Title of the Project: Statistical Methods for Daily Mortality and Multiple Environmental Risk Factors

Name and affiliations of lead investigators

- Patrick E. Brown
  - Centre for Global Health Research, St. Michael's Hospital
  - Department of Statistical Sciences, University of Toronto
- Fateh Chebana
  - Centre Eau Terre Environnement, Institut national de la recherche scientifique, Québec.
- Cindy Feng
  - School of Epidemiology and Public Health, University of Ottawa
- Meredith Franklin
  - Keck School of Medicine, University of Southern California (until July 2021)
  - School for the Environment and Department of Statistical Sciences, University of Toronto (from July 2021)

List of proposed collaborators, titles, and affiliations

Name: Kamal Rai
Title: PhD student
Affiliations: Centre for Global Health Research, St. Michael's Hospital
Department of Statistical Sciences, University of Toronto

Name: Hwashin Shin
Title: Scientist
Affiliation: Environmental Health Science and Research Bureau, Health Canada

Name: Céline Campagna
Title: Responsable scientifique
Affiliation: Équipe Changements climatiques et santé, Institut National de Santé Publique du Québec

Name: Pierre Masselot
Title: Research Fellow
Affiliation: London School of Hygiene & Tropical Medicine, UK

List of potential partner organizations

- The **Centre for Global Health Research, St. Michael's Hospital** will lead the health sciences research component of the project, providing data from the US and India and time of research staff to work on manuscripts. The Toronto-based component of the team will be located at CGHR and will be integrated into the Geospatial Mortality research group Dr. Brown leads, and a portion of the Toronto PhD student's salary will be funded though one of CGHR's research grants.
- **L'Institut National de Santé Publique du Québec** has the mandate to analyse, monitor and evaluate determinants of health, including environmental pollutants, and will give access to the Quebec provincial health databases. In-kind support will

also include health expertise for the statistical design and interpretation of research, including co-supervision of students.

- Hwashin Shin at **Health Canada** is central to this project. Her needs for an improved air quality indicator instigated the discussions which lead to this application. Dr. Shin has been funding Dr. Brown's team through Health Canada research contracts, and intends to provide at least $15,000 per year to the project.

Research Aims

Overview

There is growing interest in developing a simple, intuitive air quality index that simultaneously accounts for the health effects of multiple air pollutants (Bopp *et al.*, 2018; Dominici *et al.*, 2010; Stieb *et al.*, 2008). Health effects of air pollution depend on the composition of pollutants in the air, not simply the levels of a single pollutant (Dominici *et al.*, 2010). An air quality index that reflects this understanding should account for the various levels and relative contributions of each air pollutant in the ambient air. In this proposal, we will improve statistical methods for conducting inference on the health effects of simultaneous exposure to multiple environmental pollutants, with a focus on quantifying short-term effects of poor air quality on health outcomes at the population-level.

The *constrained groupwise additive index model* (cGAIM) is introduced by Masselot *et al.* (2020), who develops frequentist inference methods for it that use sequential quadratic programming. For a response distribution D, parameter $\theta = (\theta_1, ..., \theta_d)$, link function g, and constraints as below, the cGAIM is,

$$
\begin{aligned}
&Y_t|\lambda_t \overset{i.i.d.}{\sim} D(\lambda_t, \tau) \\
&g(\lambda_t) = X_t\beta + s(\alpha^T Z_t) + f_1(W_{1t}) + ... + f_K(W_{Kt}).
\end{aligned}
$$

Here Y_t is the outcome of interest, β is the vector of regression coefficients for linear covariates X_t, and $f_1, ..., f_K$ are smoothing functions that account for potential confounding variables W_{kt}. The distinguishing feature of cGAIM lies in s, a smooth function fit to a linear combination of environmental covariates Z_t. The α is a vector of weights on the entries of Z_t, giving the relative contribution of each component of Z_t. The smooth function s is modelled with a flexible parametric family such as cubic splines or a random walk. Estimating α, or more specifically finding the set of plausible values for α, is the main challenge of working with cGAIM.

