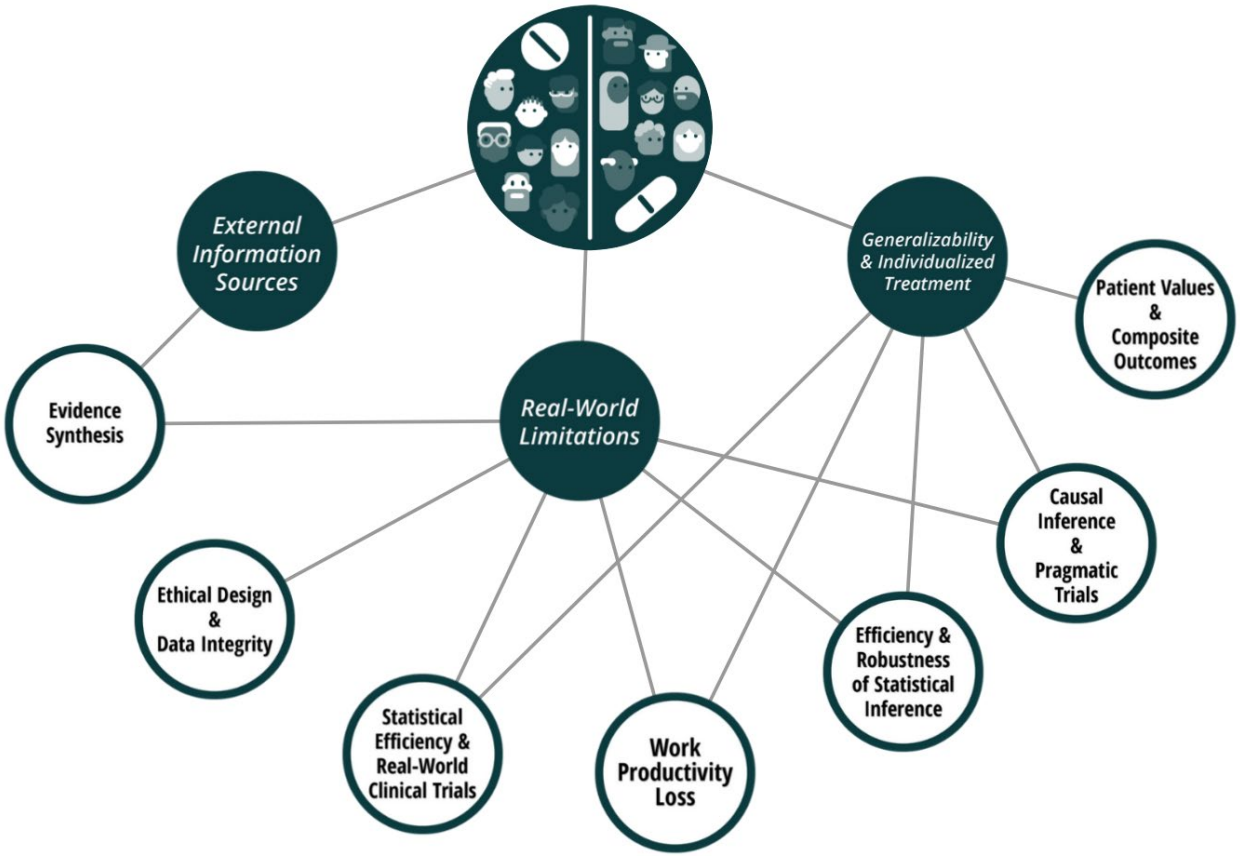
To measure work productivity loss data, we have to use complicated statistical methods.
This project asked: What are the best methods to use? And how can we best communicate the results to patients and caregivers?

Real-World Clinical Trials

Priorities

Each Cluster consulted stakeholders to discuss their priorities for patient-oriented research. The Patient-Centred Measurement Methods Cluster identified **3 priorities** for potential projects.

This Cluster then funded **7 projects** based on these priorities.



This diagram shows the connections between the priorities (solid teal) and projects (teal outline) of the Real-World Clinical Trials Methods Cluster. A list of the Cluster's priorities, and projects they funded based on them, is below.

