CANSSI Grant Proposal (Early Draft)

Title of Project

???

Name and Affiliations of lead investigators

1. Patrick Brown

   Affiliation: Centre for Global Health Research, St. Michael's Hospital

   Affiliation: Department of Statistical Sciences, University of Toronto

2. Fateh Chebana

   Affiliation: Institut national de la recherche scientifique (INRS)

3. Cindy Feng

   Affiliation: School of Epidemiology and Public Health, University of Ottawa

List of proposed callaborators, titles, and affiliations

1. Kamal Rai

   Affiliation: Centre for Global Health Research, St. Michael's Hospital

   Affiliation: Department of Statistical Sciences, University of Toronto

2. Hwashin Shin

   Affiliation: Environmental Health Science and Research Bureau, Health Canada

   Affiliation: Department of Mathematics and Statistics, Queen's University

3. Pierre Masselot

   Affiliation: London School of Hygiene & Tropical Medicine

List of potential partner organizations (optional)

Centre for Global Health Research, St. Michael's Hospital

Department of Statistical Sciences, University of Toronto

Institut National de Santé Publique du Québec (?)

Research Aims

This project aims to investigate the combined effect of multiple pollutants on various mortality outcomes by examining two main research questions.

1. What is the combined effect of multiple pollutants on various daily mortality outcomes?
2. What is the relationship between daily nCovid-19 mortality and air pollution?

Let us consider the first research question. The workhorse of the air pollution literature is a one-pollutant Poisson regression model that accounts for confounders using fixed effects and smooth functions, typically a natural cubic splines (Samet et al. 2000; Dominici et al. 2002; Laden et al. 2006). A typical model is,

$$Y_t|\lambda_t = \text{Poisson}(\lambda_t),$$
$$\log(\lambda_t) = X\beta + \gamma P_1 + \sum_{i=1}^{I} f_i(t_i).$$

Here, Y_t is the health outcome of interest, such as respiratory mortality or morbidity. The design matrix X typically contains day-of-the-week effects and seasonal terms, and the $f_i(t_i)$ are smooth functions of potential confounders such as time and temperature. When fit to Canadian mortality data, the log relative risks estimated by the one-pollutant model are very small for $PM_{2.5}$, PM_{10}, SO_2, and NO_2 (Huang, Brown, and Shin 2020). Additionally, the association between the chosen health outcome and P_1 may not be (log) linear, with higher pollutant levels having larger health impacts (Liu et al. 2019).

Modeling P_1 through a nonlinear but smooth function s_1 is one potential remedy to the second concern. A natural extension of this model to N pollutants is to fit each pollutant P_i to its own smooth function s_i ($i = 1, \ldots, N$). Then, the link function in the model becomes,

$$\log(\lambda_t) = X\beta + \sum_{i=1}^{N} s_i(P_i) + \sum_{i=1}^{I} f_i(t_i).$$

While promising, this version of the multiple-pollutant model raises the concern that the the correlation between pollutants may bias estimates, which is particularly meaningful when (log) estimates are so small. Taking inspiration from *additive index models*, discussed in Fawzi et al. (2016), this project will apply smooth functions to a convex combination of pollutants. This will allow the model to estimate the *combined* effect of these polluntants in a natural and informative way. For instance, this weighted sum naturally captures synergistic effects that can occurs when more than one pollutant is present at higher levels (Xia and Tong 2006).

Let f_i ($i = 1, \ldots, I$) denote smooth functions of confounders and s_1 a smooth function of pollutants P_1 and P_2. Thus, the link function in our proposed model is,

$$\log(\lambda_t) = X\beta + s_1(\alpha_1 P_1 + \alpha_2 P_2) + \sum_{i=1}^{I} f_i(t_i).$$

Here, α_1 and α_2 are weights that will be estimated by the model. They can be interpreted as the relative impact that each pollutant on the chosen mortality outcome.

The second research question considers the mortality outcome of daily coronavirus deaths. This has become an active area of research in recent months. For instance, Wu et al. (2020) finds that a 1 μg increase in long-term exposure to ambient $PM_{2.5}$ increases the coronavirus death rate by 15%. Additional studies that examine this relationship include (Conticini, Frediani, and Caro 2020; Sciomer et al. 2020; Setti et al. 2020).

Much work remains to be done. For instance, non-COVID-19 daily mortality data is generally not available, such that these early results are unable to obtain an accurate measure of the *excess* deaths attributable to COVID-19. This is a very important point, as COVID-19 cases (and deaths) are likely under-reported due to limited levels of testing. For another, cumulative COVID-19 mortality will continue to rise for some time, such that this question is most suitable for ongoing inquiry over the next 2-3 years.

Anticipated roles of trainees (students and post-doctoral fellows)

1. Kamal

   Role: Will implement the models?

2. Trainee: University of Toronto PhD

   Role: TBD

3. Trainee: University of Ottawa PhD

   Role: TBD

Plans for dissemination and communication

Suggested reviewers

(Possible) CVs

- Patrick
- Fateh
- Hwashin
- Meredith
- Cindy

Preliminary budget description

(Tentative) Budget:

- 50% for post-doc salary
- 10% for travel + conferences
- 20% for Laval PhD student
- 20% for UofT PhD student

Annual meetings: 2-day meeting in Ottawa, just prior to SSC (5k?)

Other funding (optional)

Are there other funding sources?

References

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Wu, Xiao, Rachel C Nethery, Benjamin M Sabath, Danielle Braun, and Francesca Dominici. 2020. "Exposure to Air Pollution and Covid-19 Mortality in the United States." *medRxiv*. Cold Spring Harbor Laboratory Press.

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