2021 Mediation Research Days

May 6-7, Virtual Meeting

April 26, 2021

Welcome Address

The goal of Mediation Research Days is to bring together researchers and students interested in the use and development of mediation methods in the traditional or causal context. Invited and contributed speakers will present on state-of-the-art mediation analysis techniques for cross-sectional or longitudinal data and discuss applications of mediation analysis in different fields (epidemiology, psychology, etc.). Presentations and discussions will focus on current challenges in mediation analysis as well as future directions for methodological development.

Thank you for your participation and we hope you enjoy the event!

Milica Miočević & Geneviève Lefebvre, Co-organizers.

Contents

Links & Schedule

This information can be found at https://www.milicamiocevic.com/mediation-days-2021 (password: indirecteffect)

Zoom link for all talks on May 6th:
https://mcgill.zoom.us/j/89027414694?pwd=SGNLT1pvM2VTZXY0TE1GZWM1MDdnZz09
Passcode: 609883

Zoom link for all talks on May 7th:
https://mcgill.zoom.us/j/89518186761?pwd=dmRJd0tJVW5NQk93eDNUYXpzNlhHUT09
Passcode: 072493

Gathertown link for all social and networking events:
https://gather.town/app/oP7xNGsWf4Mg7BgW/Mediation%20Rooftop%20Party

The student videos will be made available to all attendees on April 30th 2021. All event attendees will have the opportunity to discuss their research at social events held using Gather town. Gather town is a platform that allows each user to create an avatar, move around the rooftop bar space we created for our event, and once a group of avatars are in proximity of each other they will become part of the same video call (much like Zoom, with the option of joining different conversations by approaching different groups of avatars).

All times are EST	**MAY 6**	**MAY 7**
9:00–10:00	Dr. Milica Miočević *McGill University*	Dr. Tom Loeys *Ghent University*
10:00–11:00	Dr. Isabelle Doré *Université de Montréal*	Dr. Geneviève Lefebvre *UQAM*
11:00–12:00	Dr. Amanda Montoya *UCLA*	Dr. Matt Valente *FIU*
12:00-13:30	LUNCH BREAK	LUNCH BREAK
13:30-14:30	Dr. Denis Talbot *Université Laval*	Dr. Marie-Pierre Sylvestre *Université de Montréal*
14:30-15:30	Dr. David MacKinnon *ASU*	Gather Town *(Networking Event)*
15:30-16:30	Gather Town *(Student Presentations Q&A)*	Gather Town *(Networking Event)*

Student Presentations

Mediation by Coping Style in the Association Between Stressful Life Events and Depressive Symptoms in Young Adults

Annie Pelekanakis

Université de Montréal

Purpose: The association between stressful life events and depressive symptoms is well-established, but the role of coping style in this association is less clear. We examined whether problem-focused, emotion-focused or avoidant coping style mediated and/or moderated the association in young adults.

Methods: Data collected in self-report questionnaires were drawn from a 20-year longitudinal study that included 1294 students (age 12-13) from 10 high schools in Montreal, Canada in 1999-2000. The analytic sample included 782 participants age 24 years on average with data on covariates collected at age 20. Using VanderWeele's four-way decomposition approach, the total effect of stressful life events on depressive symptoms considering coping styles was decomposed into four components : moderation only, mediation only, mediated interaction, no mediation or moderation.

Results: We observed mediation only by emotion-focused coping ($\hat{\beta}$ (95%CI)= 0.15(0.05, 0.17)) suggesting that individuals who experienced more stressful life events also report greater use of emotion-focused coping and higher levels of depressive symptoms. We found moderation only by problem-focused coping ($\hat{\beta}$ (95%CI))=-1.51(-2.22, -1.06)) and by emotion-focused coping ($\hat{\beta}$ (95%CI))=1.16(1.05, 1.68). These results suggest that individuals reporting more problem-focused coping experienced fewer depressive symptoms after exposure to stressful life events; those reporting more emotion-focused coping experienced more depressive symptoms. Avoidant coping did not mediate or moderate the association between stressful life events and depressive symptoms.