Addressing real world limitations

Making trials feasible and efficient in real world settings (constraints on blinding, randomization, sample size, operational procedures, ethical considerations).

The projects that addressed this priority were:

- *Increasing statistical efficiency in real-world clinical trials*
- *Evidence synthesis of pragmatic clinical trial methodology*
- *Promoting ethical design and data integrity for cluster trials: issues of consent*
- *Developing & evaluating causal inference methods for pragmatic trials*
- *Improving the efficiency and robustness of statistical inference for patient-oriented treatment effect in real-world clinical trials*
- *How to analyze and present work productivity loss due to health problems in clinical trials?*

Enhancing generalizability and individualized treatment

Ensuring treatment needs in the broad population are addressed but with a focus on individual patient priorities (patient-reported outcome measures, or PROMs) and needs (precision medicine).

The projects that addressed this priority were:

- *Developing & evaluating causal inference methods for pragmatic trials*
- *Embedding patient values in randomized control trials: a case study*
- *Improving the efficiency and robustness of statistical inference for patient-oriented treatment effect in real-world clinical trials*
- *How to analyze and present work productivity loss due to health problems in clinical trials?*

Leveraging external information sources

Making use of non-trial information (published literature, health databases/medical records, expert opinion) to get answers more quickly and enhance the value of a trial.

The project that addressed this priority was:

- *Evidence synthesis of pragmatic clinical trial methodology*

Real-World Clinical Trials

Projects

Increasing statistical efficiency in real-world clinical trials

This project addressed the priority:

- *Addressing real-world limitations*

Project summary

This project developed and tested new ways of designing and analyzing clinical trials so that they are more efficient by needing fewer participants and less resources.

Two different methods of increasing efficiency were developed:

1. The first method improved the way to assign groups of patients to different treatments in cluster-randomized trials. Cluster randomization means that, for example, patients within one hospital will all get the same treatment, while the treatment will vary across different hospitals.
2. The second method improved the approach used to help doctors summarize the information that is collected from other sources (e.g., from hospital records, other studies and from their experiences with their own patients) about how well the treatment works and then to combine this information with the results from the clinical trial.
   Using information from other sources can reduce the number of patients needed in the trial to determine which treatment works better.

Publications

Ouyang, Y., Xu L., Karim M.E., Gustafson P., Wong H. CRTpowerdist: An R package to calculate attained power and construct the power distribution for cross-sectional stepped-wedge and parallel cluster randomized trials. Computer Methods and Programs in Biomedicine, Vol 208, 2021.

Ouyang, Y. Increasing the efficiency of pragmatic trials using innovative designs and analyses (T). University of British Columbia, 2021.

Ouyang, Y., Karim, M.E., Gustafson, P. et al. Explaining the variation in the attained power of a stepped-wedge trial with unequal cluster sizes. BMC Med Res Methodol 20, 166 (2020).

Wong H., Ouyang Y., Karim M.E. The randomization-induced risk of a trial failing to attain its target power: assessment and mitigation. Trials. 2019 Jun 17;20(1):360.

Team

Hubert Wong, PI; Yongdong (Derek) Ouyang; Liang Xu; Ehsan Karim; John Petkau; Paul Gustafson; Thalia Field

Evidence synthesis of pragmatic clinical trial methodology

This project addressed the priorities:

- *Addressing real-world limitations*
- *Leveraging external information sources*

Project summary

This project conducted reviews of statistical methods that has been developed to address two aspects of pragmatic trials: (1) accounting for unequal numbers of participants in clusters in a cluster-randomized trial, and (2) combining trial data with information from outside the trial to obtain more precise answers. These reviews will help trial designers more easily find the information needed to design their trials as well as identifying when new methods need to be developed. One new method was developed during this project.

In a cluster-randomized trial, participants are assigned to receive a treatment in groups, instead of individually. For example, if the trial is about testing a new way of providing care in a hospital, then all the participants (patients) within one hospital will receive the same type of care while the type of care (usual care vs new way of care) will vary across different hospitals. For this type of design, the calculations for how many participants are needed and the correct way to analyze the data is complicated. We conducted a review of literature on methods for doing these calculations for different types of cluster-randomized trials.