We will develop a Bayesian methodology for inference with the cGAIM – the bcGAIM. Compared to the cGAIM, the bcGAIM will provide two main statistical benefits. The first is quantification of the uncertainty for α; the cGAIM does not provide confidence intervals for α. Given that pollutants tend to be positively correlated, it is possible that α is not well identified and all reasonable measures of air quality are equally predictive of health outcomes. It is also possible that the posterior distribution of α is narrow and the importance of, say, nitrous oxide relative to ozone can be estimated with some certainty. Either result would be a significant contribution research on the health effects of multiple pollutant. The second advantage is that the bcGAIM will be able to accommodate a higher-dimensional α than previously used, allowing Z_t to contain pollution levels at different time lags. The joint posterior distributions of this high-dimensional α for different health outcomes will provide information on how quickly poor air quality affects various types of mortality and morbidity (or quite possibly show that multiple combinations of recent air quality measures are equally predictive).

We will also develop method for fitting a case/crossover models using bcGAIM, which offers advantages over the more standard log-linear Poisson model. The case crossover has seen

increased attention in the air pollution literature (Stringer *et al.*, 2020; Wei *et al.*, 2019). It can be viewed as a proportional hazards survival model, where each individual is in a separate strata and 'control days' are chosen to have the same baseline hazard as the event day. Additional details are given in the Methods section below.

Objectives

This proposal has three main research objectives. The first is to develop an air quality index for Canadian cities that accounts for the combined effects of multiple air pollutants. This index will be developed in collaboration with Health Canada and INSQ with the intention of it being used in a public warning system. The second aim is undertake epidemiological studies involving exposures to multiple environmental pollutants in the areas of the world where the Centre for Global Health Research has suitable data (Canada, India, USA). The third application is a specific application of the air quality index, namely investigating how exposure to different mixtures of pollutants affects daily COVID-19 mortality.

There is evidence that the health effects estimated from single pollutant models may be in fact be caused by a correlated pollutant omitted from the model. For example, Franklin and Schwartz (2008) found that the effect of ozone on non-accidental mortality was "substantially reduced" after adjusting for particle sulfate and Liu *et al.* (2019) found significant differences in the percentage change of all-cause mortality attributable to $PM_{2.5}$ and PM_{10} after adjusting for NO_2 or SO_2.

Further, there is evidence that some health outcomes are nonlinearly related to health outcomes levels (Feng *et al.*, 2016). Achieving the three objectives requires a non-linear (or semi-parametric) dose-response curve and a combined-effect multi-pollutant exposure model. Our bcGAIM model will meet the requirements necessary to fulfil these objectives due to its being able to estimate weights using data, allowing for nonlinear relationships between pollutants and health outcomes, and applicable to both Poisson time series and case-crossover models.

Interpretability of model outputs is another requirement of this project, and many 'unsupervised' methods (i.e. principle components analysis and clustering) are difficult to interpret (Davalos *et al.*, 2017). A popular nonparametric method is the Bayesian Kernel Machine Regression (BKMR), introduced in Bobb *et al.* (2015), which models an exposure-response surface via a kernel function. Using a hierarchical Bayesian variable selection method, it can select one pollutant from a group of correlated ones, and is interpreted by visualizing cross-sections of a potentially high-dimensional exposure-response surface. The bcGAIM will provide some of the flexibility of BKMR and clustering while being sufficiently interpretable to meet the communication needs of an inter-disciplinary research team.

The relationship between daily COVID-19 deaths and air pollution levels has recently become an active area of research. For instance, Wu *et al.* (2020) apply a zero-inflated negative binomial to model U.S. data, where the zero-inflation accounts for counties with no COVID-19 deaths. They find that a 1 μg increase in long-term exposure to ambient $PM_{2.5}$ increases the COVID-19 death rate by 15%. We will use variations on bcGAIM to examine the relationship between COVID-19 deaths and combinations of air pollutants. As well as exploring daily variations in the case fatality rate (and its relation to air quality), the model will be

adapted to consider long-term exposures and COVID-19 incidence rates.

Methods

The bcGAIM will make four methodological advancements for modeling the health effects of mixtures of pollutants. These are:

1. extending the cGAIM to higher dimensional problems;
2. fully exploring the parameter space to identify all plausible values for α;
3. developing priors for shape-constrained Bayesian inference on the smooth function s; and
4. using case crossover models in place of the Poisson response variable.