Conclusion: Interventions that aim to reduce depressive symptoms in young adults who experienced stressful life events may need to reinforce problem-focused coping and minimize emotion-focused coping strategies.

Cardiovascular Risk Factors and Carotid Intima Media Thickness: Mediation and Interaction by Grip Strength

Christian W. Mendo
Université de Montréal

Frailty is often described as an increased vulnerability to the effects of stressors. There is little research investigating the specific role of frailty in the association between cardiovascular risk factors such as type 2 diabetes and hypertension and vascular atherosclerosis. Using the 4-way decomposition method elaborated by VanderWeele, we investigate the role of grip strength, as a physical marker of frailty, and the effect of cardiovascular risk factors (specifically type 2 diabetes as well as hypertension) on the vascular atherosclerotic burden of individuals [measured using carotid intima media thickness (cIMT)]. We present analyses of the Canadian Longitudinal Study on Aging, focusing on the 30,000 study participants who underwent serial physical evaluations at one of 11 data collection sites between 2011 and 2018. Our findings suggest that grip strength does not mediate associations between T2D and cIMT, nor between hypertension and cIMT [pure indirect effect (95% CI) = 0.02 (-0.01, 0.05) and 0.03 (-0.03, 0.04), respectively]. We found evidence of strong interactions between grip strength and T2D as well as hypertension, in their association with cIMT (mediated interaction and interaction only effects ranging from 18.4% to 30.7%).

Joint work with Mark Robert Keezer (MDCM, PhD) and Marie-Pierre Sylvestre (PhD).

Keywords: carotid intima media thickness, grip strength, mediation, interaction, CLSA

Assessing Mediator to Outcome Confounding Bias in Mediation Analysis using Sensitivity Analysis

Diana Alvarez Bartolo
Arizona State University

Confounding represents a threat to the causal interpretation in mediation analysis. For instance, if X represents random assignment, the effect of the independent variable (X) on the mediator (M) and the effect of the independent variable (X) on the outcome (Y) have a causal interpretation under certain reasonable assumptions. However, the randomization of X does not allow for a causal interpretation of the mediator (M) to outcome (Y) effect unless certain confounding assumptions are satisfied. Several techniques help strengthen the causal interpretation of the M to Y effect in mediation analysis. For instance, sensitivity analysis is a group of methods that help deal with confounding bias when there is no measure of the potential confounders. This presentation will describe a project that aims to develop a significance test, confidence interval estimation, and an effect size comparison for two confounder sensitivity analysis methods: Left Out Variable Error (L.O.V.E) and correlated residuals.

Outcome-Adaptive Lasso for Causal Mediation Analysis: Variable Selection for Direct and Indirect Effects

Ismaila Baldé
Université du Québec à Montréal (UQAM)

Causal inference strives for constructing unbiased estimators of the effect of treatment on the outcome. When seeking to estimate the total effect, propensity score (PS) methods are widely used to control for confounding bias from observational data. Today, it is well established that only the confounders and the predictors of the outcome are necessary to avoid bias and improve accuracy. However, for causal mediation analysis, the appropriate variables to include in the models are not clearly known in the literature. We propose the outcome adaptive lasso for causal mediation analysis (MOAL) that combines the strengths of the methods OAL (Shortreed and Ertefaie, 2017) and Sequential g-estimator (Vansteelandt, 2009) to select appropriate variables. Unlike many existing methods in causal mediation, MOAL can be used in the presence or absence of intermediate confounders. Simulation results show that for the direct effect, MOAL selects the PS model that includes the confounders (treatment-response and mediator-response) and the predictors of the response, while excluding the remaining variables. The indirect effect is deduced by the difference method. We also illustrate variable selection using the MOAL approach using data from the Harvard School of Public Health College Alcohol Study, 1999.

Joint work with Geneviève Lefebvre.

