

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 collaborators, 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 COVID-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 $\text{PM}_{2.5}$, 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 ($i = 1, \dots, N$). 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 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 pollutants in a natural and informative way. For instance, this weighted sum naturally captures synergistic effects that can occur when more than one pollutant is present at higher levels (Xia and Tong 2006).

Let f_i ($i = 1, \dots, I$) 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 $1 \mu\text{g}$ increase in long-term exposure to ambient $\text{PM}_{2.5}$ 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 yet available, such that we do not have an accurate measure of *excess* deaths attributable to COVID-19. These excess deaths could be attributable to under-reported COVID-19 case and death counts (due to limited testing) or restricted access to care for patients with other health conditions. Moreover, cumulative COVID-19 mortality will likely continue to rise for some time, making the question of excess deaths best suited for an ongoing inquiry that help inform public health responses.

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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- Laden, Francine, Joel Schwartz, Frank E Speizer, and Douglas W Dockery. 2006. "Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study." *American Journal of Respiratory and Critical Care Medicine* 173 (6). American Thoracic Society: 667–72.
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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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