UTOPIAN Primary Care Trials Group – Session 6 *Minutes*

Thursday, June 18th, 2020 from 4:00 p.m. to 5:00 p.m., Zoom teleconference

Attendance:

Andrew Pinto (AP) – Chair
Aashka Bhatt (AB)
Noah Crampton (NC)
Giles Pereira (GP)
Marjan Moeinedin (MM)
Rahim Moineddin (RM)
Braden Gregory O'Neill (BGO)
Michelle Greiver (MG)
Eva Grunfeld (EG)
Ross Upshur (RU)
Donatus Mutasingwa (DM)
Carolyn Steele Gray (CSG)
Sumeet Kalia (SK)
Ann Burchell (AB)
Sheila Dunn (SD)
Rosemarie Lall (RL)
Sumeet Kalia (SK)
Noah Ivers (NI)
Tony D'Urzo (DU)
Peter Selby (PS)
Chris Meaney (CM)
Joanne King (JK)
Jennifer Rayner (JR)

Regrets:

Payal Agarwal (PA)
Aisha Lofters (AL)
Abhimanyu Sud (AS)

Item	Topic	Minutes	Action	Responsible
1	Introductions (Andrew Pinto)	• Andrew Pinto introduced those present on the phone.		
2	Review and approval of May 27, 2020 draft meeting minutes (All)	• Minutes of the previous meeting were approved by those present.	• Approved	• All
3	Learning topic: Causal effects in randomized trials and observational studies (Sumeet Kalia)	• Goals of presentation: 1. To describe causal effects using directed acyclic graphs 2. To describe the importance of randomization procedures 3. To compare intention-to-treat analysis with per-protocol analysis • Causality at individual level: ○ Hernan and Robins (2020) define "causality at individual level" as:		

Definition

- Consider binary exposure A (1: smoker; 0: non-smoker) and binary outcome Y (1: lung cancer; 0: No lung cancer).
- Let $Y^{a=1} = Y^1$ be the observed outcome for smoker; likewise $Y^{a=0} = Y^0$ be the observed outcome for non-smoker.
- The causal effect at the individual level is described as the difference between Y^1 and Y^0.

  - The causal effect at the individual level is described as the difference between Y^1 and Y^0. Together, Y^1 and Y^0 are referred to as potential (or counterfactual) outcomes

- Causality of Population Level (average causal effect):
  - Hernan and Robins (2020) define "causality at population level" as:

Definition

- An average causal effect is present if the risk of developing lung cancer among smokers is different from the risk of developing lung cancer among non-smokers:

$$Pr(Y^1 = 1) \neq Pr(Y^0 = 1)$$

  - Alternatively, average causal effect may not exist in the population if risk of death is the same in treatment and control group: $Pr(Y^1 = 1) = Pr(Y^0 = 1)$

- Randomized Trials:
  - Prospective randomized experiments are often conducted to assess the effectiveness of a treatment
  - Ideal randomized experiments with following properties allow researchers to estimate causal relationships using associations:
    - No loss to follow-up
    - No non-compliance of assigned treatment
    - Single version of treatment
    - Double-blinded treatment assignment
  - Causal inference becomes difficult in some randomized trials with:
    - Informed drop-out (e.g. systematic loss to follow-up for patients with severe conditions)
    - Non-compliance (e.g. participants do not receive intervention to which they were randomized)

- Treatment Assignment Using Randomization

  - How does randomization ensure causal effect of treatment A on outcome Y for baseline confounder L?
    - Randomization ensures balance in both measured and unmeasured confounders across treated and untreated group

		▪ Randomization ensures that the treatment groups are exchangeable (i.e. same effect measures are expected if the labels for treated and untreated groups are switched) ▪ Randomization ensures that the missing values of potential (or counterfactual) outcome Y^a occur only due to chance (i.e. missing at random). This allows the causal effect measures to be consistently estimated • Why is randomization preferred? o Identifiability conditions of causal inference are enforced in the design of randomized trials and thus causal relationships can be estimated using associations o Identifiability conditions of causal inference are needed to be assumed in observational studies and thus causal relationship cannot be estimated using associations ▪ "No unmeasured confounding" and "consistency" assumptions are untestable in observational studies; ▪ Violation of "positivity" assumption can be determined by data exploration; ▪ The validity of DAGs cannot be tested to explain the real-life phenomena. We assume DAG holds to estimate the causal effects		
5	Discussion of trial proposals and ongoing work (All)	• Aashka is maintaining a list of all the COVID-related studies happening in the DFCM and across UTOPIAN sites. In addition, we are also maintaining a list of investigators who are connected to different sites and the different trials they are connected to. o The advantage of keeping track of this information, is that when trial ideas emerge from our work, we can quickly link these ideas with sites and investigators. • 13 COVID-19 trials ongoing at DFCM and UTOPIAN sites (2 funded, 11 pending funding) o We will continue to update this list, and share it with this group in a frequent communication • We have secured an email: covid.trials@utoronto.ca • Clinical Trials Bootcamp: o A series of sessions that will run at lunchtime over a two-week span during the summer (similar to a summer institute model) o Will cover the basics of trials o We will be seeking people to present	• Maintaining list and sending out weekly communication • Email communication from: covid.trials@utoronto.ca	• Andrew Pinto and Aashka Bhatt
Meeting adjourned at 5:00 p.m.				
Next meeting: September 23, 2020; 4:00 p.m.-5:00 p.m. (virtual)				