UTOPIAN Primary Care Trials Group – Session 4 *Minutes*

Wednesday, May 27th, 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 April 30, 2020 draft meeting minutes (All)	• Minutes of the previous meeting were approved by those present.	Approved	

3	Learning topic: Adaptive Trial Design (Dr. Ross Upshur)	• Clinical trials, their design and analysis are constantly evolving field
		• Structure of RCT: Standard architecture:
		  ○ Inception Cohort (sampling, inclusion and exclusion criteria)
		  ○ Method of Randomization (allocation to Treatment and Control groups)
		  ○ Observer groups over time and measure the outcomes (relevant issue is the difference between the Treatment and Control Groups)		

		• Theory of RCT:
		  ○ Randomization balances known and unknown co-variates, such that we have an un-biased estimator (outcome measure) that tells us the difference between the Treatment and Control
		  ○ We are trying to set up a form of inference on the basis of the data
		• Adaptive Designs for Clinical Studies:
		  1. Model-based/Continual Assessment Designs
		  2. Group Sequential/Sample-Size Re-Estimation Designs
		  3. Group Sequential/Response Adaptive Designs
		  4. Adaptive Randomization Designs
		• Characteristics of Adaptive Designs:
		  ○ Streamlined
		  ○ Flexible
		  ○ Optimized
		  ○ Data-driven
		  ○ Systematic
		  ○ Decision-oriented
		  ○ Validity
		  ○ Integrity
		  ○ Bayesian
		  ○ Simulation
		  ○ Real-time
		  ○ Robust
		  ○ Cost-efficient
		  ○ Sequential learning
		  ○ Dynamic
		• 8 Common Types of Adaptations
		  ○ Stopping early (or late, i.e. extending accrual) with a conclusion of superiority or futility
		  ○ Adaptively assigning doses to more efficiently assess the dose-outcome relations
		  ○ Adding or dropping arms or doses (perpetual motion machines)
		  ○ Seamless phases of drug development within a single trial
		  ○ Changing the proportion of patients randomized to each arm
		  ○ Adaptively identifying in on an indication or responder population
		  ○ Changing accrual rate
		  ○ *Many of these 'types' can be set up in advance (i.e. planned adaptations)
		• Adaptive Trials Components:
		  ○ Interim Analysis: Frequent
		  ○ Randomization: Variable
		  ○ Number of Arms: Few to many		

		○ Use of Incomplete Data: Imputation at all stages ○ Philosophy: Bayesian or Frequentist ○ Control of Errors Rate: Via Extensive Simulation		
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. ○ 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) ○ 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: ○ A series of sessions that will run at lunchtime over a two-week span during the summer (similar to a summer institute model) ○ Will cover the basics of trials ○ 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: Thursday, June 18, 2020; 4:00 p.m.-5:00 p.m. (virtual)				