In Masselot *et al.* (2020), the cGAIM uses an iterative two-step optimization scheme – α is updated using a quadratic program, then s is updated using the shape-constrained additive model methodology of Pya and Wood (2015). The bcGAIM will initially be implemented in Stan, a statistical modeling language that performs optimization using Hamiltonian Monte Carlo (Carpenter *et al.*, 2017). The Stan modeling language makes it straightforward (in theory) to extend the bcGAIM to include additional pollutants, additional lags for pollutants in the model, and additional smooth functions s. It is expected that the α parameters will not always be well identified, and results will be sensitive to model assumptions and prior distributions. One task in this component of the research will be to find reparametrizations and multivariable prior distributions which enable prior elicitation from subject-area specialists.

Following its implementation in Stan, the bcGAIM will be implemented using non-MCMC inference methods, similar to Integrated Nested Laplace Approximation (INLA) (Rue *et al.*, 2009). One such algorithm for single-pollutant case-crossover models was recently developed by Stringer *et al.* (2020), and this approach will be extended to allow for inference on the α parameters in bcGAIM. These non-MCMC methods provide significant computational and ease-of-use benefits, and will expand the types of problems and number of users who can use the bcGAIM methodology. To facilitate use by other researchers, all bcGAIM software will be released in an R package.

After bcGAIM is implemented for a three-dimensional α, more specifically ozone, fine particulates, and nitrous oxide at two day lags, additional time lags will be added with the resulting α being 9- or 12 dimensional. The computational and methodological challenges at this stage are expected to be significant, and parallelizing the algorithm on cloud platforms will be used to dramatically increase the number of candidate values of α considered.

Another major task in developing the bcGAIM is in developing random effect distributions for shape-constrained Bayesian inference on s. In addition to having desirable statistical properties, the chosen models should be simple and interpretable so that it can be elicited from non-statistical experts. This is difficult to achieve for shape constraints. The first reason for this is that s may not have any parameters related to the desired constraint; for example, a 1^{st}-order random walk has no parameters related to monotonicity. To overcome this, s could be re-parameterized, the functional form of s could be exploited, or data augmentation schemes that introduce derivative observations could be used (Riihimäki and Vehtari, 2010).

The second reason is that substantial mathematical analysis is required to ensure priors do not introduce unwanted behavior. For example, a truncated multivariate normal (tMVN) prior can induce monotonicity when placed on the coefficients $\beta^{'}$ of a finite basis expansion of s (Maatouk and Bay, 2017). However, the tMVN prior places negligible mass on near-flat regions of s. While Zhou *et al.* (2020) remedy this by introducing a scale parameter to the coordinates of the tMVN distribution, the modified tMVN prior is placed on $\beta^{'}$, not s. In comparison to the tMVN prior, we seek a prior on s and not its basis expansion. Such a prior will be less encumbered by mathematical details and more easily understood by non-statistical experts. This ease of interpretation should encourage adoption of the bcGAIM among non-statistical experts, which is one of the goals of this project.

References

Bobb, J. F., Valeri, L., et al. (2015) Bayesian kernel machine regression for estimating the health effects of multi-pollutant mixtures. *Biostatistics*, **16**, 493–508.

Bopp, S., Richarz, A., et al. (2018) Something from nothing: Ensuring the safety of chemical mixtures. *Ensuring the safety of chemical mixtures, Publications Office of the European Union, EUR*, **29258**.

Carpenter, B., Gelman, A., et al. (2017) Stan: A probabilistic programming language. *Journal of Statistical Software*, **76**.

Davalos, A. D., Luben, T. J., et al. (2017) Current approaches used in epidemiologic studies to examine short-term multipollutant air pollution exposures. *Annals of Epidemiology*, **27**, 145–153.

Dominici, F., Peng, R. D., et al. (2010) Protecting human health from air pollution: Shifting from a single-pollutant to a multi-pollutant approach. *Epidemiology (Cambridge, Mass.)*, **21**, 187.

Feng, C., Li, J., et al. (2016) Impact of ambient fine particulate matter (pm 2.5) exposure on the risk of influenza-like-illness: A time-series analysis in Beijing, China. *Environmental Health*, **15**, 17.

Franklin, M. and Schwartz, J. (2008) The impact of secondary particles on the association between ambient ozone and mortality. *Environmental Health Perspectives*, **116**, 453–458.