Real-world trials often involve comparisons of interventions to routine care or to interventions that have already been tested previously. This means that often there is knowledge about how well the interventions being compared work even before the trial is conducted. We conducted a review of literature on Bayesian methods for combining existing knowledge with trial data to get more precise answers.

The new method developed in this project showed how to increase the precision of the treatment effect from a stepped-wedge cluster-randomized trial by taking into

account outside information on the changes in outcome rate over time using Bayesian methods.

Publications

Zhan D, Ouyang Y, Xu L, Wong H. Improving efficiency in the stepped-wedge trial design via Bayesian modeling with an informative prior for the time effects. Clin Trials. 2021 Jun;18(3):295-302. Epub 2021 Apr 5.

Zhan D, Xu L, Ouyang Y, Sawatzky R, Wong H (2021) Methods for dealing with unequal cluster sizes in cluster randomized trials: A scoping review. PLoS ONE 16(7): e0255389.

Team

Hubert Wong, PI; Denghuang (Jeff) Zhan; Yongdong (Derek) Ouyang; Liang Xu; Rick Sawatzky

Promoting ethical design and data integrity for cluster trials: Issues of consent

This project addressed the priority:

- *Addressing real-world limitations*

Project summary

Cluster randomized controlled trials (cRCTs) are increasingly popular in health services research. Our project is looking at the research ethics of these trials.

What is a cRCT?

- A "randomized controlled trial" (RCT) is a type of research study that tests a new treatment, procedure or practice (i.e., an "experimental intervention"). To do this, RCTs randomly assign participants to either keep doing what they did before (e.g., do their usual treatment) or try something new (e.g., start a new, experimental treatment).
- A "cluster randomized controlled trial" compares "clusters" of people instead of individual people. "Clusters" might be different hospital wards or clinics.

For example, a new handwashing protocol may be assigned to half the hospital wards while the other wards continue to do their old handwashing protocol. The study mainly collects data about health care providers' handwashing behaviour, but also looks at whether infection rates in hospital units that use the new protocol differ from the ones that are not using this new protocol.

How are we studying cRCTs?

We're asking: who should be required to provide consent for these different trials? Clinic or hospital administrators? Doctors and other care team members involved? Patients?

To investigate these questions, we conducted a systematic review and qualitative interviews to explore patients', cRCT researchers', and research ethics boards' perspectives on ethical consent processes for different types of cRCTs.

Based on our findings, we are developing a framework and online module to guide researchers and research ethics boards on ethical design of cRCTs, with emphasis on issues of consent.

Project findings

Our preliminary findings suggest that these questions are challenging to navigate.

- Some believe that the data in clinical databases should be available without explicit consent for data to be used in research as long as patient safety, privacy, and confidentiality is maintained:
    - But how can we judge if this safety, privacy, and confidentiality has been met?
    - Interviewees also emphasized that, even if there is a waiver of consent and no consent process, there should still be an information process to respect the participants.
- Some believe that waiving individual consent for cluster trails that pose little to no harm can be acceptable, especially if seeking individual-level consent can incur undue burden on the research team.
- Some suggested instituting a "gatekeeper" who has the best interests of participants in mind.
- Questions arose around how to distinguish between cluster trials and quality improvement projects.
- Participants voiced a need for guidelines that are more focused on patients' perspectives, not only health system perspectives.
    - We will develop patient-oriented guidelines upon completion of our data analysis.

Our data analysis is ongoing. We are currently in the process of producing video and educational modules on our findings and on questions around ethical cluster trials more generally.

Team

Anita Ho, PI; John (Kip) Kramer, Co-PI; Kathryn Banks; Mike Burgess; Pia Ganz; Holly Longstaff; Michael McDonald; Danielle Behn Smith; Soodi Joolaee; Don Grant; Michele White; Eirikur Palsson; Mariko Ikeda

Developing & evaluating causal inference methods for pragmatic trials

Contact: ehsan.karim@ubc.ca

This project addressed the priorities:

- *Addressing real-world limitations*
- *Enhancing generalizability and individualized treatment*

Project summary

In medical research, to find out whether a treatment works for a disease typically depends on comparing the results of two groups of people: those who get the treatment, versus those who do not, ideally in a clinical trial.

