# UTOPIAN Clinical Research Group Meeting
# MINUTES

March 31, 2022
Time: 4:00 PM – 5:00 PM EST
Teleconference (Zoom)

**Action Items**:

1. Jamie to circulate information regarding the CHEAP trial to interested sites/physicians once reviewed and approved by the UTOPIAN Scientific Advisory Committee.
2. UTOPIAN is planning a workshop in July 2022 on CIHR Project Grant Writing – Details to be shared soon.

## Review & Approval of Minutes

- Minutes from the previous UTOPIAN Clinical Research Group (CRG) meeting were **approved**.

## Lecture Series 3: Common approaches to Analyzing Data from Clinical Trials in Primary Care

*Presenter: Dr. Rahim Moineddin*

Introduction

- The strategy for data analysis depends on the study design (e.g., what randomization method and randomization unit are being used, whether it is a single or multi-centre study, etc.)

Intention to Treat Analysis

- A major threat to the validity of clinical trials is loss to follow up and participants not following the protocol appropriately (e.g., not taking medications as prescribed).
    - A strategy to address this is using intention to treat (ITT) analysis, which analyzes data by the study arm participants were assigned to, regardless of whether they followed the protocol.
    - An alternative approach is analyzing the data per protocol, sometimes called modified ITT, which removes participants that did not follow the protocol.

Baseline Characteristics by Treatment Groups

- Before conducting statistical analysis, studies must determine the 'balance' between participants in study arms (i.e., important demographic and clinical characteristics using descriptive statistics).
    - Randomization is expected to produce similar baseline statistics across groups.
    - This process may help identify potential confounders.

Adjusted Analysis

- An adjusted analysis takes into account differences in baseline characteristics between groups that may influence the outcome (i.e., confounders; e.g., if one group has older participants, the difference in the outcome (or lack of difference) could be attributed to the age imbalance).
    - Adjusted analysis account for confounders using the appropriate statistical method (e.g., a regression model).

Effect Modifiers and Stratified Analysis

- Effect modification occurs when an exposure has a different effect among different subgroups. Effect modification is associated with the outcome but not the exposure (e.g., a cancer treatment that has a different effect in males versus females).

Secondary Analysis

- In many trials, there is the primary analysis and secondary analysis. The secondary analyses may not always be pre-specified in the protocol as they are supplemental and can range from being conclusive to hypothesis generating.

Sensitivity Analysis

- Sensitivity analysis is a method used to determine the robustness of an assessment by examining the extent to which results are affected by changes in methods, models, values of unmeasured variables, and/or assumptions.
    - Consistency between the results of the primary analysis and sensitivity analysis may strengthen conclusions being made.
    - This is important because clinical trials often rely on assumptions that may have some impact on conclusions if they are not met.

Subgroup Analysis

- Subgroup analysis is the analysis of results in certain subgroups. These should be specified in the protocol in advance.
    - There are conflicting opinions on the value of subgroup analysis. Opponents suggest it is a fishing expedition, whereas advocates highlight the risk of missing important differences in treatment effects.

## Project Presentation: The Cost, Health, and Effectiveness Assessment of the Portfolio Diet in Primary Care (CHEAPP) Program

*Presenter: Dr. John L. Sievenpiper*

Introduction

- The Portfolio diet is a plant-based, dietary portfolio of cholesterol-lowering foods.
    - This includes nuts, vegetable proteins (e.g., soy products), viscous fiber (e.g., oats, barley, eggplant, etc.), plant sterols (e.g., plant sterol margarine, oil, supplements), and heart healthy oils (e.g., extra virgin olive oil).
    - Previous single centre study comparing the Portfolio diet to Statin found a similar -30% change from baseline in LDL cholesterol at one month.
    - Similar results were found in a more real-world based trial involving 4 sites, 345 participants, and a six-month follow up.

How up Translate the Guidelines into Clinical Practice?

- International health organizations supported the Portfolio diet for cardiovascular disease risk reduction.
- Presented findings using an infographic, which was posted on the Canadian Cardiovascular Society website and provides background and tips.
- The study team has also developed an app to share findings with a wider audience. Viewers can see how they are performing compared to other users, access cookbooks, tip sheets, and videos, etc.

Study Proposal

- **Study Design**: Parallel RCT with 2 groups (N=500/group) for assessment of efficacy, adherence, recruitment, retention and cost of the Portfolio diet.
    - Participants randomized to either the Portfolio diet group or standard of care and followed for one year.
- **Participants & Recruitment**: Primary and secondary prevention participants at high cardiovascular disease risk on background statin therapy.

    - Recruit 10 sites (UTOPIAN) with 34 physicians and 30 participants per physician over two-years.
- **Data Collection**: Food frequency and other questionnaires (REDCap), bloodwork (LifeLabs), clinical events (ICES).
- **Primary Outcome**: Proportion of participants achieving a ≥10% reduction in LDL cholesterol or non-HDL cholesterol at one year.

## Recent Publications


- Garrison SR, Kolber MR, Allan GM, Bakal J, Green L, Singer A, Trueman DR, McAlister FA, Padwal RS, Hill MD, Manns B, McGrail K, O'Neill B, Greiver M, Froentjes LS, Manca DP, Mangin D, Wong ST, MacLean C, Kirkwood JE, McCracken R, McCormack JP, Norris C, Korownyk T. Bedtime versus morning use of antihypertensives for cardiovascular risk reduction (BedMed): protocol for a prospective, randomised, open-label, blinded end-point pragmatic trial. BMJ Open. 2022 Feb 24;12(2):e059711. doi: 10.1136/bmjopen-2021-059711. PMID: 35210352.
- Shuldiner J, Schwartz KL, Langford, BJ, Taljaard M, Grimshaw JM, Lacroix M, Tadrous M, Leung V, Brown K, Morris AM, Garber G, Presseau J, Thavorn K, Leis JA, Witteman HO, Brehaut J, Daneman N, Silverman M, Greiver M, Gomes T, Kidd, MR, Francis JJ, Zwarenstein M, Lam J, Mulhall C, Gushue S, Uppal S, Wong A. Optimizing responsiveness to feedback about antibiotic prescribing in primary care: protocol for two interrelated randomized implementation trials with embedded process evaluations. Implementation Sci. 2022 Feb. 17(17):1-17 https://doi.org/10.1186/s13012-022-01194-8.
- Crampton N, Greiver M, Woods N, Singer A, Domb S, Orava M, Shachak A. Teaching electronic medical record (EMR) data discipline to clinical trainees: A Canadian pilot study. Int J Med Inform. 2022 Mar;159:104664. doi: 10.1016/j.ijmedinf.2021.104664. Epub 2021 Dec 29. PMID: 34999411.
- Naimer, M.S., Aliarzadeh, B., Bell, C.M. et al. Specialist wait time reporting using family physicians' electronic medical record data: a mixed method study of feasibility and clinical utility. BMC Prim. Care 23, 72 (2022). https://doi.org/10.1186/s12875-022-01679-x