Introducing an Exact Regression-Based Natural Effect Estimator for Binary Outcome and Continuous Mediator

Mariia Samoilenko
Université du Québec à Montréal (UQAM)

Several regression-based approaches to estimate natural effects (NE) have been developed over the last decade for a continuous mediator and a binary outcome. VanderWeele and Vansteelandt derived approximate expressions for the NE on the odds ratio scale under the rare outcome assumption. Recently, Gaynor et al. derived approximate NE estimator for a common outcome using the relationship between logit and probit models. In line with this body of work, we propose a NE estimator based on linear mediator and logistic outcome regressions, but derived without simplifying approximations. Unlike the aforementioned estimators, our exact NE estimator relaxes the rareness/commonness assumptions for the outcome. We will introduce the proposed estimator on the risk/odds ratio and risk difference scales with corresponding formulas for error estimation by delta method. We will also illustrate its performance in simulation scenarios where the outcome is rare or common.

Joint work with Geneviève Lefebvre.

May 6 Invited Presentations

Bayesian Mediation Analysis with Informative Prior Distributions Based on Historical Data

May 6
9:00-10:00, EST

Milica Miočević

Department of Psychology, McGill University

Bayesian analysis is exact for small samples and is often suggested as a solution for convergence issues and low power (e.g., Depaoli, 2013; Lee & Song, 2004; Yuan & MacKinnon, 2009). However, as was pointed out in a recent systematic review (Smid, McNeish, Miočević, & van de Schoot, 2020), Bayesian methods have advantages over classical methods almost only with accurate informative prior distributions, and consequences of using inaccurate informative priors can be detrimental for the statistical properties of parameters of interest (see e.g., Depaoli, 2014; Holtmann, Koch, Lochner, & Eid, 2016; Miočević, Levy, & MacKinnon, 2020).

This talk describes how power prior distributions (Ibrahim & Chen, 2000) based on a historical data set can be used to increase power to detect the indirect effect in Bayesian mediation analysis (Miočević & Golchi, 2021). The only requirements for implementing the procedure are that the data from the current study constitute a representative sample from the population of interest, and that the historical and current data sets contain measures of the same covariates and independent variable, mediator, and outcome. The simulation study findings show that the proposed method leads to appropriate amount of borrowing from the historical data set, which leads to increases in precision and power when the historical data and current data are exchangeable and does not induce bias when the historical and current studies are not exchangeable.

Investigating Mechanisms Underpinning Physical Activity Benefits on Mental Health: Using Mediation Analysis to Inform Public Health Interventions

May 6
10:00-11:00, EST

Isabelle Doré

School of Kinesiology and Physical Activity Sciences, Faculty of medicine, Université de Montréal; School of Public Health, Université de Montréal (second affiliation); Regular researcher, CHUM Research Center.

It is well known that physical activity can promote mental health and prevent common mental disorders symptoms such as anxiety and depression. However, few studies investigate the psychosocial mechanisms underpinning this association, thus limiting the potential to develop and implement effective public health interventions targeting these mechanisms. Using two examples of mediation analysis in physical activity and mental health research, this presentation proposes to 1) provide a brief overview of natural effect definitions and assumptions for mediation analysis in the counterfactual framework, 2) explore specificities of different R packages for causal mediation analysis, and 3) present results from single and multiple mediator models. Data used for these examples were collected among youth participating in MATCH (Monitoring Activities of Teenagers to Comprehend their Habits study), an ongoing longitudinal study (2011-. . .) investigating patterns of physical activity participation during adolescence and young adulthood and various physical and mental health outcomes. The first example examined whether the perception of three basic psychological needs (autonomy, competence and relatedness, specifically in the context of physical activity) and moderate-to-vigorous physical activity (MVPA) mediates the association between the number of years participating in physical activity and mental health in youth. The second example investigated the association between physical activity motives (enjoyment, competence, fitness, appearance and social) and mental health and the potential mediating effect of physical activity volume on these associations among youth.