To avoid bias in results, researchers who design clinical trials make sure that the people in both groups are very similar (e.g., same age, seriousness of the disease, equal length of time with the disease, so on). Unfortunately, this type of research design often does not include patients who are the sickest, of older age, or are from different ethnic groups, and thus it is impossible to know whether the drug will actually work on these types of patients.

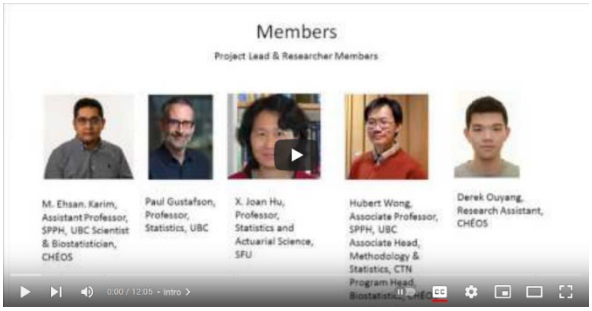
Pragmatic trials are a new kind of trial design, which aims to include these more vulnerable groups of patients. However, because these patients are less similar, it is difficult to analyze the data.

Our study focused on cases of **"incomplete treatment adherence," "partial adherence,"** and **"non-adherence"** within a sample. For example, within a study, often some patients are not able to continue with the treatment, need to take less of the drug, or have to drop out of the study.

The current ways to analyze the data often ignore most of these details, and therefore the results are not very useful to a patient or a doctor in making

treatment decisions. Sophisticated statistical methods are currently being developed, but often these methods are not well understood or accessible to the analysts.

So, we studied emerging methods of accounting for this variety within the data.



Watch a brief overview by the team **summarizing the proposal** for this project.

Runtime: 12:07

Read an in-depth overview, terminologies, findings and outputs at Ehsan Karim's personal website.

Project findings

Objective 1: Incomplete treatment adherence

We evaluated different statistical methods to account for **incomplete treatment adherence,** and contrasted the performances of these methods to some of the commonly used methods, under different realistic clinical settings where patients were supposed to follow a sustained treatment strategy. We paid particular attention to the challenging setting for data where patients' lab tests are done infrequently, evaluating various missing data analysis techniques to address such challenges.

Learn more at ehsanx.github.io

Objective 2: Partial adherence

There is some analytical guidance on estimating treatment effects when some patients are fully adherent, and some patients are not adherent at all (i.e., two categories of adherence). However, most patients are **partially adherent** in the real world—they start to take the treatment and then decide to discontinue it for various reasons.

Our research has extended the existing analytic approach to accommodate for this (i.e., considering a third category of adherence).

Learn more at ehsanx.github.io

Objective 3: Non-adherence

For dealing with medication **non-adherence,** a few methods are proposed in the economic literature (popularly known as "instrumental variable analysis"). However, it is currently unknown how good these economic methods are compared to statistical methods if we apply them to the same context, such as pragmatic trials.

In our project, we explored the characteristics of both these methods and determined how practical these methods are in various clinical scenarios.

Learn more at ehsanx.github.io

Publications

Peer-reviewed articles

Sanders, E, Gustafson, P, Karim, ME. Incorporating partial adherence into the principal stratification analysis framework. Statistics in Medicine. 2021; 40: 3625–3644.

Hossain, M.B., Mosquera, L. & Karim, M.E. Analysis approaches to address treatment nonadherence in pragmatic trials with point-treatment settings: a simulation study. BMC Med Res Methodol 22, 46 (2022).

Conference proceedings

1. Hossain MB, Mosquera L, Karim ME. Performance of statistical methods to address treatment non-adherence in pragmatic clinical trials with point treatment settings: a simulation study. University of Toronto Journal of Public Health. 2021; 2(2). (**Objective 3**)

2. Mosquera, L., & Karim, M. E. (2021, February). Evaluating Adjusted Per-Protocol Effect Estimators in Pragmatic Trials to Address Treatment Non-Adherence. In International Journal Of Clinical Pharmacy (Vol. 43, No. 1, pp. 298-298). Netherlands: Springer. (**Objective 1**)