Liu, C., Chen, R., et al. (2019) Ambient particulate air pollution and daily mortality in 652 cities. *NEJM*, **381**, 705–715.

Maatouk, H. and Bay, X. (2017) Gaussian process emulators for computer experiments with inequality constraints. *Mathematical Geosciences*, **49**, 557–582.

Masselot, P., Chebana, F., et al. (2020) Constrained groupwise additive index models. *Submitted*.

Pya, N. and Wood, S. N. (2015) Shape constrained additive models. *Statistics and Computing*, **25**, 543–559.

Riihimäki, J. and Vehtari, A. (2010) Gaussian processes with monotonicity information. In: *Proceedings of the thirteenth international conference on artificial intelligence and statistics*, 2010, pp. 645–652.

Rue, H., Martino, S., et al. (2009) Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. *JRSS: Series B*, **71**, 319–392.

Stieb, D. M., Burnett, R. T., et al. (2008) A new multipollutant, no-threshold air quality

health index based on short-term associations observed in daily time-series analyses. *Journal of the Air & Waste Management Association*, **58**, 435–450. Taylor & Francis.

Stringer, A., Brown, P. E., et al. (2020) Approximate Bayesian inference for case-crossover models.

Wei, Y., Wang, Y., et al. (2019) Short term exposure to fine particulate matter and hospital admission risks and costs in the medicare population: Time stratified, case crossover study. *BMJ*, **367**.

Wu, X., Nethery, R. C., et al. (2020) Exposure to air pollution and covid-19 mortality in the United States. *medRxiv*.

Zhou, S., Ray, P., et al. (2020) On truncated multivariate normal priors in constrained parameter spaces. *arXiv preprint arXiv:2001.09391*.

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

Kamal Rai will complete his PhD in 2021 and will work on this project as a postdoc. He will develop the Bayesian implementation of the GAIM models in Stan. This includes exploring determining appropriate prior distributions for the weights α, developing visualizations that communicate modeling results, and assisting other project members in developing shape constraints. He will be responsible for producing paper(s) summarizing the results of this model when run on Canadian air pollution and mortality data. To facilitate team communication and cohesion, he will also split time between Toronto (at the Centre for Global Health Research) and Ottawa (at the University of Ottawa), and use the proximity of the University of Ottawa to Quebec to occasionally visit project collaborators located there.

The University of Toronto PhD student will develop the INLA-like Bayesian computations to conduct inference on the GAIM, and compare its results from those obtained from the Stan implementation. A University of Laval or University of Ottawa PhD student will develop methods to conduct shape-constrained (Bayesian) inference, and examine the relationship between COVID-19 deaths and air pollution levels.

Plans for dissemination and communication

The lead investigators of this proposal have a track record of publishing research results in leading statistical and epidemiological journals, and aim to publish the results of this project in high-impact journals. The results and findings of this multiple pollutant inquiry will also be shared with Health Canada and the Institut National de Santé Publique du Québec. Drs Shin and Campagna will use the methodologies developed in their ongoing research and programatic work, and facilitate the adoption of the methods more widely in their organizations.

Suggested reviewers

- Jim Zidek, University of British Columbia. www.stat.ubc.ca/users/james-v-zidek-frsc-oc. Prof. Zidek is one of the world's foremost researchers on statistical method for environmental health.
- Rhonda Rosychuk, University of Alberta sites.ualberta.ca/~rhondar. Dr. Rosychuk has published extensively in both the health sciences literature and statistical journals, including on spatial and longitudinal models for environmental health problems.
- Samir Bhatt, Imperial College London www.imperial.ac.uk/people/s.bhatt, develops Bayesian inferential methods for complex models in public health research.

Preliminary budget description

The CANSSI Collaborative Research Team grant is for $60,000/year for 3 years. We propose an annual budget of:

1. $30,000/year to support a post-doctoral fellow.
2. $24,000/year to support two PhD students ($12,000 per student).
3. $6,000/year to support travel to/from the cities of the lead investigators – Toronto, Ottawa, and Quebec – and annual team meetings held around the Statistical Society of Canada conference.

In addition to the CANSSI funding, Hwashin Shin will provide $15k/year towards the post-doc salary. This will likely be in the form of research contracts.