Moderated Mediation for Repeated-Measures Designs

May 6
11:00-12:00, EST

Amanda Kay Montoya

Department of Psychology, University of California Los Angeles (UCLA)

Mediation and moderation are both commonly used analytical approaches for more deeply understanding the relationship between two variables (X and Y). Mediation analysis evaluates indirect effects, where a third variable acts as a pathway by which X effects Y, while moderation analysis evaluates whether the relationship between X and Y depends on a third variable. Integrating mediation and moderation together into moderated mediation analysis, elucidates how indirect effects may depend on a moderator variable. These models are very popular in psychology, consumer behavior, and many other fields when applied to between-subject data (experiments or cross-sectional). Recent developments in within-subject mediation and moderation allow for the introduction of moderated mediation analysis in within-subject

designs. In this talk, I show how to conduct this new analysis, it's equivalence in special cases to multilevel moderated mediation, and introduce a new version of MEMORE (available for SPSS and SAS) to fit these models.

The Impact of Adjusting for Pure Predictors of Exposure, Mediator and Outcome on the Variance of Natural Direct and Indirect Effect Estimators

May 6
13:30-14:30, EST

Denis Talbot

Département de médecine sociale et préventive, Université Laval

It is now well established that adjusting for pure predictors of the outcome, in addition to confounders, allows unbiased estimation of the total exposure effect on an outcome with generally reduced standard errors. However, no analogous results have been derived for mediation analysis. Considering the simplest linear regression setting, we develop theoretical results showing how the variance of estimators of the natural indirect effect and natural direct effect on the difference scale are affected when adjusting for pure predictors of the exposure, mediator and outcome. We also present simulation results that confirm these results and suggest they extend to multiple other situations, including cases where the mediator or the outcome is binary, or to the risk ratio and odds ratio scales. A real-data illustration employing data from the Canadian Study of Health and Aging is provided. This analysis is concerned with the mediating effect of vitamin D in the effect of physical activity on dementia and its results are overall consistent with the theoretical and empirical findings.

Joint work with Awa Diop, Geneviève Lefebvre, Caroline S Duchaine, Danielle Laurin.

Mediation Days and Nights: Moving from Traditional to Causal Mediation Analysis

May 6
14:30-15:30, EST

David Mackinnon

Department of Psychology, Arizona State University

The presentation describes some challenges in moving from traditional social science approaches for mediation analysis to methods based on the potential outcomes framework. I use the analysis of experimental data with a continuous mediator and outcome to link potential outcomes and traditional mediation analysis. Potential outcomes estimators correspond to tests of simple effects in traditional statistical analysis. The two approaches lead to different interpretation of results and different emphasis on assumptions such as confounding, measurement, and temporal precedence. Traditional and potential outcomes methods are applied to data from eight benchmark memory studies where the mediated effect can be considered known to exist. Methods include natural effects models, ratio of mediator probability weighting models, and traditional mediation analysis with the product of coefficients method. Strategies and roadblocks to motivating the transition to potential outcomes methods are discussed.

May 7 Invited Presentations

Disentangling Indirect Effects Through Multiple Mediators Without Assuming any Causal Structure Among the Mediators

May 7
9:00-10:00, EST

Tom Loeys

Department of Data Analysis, Ghent University

When there are multiple mediators on the causal pathway from treatment to outcome, path analysis is commonly used to disentangle the indirect or mediated effects transmitted through each of the mediators. However, decomposing the total effect into separate indirect effects along causal paths linking several mediators is valid only under stringent assumptions, such as a correctly specified causal structure of the mediators, and no unobserved confounding of the mediators.

In this talk, we introduce a new definition of direct and indirect effects for multiple mediators, called interventional effects, from the causal inference and epidemiology literature. Interventional direct and indirect effects are well-defined and can be unbiasedly estimated without relying on the aforementioned assumptions. We will focus on a particular class of linear models widely used for multiple mediation analysis. We demonstrate how the interventional indirect effects through each distinct mediator can be estimated using existing path analysis methods within the linear structural equation modeling framework.

Interestingly, the proposed interventional effect estimators adopt the same mean models for the mediators and outcome as prevalent path analysis estimators that (incorrectly) assume no causal effects among the mediators. These existing path analysis estimators are therefore endowed with a causal interpretation that is valid regardless of the underlying causal structure of the mediators when estimating interventional effects. Furthermore, the estimators are unbiased even when the mediators share hidden or unobserved common causes.