3. Hossain MB, Karim ME. (2021, February). ESPACOMP-20-011: Comparison of statistical methods to address treatment nonadherence in pragmatic trials with only baseline covariate-measurements. In International Journal Of Clinical Pharmacy (Vol. 43, No. 1, pp. 298-298). Netherlands: Springer. (**Objective 3**)

Theses by trainees

1. Sanders E. Incorporating Partial Adherence into the Principal Stratification Analysis Framework, Statistics, UBC, MSc thesis, 2019. (**Objective 2**)

2. Mosquera,L. Exploring inverse probability weighted per-protocol estimates to adjust for non-adherence using post-randomization covariates : a simulation study, Statistics, UBC, MSc thesis, 2020. (**Objectives 1**)

International conference presentations

1. Karim ME (joint work with Hossain MB) Implications of choosing different imputation methods while inferring about per-protocol effects of sustained treatment strategies, ESPACOMP Conference (Virtual conference), Seraing, Belgium; 21 Oct 2021. (**Objective 1**)

2. Hossain MB (joint work with Karim ME) Addressing differential medication non-adherence in pragmatic trials with point-treatment settings: a simulation study. 25th ESPACOMP Conference (Virtual conference), Seraing, Belgium; 21 Oct 2021. (**Objective 3**)

3. Hossain MB (joint work with Karim ME) Comparison of statistical methods to address treatment nonadherence in pragmatic trials with only baseline covariate-measurements. 24th ESPACOMP: International Society for Medication Adherence Conference (Virtual conference), Seraing, Belgium; 10 Nov 2020. (**Objective 3**)

4. Mosquera LK (joint work with Karim ME) Evaluating Adjusted Per-Protocol Effect Estimators in Pragmatic Trials to Address Treatment Non-Adherence. 24th ESPACOMP: International Society for Medication Adherence Conference (Virtual conference), Seraing, Belgium; 10 Nov 2020. (**Objective 1**)

5. Hossain MB (joint work with Karim ME) Review of statistical methods to address treatment nonadherence in the pragmatic trial context. 41st Annual Conference of the International Society for Clinical Biostatistics (ISCB), Kraków, Poland, August 18, 2020 [RP3.28] (**Objective 3**)

6. Mosquera LK (joint work with Karim ME) Properties of Adjusted Per-Protocol Effect Estimators to Address Treatment Non-Adherence in Pragmatic Trials. 41st Annual Conference of the International Society for Clinical Biostatistics (ISCB), Kraków, Poland, August 18, 2020 [RP3.26] (**Objective 1**)

7. Mosquera LK (joint work with Karim ME) Comparing instrumental variable and naive methods for estimating the causal effect of treatment in pragmatic trials with non-compliance, The 2019 Atlantic Causal Inference Conference (ACIC), Montreal, May, 2019 (**Objective 1**)

National conference presentations

1. **Sanders E** (joint work with Gustafson P, Karim ME) Incorporating Partial Adherence into the Principal Stratification Analysis Framework, Annual Meeting of the Statistical Society of Canada, Calgary, May, 2019 (**Objective 2**)

2. **Hossain MB** (joint work with Karim ME) Comparing methods to address sparse follow-up issues in estimating per-protocol effects in pragmatic clinical trials: a simulation study. The ninth annual Canadian Statistics Student Conference (Virtual conference), Ottawa, Canada; 26 May 2021 (**Objective 1**)

3. **Hossain MB** (joint work with Karim ME) Statistical approaches to deal with treatment nonadherence in the pragmatic trial context. Canadian Statistics Student Conference 2020 (Virtual conference), Ottawa, Canada; 30 May 2020. (**Objective 3**)

4. **Hossain MB** (joint work with Karim ME) Comparing statistical methods in estimating per-protocol effects to address sparse follow-up issue in pragmatic clinical trials with treatment non-adherence. 6th Canadian Conference in Applied Statistics (Virtual conference), Montreal, Canada; 15 May 2021 (**Objective 1**)

Workshop and seminar presentations

1. **Hossain MB** (joint work with Karim ME) Performance of statistical methods to address treatment non-adherence in pragmatic clinical trials with point-treatment settings: a simulation study. 2021 SORA-TABA Annual Workshop & DLSPH Biostatistics Research Day, May 27-28, 2021, Online. (**Objective 3**)

