**Course Title:** Combining randomized and non-randomized studies in evidence synthesis: Why, how, and when?

**Presenters:** Dr.Chris Cameron, Mr. Tim Disher, Dr. Marsha Campbell-Yeo

**Course Type:** Half day

**Course Level:** Intermediate

**Course Limit, if any (maximum number of attendees):** ??

**Overview:** This course will provide an overview of methods for combining randomized controlled trials (RCTs) and non-randomized studies (NRS) in meta-analysis. We will discuss the theoretical and practical reasons for considering combining evidence from RCTs and NRS, as well as common pitfalls. We will also complete a hands-on application where we combine RCTs and NRS using three common analytic approaches, and provide guidance for assessing whether a combined analysis is appropriate.

**Background:** Historically, synthesis of RCTs and NRS have been avoided out of concern for introducing bias into decision making. The increase in the use of high-quality non-randomized designs challenges this paradigm, as it is becoming increasingly difficult for decision-makers to justify ignoring NRS entirely. When NRS are excluded from meta-analysis, there is a risk that they will be incorporated informally which reduces transparency and may lead to inappropriate decisions. These undesirable outcomes can be avoided through the appropriate synthesis of RCTs and NRS using existing models that allow for downweighting and bias-adjustment of NRS including expert elicitation, incorporation of NRS as prior information, and Bayesian hierarchical modeling. This course will provide an overview of when these methods are appropriate, and also provide a hands-on application using simulated and real datasets.

**Format and Requirements:** The course will combine didactic and interactive approaches consisting of short presentations, and hands on exercises, as well as discussion. Participants will be required to bring laptops with R and RStudio installed for participation in exercises. Installation instructions will be provided in advance of the course. The workshop will be formatted to be informative, engaging and be targeted to participants with clinical, policy or stakeholder, or statistical backgrounds. We will assume a basic understanding of systematic reviews and meta-analysis.

**Course Description and Objectives:**  We will begin by reviewing the motivation for combining RCTs and NRS motivated by examples in the literature. Following this, we will highlight through theory and simulated examples the potential risks of introducing evidence from NRS. We will conclude with a review of existing methods for the transparent synthesis of RCTs and NRS, including hands-on exercises with example code. These methods will include adjustment of NRS through:

1. Incorporation of expert opinion, including a simple elicitation exercise.
2. Use of observational trials as prior evidence
3. Bayesian hierarchical models

We will subsequently discuss how findings from such studies can be used to support healthcare decision making.

Objectives:

Following this short-course, participants will:

* Understand why the synthesis of RCTs and NRS may be desirable;
* Appreciate the limitations and potential biases involved with combining RCT and NRS ;
* Describe the main approaches for synthesis of RCTs and NRS and the conditions under which each is optimal;
* Have familiarity running and interpreting a synthesis of RCTs and NRS