Patrick Brown

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date prepared: June 8, 2020

Current employment

- Associate Professor, Department of Statistical Sciences, University of Toronto. 2018-
- Centre for Global Health Research, Li Ka Shing Knowledge Institute, St. Michael's Hospital. 2017-

Degrees:

PhD in Statistics, Lancaster University, UK. Part-time and full-time study from August 1997 to January 2003.

MSc in Statistics, London School of Economics, UK. October 1996 - June 1997.

BA (Hons) in Economics and Statistics, Queen's University, Canada. September 1992 - May 1996.

Selected Research Awards

NSERC Discovery Grant Latent-Gaussian Spatio-temporal models for complex problems, 2017-2022 $120k Patrick E. Brown -

NSERC Discovery Grant Inference on Spatio-Temporal Log-Gaussian Cox Processes for Spatially Aggregated Disease Incidence Data, 2012-2017 $60k Patrick E. Brown

Selected recent publications

1 R Entezari, PE Brown, and JS Rosenthal. 2020.
"Bayesian spatial analysis of hardwood tree counts in forests via MCMC".
Environmetrics to appear, e2608.

2 M Mahsin, R Deardon, and PE Brown. 2020.
"Geographically-dependent individual-level models for infectious diseases transmission".
Biostatistics. to appear.

3 EH Yoo, PE Brown, and Y Eum. 2018.
"Ambient air quality and spatio-temporal patterns of cardiovascular emergency department visits".
International Journal of Health Geographics 17.18, pp. 1–16.

4 JSW Lee, P Nguyen, PE Brown, J Stafford, and N Saint-Jacques. 2017.
"A local-EM algorithm for spatio-temporal disease mapping with aggregated data".
Spatial Statistics 21, pp. 75–95.

5 PE Brown. 2016.
"Maps, Coordinate Reference Systems and Visualising Geographic Data with mapmisc".
R-journal 8.1, pp. 64–91.

6 PE Brown, H Jiang, S Ezzat, and AM Sawka. 2016.
"A detailed spatial analysis on contrasting cancer incidence patterns in thyroid and lung cancer in Toronto women".
BMC Public Health 16.1, p. 950.

7 PE Brown. 2015.
"Model-based Geostatistics the easy way".
Journal of Statistical Software 63.

Professional Service

Statistical Society of Canada, 2007-

- Treasurer 2019-
- Biostatistics President (elect/current/past) 2017-2020
- Biostatistics Treasurer 2009-2015
- Local organizer for 2014 Annual Meeting
- Finance procedures committee 2017-2019
- Finance committee 2012-2016

Supervision

PhD

- Alex Stringer, PhD in Statistics DoSS, Sept 2018-: Integrated nested variational inference for non-linear latent-Gaussian models. Co-supervision with Jamie Stafford
- Ruoyong Xu, PhD in Statistics DoSS, Sept 2018-: Highly parallelized spatial computations on GPU's
- Kamal Rai, PhD in Statistics DoSS, Sept 2017- : MCMC methods for complex spatial models (geometric anisotropy, conditional likelihoods) are being developed.

Postdoctoral

- Guowen Huang, 2018-: Short-term impacts of air quality on mortality and morbidity in Canada.
- Luc Villandré, 2018-: Multiresolution approximations for spatial modeling of satellite data.

FATEH CHEBANA
Full professor (INRS), fateh.chebana@ete.inrs.ca
Institut National de la Recherche Scientifique (INRS), Centre Eau, Terre et Environnement (ETE), Québec

Education: Msc (late 1999) and Ph.D (late 2003) in Statistics, University Paris 6, France
Main research interests: Applied Statistics; Hydrological statistics; Environmental and Climate effects on Health

MAIN PROFESSIONAL ACTIVITIES

- Director MSc Professional program in Water Sciences, INRS-ETE, June 2017-…
- Associate Editor, *Environmetrics* (Wiley), 2020-…
- Associate Editor, *Journal of Hydrology* (Elsevier), 2015-…
- Guest-editor, special issue "Special Issues for Advances in Meteorology 2015"
- Guest-editor, special issue "Statistical Methods in Environmental Epidemiology 2020"
- Co-editor, *Encyclopedia Environmetrics*, 2nd ed. 2013, Wiley (Major work, 650 authors, 4000 pages)
- Chair (scientific and organization), Statistical Hydrology Commission workshop, Quebec, 2016
- Co-chair, International CRM–CANSSI Workshop, New Horizons in Copula Modeling. Montréal, 2014