2. **Sanders E** (joint work with Gustafson P, Karim ME) Incorporating Partial Adherence into the Principal Stratification Analysis Framework, Statistics Seminar, Department of Statistics, University of British Columbia, August 15, 2019. (**Objective 2**)

Team

Ehsan Karim, PI ✉; Paul Gustafson; Joan Hu; Hubert Wong; Samar Hejazi; Sharon Roman; Derek Ouyang; Md Belal Hossain; Lucy Mosquera; Eric Sanders

Embedding patient values in randomized control trials: A case study

This project addressed the priority:

- *Enhancing generalizability and individualized treatment*

Project summary

Clinical trials compare treatments or interventions to determine which treatment or intervention is best. However, the importance of various health outcomes and treatment requirements (for example, how a treatment is taken) varies between people, and this varying importance can influence ether or not a person chooses to take a given treatment. Traditional trial methods do not consider these variations, and often study outcomes that are important to researchers and clinicians, rather than patients.

Our project aimed to develop and test new methods to determine patient-oriented composite outcomes.

Project findings

Our team identified which health outcomes and treatment requirements were most important for pregnant people choosing a treatment approach for high blood pressure in pregnancy. We then developed new methods that reflect how patients assign importance to outcomes and treatment requirements.

Using these new methods, we found that no single treatment approach was best for all individuals. The best approach depended on which health interventions and health outcomes were most important to the individual.

Publications

Metcalfe, Rebecca K. et al. Patient Preferences and Decisional Needs When Choosing a Treatment Approach for Pregnancy Hypertension: A Stated Preference Study. Canadian Journal of Cardiology, Volume 36, Issue 5, 775 – 779 2020.

Presentations

Metcalfe, R. K., Harrison, M., Singer, J., Lewisch, M., Magee, L. & Bansback, N. (Accepted). *Integrating Patient Values into Clinical Trials Using Composite Endpoints: A Case Study Using the Control of Hypertension in Pregnancy Study*. Oral Presentation at the Annual Meeting of the Society for Clinical Trialists, San Diego, USA.

Metcalfe, R. K., Harrison, M., Singer, J., Lewisch, M., Magee, L. & Bansback, N. (Accepted*). What does this trial mean for me? Integrating patient values into clinical trials.* Oral Presentation the 4th Annual Meeting of the B.C. SUPPORT Unit, Online.

Metcalfe, R. K., Harrison, M., Singer, J., Lewisch, M., Magee, L. & Bansback, N. (2022). *From Trials to Treatment: New Methods to Integrate Patient Values and Clinical Evidence.* Oral Presentation to Meeting of Clinical Trials BC, Canada.

Metcalfe, R. K., Harrison, M., Singer, J., Hutfield, A., Lewish, M., Muramatsu, M., Magee, L. & Bansback, N. (2019). *The Importance of Emotion in Healthcare Decision-making in Pregnancy: Insights from a Qualitative Study*. Poster presented at the 4th Annual Meeting of the B.C. SUPPORT Unit, Vancouver, Canada.

Team

Joel Singer, PI; Nick Bansback, Co-I; Mark Harrison, Co-I; Mary Lewisch; Laura Magee; Peter von Dadelszen; Rebecca Metcalfe; Terry Lee – Statistician

Improving the efficiency and robustness of statistical inference for patient-oriented treatment effect in real-world clinical trials

Contact: xiehuix@sfu.ca

This project addressed the priorities:

- *Addressing real-world limitations*
- *Enhancing generalizability and individualized treatment*

Project summary

The randomized clinical trial (RCT) is the preferred study design for assessing causal effects of medical interventions. A patient and their treatment decision makers are often interested in intervention efficacy that informs what to expect when the patient actually complies with treatment.

In many real-world RCTs, however, the patient-oriented intervention effect is often challenging to evaluate because of limited sample size, a small number of compliers due to low compliance rate and small to moderate effect size on outcome measures, which can significantly reduce the power to detect intervention efficacy.