Joint work with Wen Wei Loh, Beatrijs Moerkerke and Stijn Vansteelandt.

May 7
10:00-11:00, EST

Bayesian Joint Modeling for Causal Mediation Analysis With a Binary Outcome and a Binary Mediator

Geneviève Lefebvre

Département de mathématiques, Université du Québec à Montréal (UQAM)

Mediation analysis with a binary outcome is notoriously more challenging than with a continuous outcome. In this talk, we will present a new approach for performing causal mediation with a binary outcome and a binary mediator. Our proposal relies on the Student-t approximation to the Bayesian multivariate regression logistic model introduced by O'Brien and Dunson (*Biometrics*, 2004). We will explain how this latent multivariate model can be used to estimate the natural direct and indirect effects of an exposure in any measure scale of interest (e.g., odds or risk ratio, risk difference). Our novel mediation approach has several valuable features which, to our knowledge, are not found together in current binary-binary mediation models. The model will be illustrated and compared to two existing approaches for conducting causal mediation analyses with this type of data.

Joint work with Miguel Caubet Fernandez and Mariia Samoilenko.

May 7
11:00-12:00, EST

Causal Mediation Effects in Single-Case Experimental Designs (SCEDs)

Matthew J. Valente

Department of Psychology, Florida International University

Single Case Experimental Designs (SCEDs) are used to test treatment effects in a wide-range of fields and consist of repeated measurements for a single case throughout one or more baseline phases and throughout one or more treatment phases. The repeated measurements over time form a time series and manipulation of the baseline and treatment phase make SCEDs a type of interrupted time series design which is considered one of the most effective quasi-experimental designs for causal inference. Recently, mediation analysis has been applied to SCEDs. Mediation analysis decomposes the total treatment-outcome effect into a direct and indirect effect, and therefore helps unravel the causal processes underlying treatment-outcome effects. The most recent methodological advancement for mediation analysis is the development of causal mediation analysis methodology which clarifies the necessary causal assumptions of mediation analysis. The goal of this presentation is to describe and apply causal mediation effect definitions to commonly used piecewise linear regression models that are used in SCEDs. An empirical example is presented to demonstrate the newly-derived causal mediation effects in SCEDs.

Direct and Indirect Effects in the Presence of Time-Varying Confounding : The Mediating Effect of Friends Smoking in the Association Between Depressive Symptoms and Smoking in Youth

May 7
13:30-14:30, EST

Marie-Pierre Sylvestre

Département de médecine sociale et préventive, Université de Montréal

We recently reported that the mediating role of friends smoking in the association between depressive symptoms and cigarette smoking is attenuated during late adolescence (Mendo et al. 2021). In this analysis, we examine data restricted to younger adolescents and we relax several assumptions made previously. For example, we treat the confounders, exposure, mediator and outcome as time-varying variables during young adolescence, we account for time-varying confounding, and we allow for past values of the mediator to affect subsequent values of the exposure. We use data from the Nicotine Dependence In Teens study (NDIT) a prospective investigation of 1294 students from 10 high schools in Montréal, Canada. We focus the analysis on cycles 4 to 8, when participants were 13-14 years old (n=1189). We conducted longitudinal mediation analysis to account for time-varying depressive symptoms and number of friends who smoke. Direct and indirect effects were estimated using the weighting approach proposed by VanderWeele & Tchetgen Tchetgen (2017), which is based on combining the results of two marginal structural models. In addition to time-invariant variables (e.g., sex, mother's education), models were adjusted for potential time-varying confounders, including alcohol consumption, parents who smoke, age, participation in a team sport and cigarette consumption in previous cycles. 95% confidence intervals were based on bootstrap. The estimated overall effect of depression symptoms on cigarette smoking was 1.08 (95% CI: [0.18 – 2.46]). The estimated direct effect was 0.74 (95% CI [-0.12 – 2.01]). Friends smoking mediated the association between depressive symptoms and cigarette smoking with an estimated indirect effect of 0.34, 95% CI: [0.09 – 0.90]).

Joint work with Miceline Mésidor and Jennifer O'Loughlin.

Speaker Index