FUNDS (MAIN PROJETCS as PI SINCE 2014)

Names	Topic	Amount	Source
Chebana	Water demand forecasting	25 K$ 2020	NSERC-ENGAGE
Chebana	Advanced statistical approaches for hydrological frequency analysis	215 K$ 2019-2024	NSERC-Discovery
Chebana, Campagna	Health-Weather alerte system	300 K$ 2017-20	Ouranos
Chebana	Long term streamflow forecasting	25 K$ 2018	NSERC-ENGAGE
Chebana, Bélanger, Gosselin, Ouarda	Health and Climate : knowledge transfer	100 K$ 2016-17	Ministère de la santé et des services sociaux de Québec
Chebana, St-Hilaire, Bergeron	Laboratoire analyse modélisation habitats aquatiques	500 K$ 2016	Canada Foundation for Innovation
Chebana	Urban Water Demand	25 K$ 2016	ENGAGE-NSERC
Chebana, Ouarda	Software update	50 K$ 2015	Ministère Transports Québec Ministère Enviro. Québec
Chebana, Dabo-Niang, Ouarda	Fonctionnal data analysis	22 K$ 2013-15	Ministère relations internationals, Québec
Chebana	Regional frequency analysis	138 K$ 2012-18	NSERC-Discovery
Chebana, Bélanger, Gosselin, Ouarda	Research program on Health and Climate Change	918 K$ 2011-16	Ministère de la santé et des services sociaux de Québec

SELECTED PUBLICATIONS since 2014, total 105 peer reviewed papers (FC = Fateh Chebana)

1. Ben Alaya, Ternynck, Dabo-Niang, FC, Ouarda (2020). Change point detection of flood events using a functional data framework. *Adv. Water Resour.*,
2. Serinaldi, FC, Kilsby (2020). Dissecting innovative trend analysis. *Stoch. Environ. Res. Risk Asses.*,
3. Alobaidi, Meguid, FC (2019). Predicting seismic-induced liquefaction through ensemble learning frameworks. *Nature Scientific Reports*,
4. Ben Nasr, FC (2019). Homogeneity testing of multivariate hydrological records, using multivariate copula L-moments. *Adv. Water Resour*
5. Ben Nasr, FC (2019). Multivariate L-moment based tests for copula selection, with hydrometeorological applications. *J. Hydrol.*,
6. Curceac, Ternynck, Ouarda, FC, Dabo-Niang (2019). Short-term air temperature forecasting using Nonparametric Functional Data Analysis and SARMA models. *Environ. Model. Soft.*,
7. Masselot, FC, Lavigne, Campagna, Gosselin, Ouarda (2019). Toward an improved air pollution warning system in Quebec. *Int. J. Environ. Res. Public Health*,