Furthermore, in many RCTs, especially when evaluating multifaceted interventions for chronic diseases, such as arthritis, the endpoints often involve multiple outcomes to measure a complex trait. This raises the challenge of how to optimally pool treatment efficacy estimation across outcome measures. The “complier-average causal effect” (CACE) approaches have become popular in informing such patient-oriented treatment effects.

Project findings

Our study has developed a novel CACE approach, called the MCACE model, to analyze the complicated data from real-world RCTs.

Comparing the new approach to existing approaches, such as the intention-to-treat and univariate CACE analysis, our new methods have shown improved efficiency and robustness—specifically, for estimating intervention efficacy, and on multiple endpoints in real-world clinical trials.

Presentations

ENAR **2021** Spring Meeting

2021 Joint Statistical Meetings

2018 and 2019 Annual workshop on research methods for patients and researchers at Arthritis Research Canada, by trainees

2021 Monthly Research Webinar in Arthritis Research Canada, by trainee

Publications

Guo, L., Qian, Y., and Xie, H (2022) Assessing Complier Average Causal Effects from Longitudinal Trials with Multiple Endpoints and Treatment Noncompliance: an Application to a Study of Arthritis Health Journal. Statistics in Medicine.

Team

Hui Xie, PI ✉; Joan Hu; Ehsan Karim; Diane Lacaille; Linda Li; Yi Qian; Hubert Wong; Kelly English; Yue Ma; Lulu Guo; Kai Li; Bocheng Jing

How to analyze and present work productivity loss due to health problems in clinical trials?

Contact: wzhang@cheos.ubc.ca, jlheureux@cheos.ubc.ca

This project addressed the priorities:

- *Addressing real-world limitations*
- *Enhancing generalizability and individualized treatment*

Project summary

Health problems can have an adverse impact on work productivity of patients and their caregivers. Patients and caregivers might have to stop working, reduce their routine work hours, miss work days, or may not be able to perform their work at their full capacity.

Work productivity loss is an important outcome to measure in clinical trials. However, analyzing work productivity loss data often requires complicated statistical methods due to the nature of the data—namely, that the data usually contains a relatively high proportion of people who have zero losses and a high proportion of people who stop working, i.e., lose all work time.

Our two objectives were:

1. To compare the **statistical performance** of different work productivity loss analysis methods.
2. To develop and assess **different ways of communicating** analysis results to non-technical users (e.g., patients and caregivers)

Project findings

Objective one: Comparing statistical methods

We found there is a **lack of consensus** on how to measure, analyze, and present work productivity loss outcomes in recent clinical trials. We found that work productivity loss in recent clinical trials is often partially measured and commonly analyzed using assumptions that may not be met. Our study suggests that selecting an appropriate statistical method to analyze work productivity loss depends on the sample size and the data distribution of work productivity loss outcomes in each treatment arm of a clinical trial.

The diversity of measurement and analysis methods used in literature may make comparability challenging. There is a **need for guidelines** providing recommendations to standardize the methods used to measure, analyze, and report work productivity loss outcomes in each treatment arm of a clinical trial.

Objective two: Ways of communicating work productivity loss results to patients and caregivers

We found, in our interviews, that patients and caregivers want to be provided with:

- Lay terms about what each work productivity loss outcome means
- Visual support for each productivity loss result
- Calculation examples when cost results are presented

From our survey, we found that:

- Patients and caregivers identify the same work productivity loss outcomes as “important to report”
- Patients and caregivers think it is important to report all outcomes in days and in cost

Presentations

December 2021: Dr. Wei Zhang and Jacynthe L'Heureux presented preliminary findings in the Work in Progress Seminar Series held at the Centre for Health Evaluation and Outcome Sciences. **(Objective 2)**

March 2022: BC SUPPORT Unit Conference: Putting Patients First. **(Objective 2)**

Publications

Zhang, W., Sun, H. How to analyze work productivity loss due to health problems in randomized controlled trials? A simulation study. BMC Med Res Methodol 21, 130 (2021). **(Objective 1)**

Team

Wei Zhang, PI ✉; Huiying Sun; Paige Tocher; Julie Sou; Lin Chen; Jacynthe L'Heureux ✉; Gary Johns; Theodore Steiner; Helen McTaggart-Cowan; Yike Huang