8. Alobaidi, Chebana, Meguid (2018). Robust ensemble learning framework for day-ahead forecasting of household based energy consumption. *Appl. Ener.*,
9. Chiu, Abdous, Bélanger, Gosselin (2018). Mortality and morbidity peaks modeling: An extreme value theory approach. *Stat. Methods Med. Res.*,
10. Larabi, St-Hilaire, FC, Latraverse (2018). Using functional data analysis to calibrate and evaluate hydrological model performance. *J. Hydrol. Eng.*,
11. Larios, FC, Godbout, Brar, Valera, Palacios, Avalos Ramirez, Saldoval-Salas, Larouche, Medina-Hernàndez, Potvin (2018). Analysis of atmospheric ammonia concentration from four sites in Quebec City region over 2010-2013. *Atmos. Pollut. Res.*,
12. Masselot, FC, Bélanger, St-Hilaire, Abdous, Gosselin, Ouarda (2018). Aggregating the response in time series regression models, applied to weather-related cardiovascular mortality. *Sci. Total Environ.*,
13. Masselot, FC, Ouarda, Bélanger, St-Hilaire, Gosselin (2018). A new look at weather-related health impacts through functional regression. *Scientific Reports*,
14. Ouarda, Charron, Hundecha, St-Hilaire, FC (2018). Introduction of the GAM model for regional low-flow frequency analysis at ungauged basins and comparison with commonly used approaches. *Environ. Model. Soft.*,
15. Rahman, Charron, Ouarda, FC (2018). Development of regional flood frequency analysis techniques using generalized additive models for Australia. *Stoch. Environ. Res. Risk Asses.*,
16. Masselot, FC, St-Hilaire, Abdous, Gosselin, Ouarda 2018 EMD-regression for modelling multi-scale relationships, and application to weather-related cardiovascular mortality. *Sci. Total Environ.*,
17. Requena, FC, Ouarda 2018 A functional framework for flow-duration-curve and daily streamflow estimation at ungauged sites. *Advances in Water Resources*
18. Genest, FC 2017 Copula modeling in hydrologic frequency analysis. *Handbook App. Hydrology*,
19. Masselot, FC, Ouarda 2016 Fast and direct nonparametric procedures in the L-moment homogeneity test. *Stoch. Environ. Res. Risk Asses.*,
20. Durocher, FC, Ouarda 2016 On the prediction of extreme flood quantiles at ungauged locations with spatial copula. *J. Hydrol.*
21. Ouali, FC, Ouarda 2016 Non-linear canonical correlation analysis in regional frequency analysis. *Stoch. Environ. Res. Risk Asses.*,
22. Ouali, FC, Ouarda 2016 Quantile regression in regional frequency analysis: a better exploitation of the available information. *J. Hydrometeorol.*,
23. Requena, FC, Mediero 2016 A complete procedure for multivariate index-flood model application. *J. Hydrol.*
24. Masselot, Dabo, FC, Ouarda 2016 Streamflow forecasting using functional regression. *J. Hydrol.*
25. Wazneh, FC, Ouarda 2016 Identification of hydrological neighborhoods for regional flood frequency analysis using statistical depth function. *Adv. Water Resour.*,
26. Ternynck, Ben Alaya, FC, Dabo, Ouarda 2016 Streamflow Hydrograph Classification Using Functional Data Analysis. *J. Hydrometeorology*
27. Ben Alaya, FC, Ouarda 2016 Multisite and multivariable statistical downscaling using a Gaussian copula quantile regression model. *Climate Dynamics*
28. Ben Alaya, FC, Ouarda 2015 Probabilistic Multisite Statistical Downscaling for Daily Precipitation Using a Bernoulli–Generalized Pareto Multivariate Autoregressive Model. *J. Climate*
29. Alobaidi, Marpu, Ouarda, FC 2015 Regional frequency analysis at ungauged sites using a two-stage resampling generalized ensemble framework. *Adv. Water Resour.*,
30. Durocher, FC, Ouarda 2015 A nonlinear approach to regional flood frequency analysis using projection pursuit regression. *J. Hydrometeorology*
31. Brahimi, FC, Necir 2015 Copula representation of bivariate L-moments: A new estimation method for multiparameter 2-dimentional copula models, *Statistics*,
32. Ben Alaya, FC, Ouarda 2014 Probabilistic Gaussian Copula Regression Model for Multisite and Multivariable Downscaling. *Journal of Climate*

SUPERVISING

Postdocs (1 current, 6 finished); PhD students (4 current, 9 finished), Master (2 current, 3 finished), Trainees (0 current, 19 finished). Because of Covid-19, I don't have any trainee this summer.

Curriculum Vitae: Cindy Xin Feng

Education
PhD in Statistics, Simon Fraser University, 2007-2011
MSc in Statistics, Simon Fraser University, 2004-2006
BSc in Applied Mathematics, Beijing University of Technology, Beijing, China, 1999-2003

Employment History
Associate Professor, School of Epidemiology and Public Health, University of Ottawa, Jan2020-now
Associate Professor (tenured), School of Public Health, University of Saskatchewan, July 2018-now
Assistant Professor, School of Public Health, Sept.2012-June 2019
Adjunct Professor, Department of Mathematics and Statistics, Sept 2016-present

Graduate Student Supervision:
Current students:
1 PhD in Biostatistics, 1 MSc in Biostatistics and 2 PhDs in Epidemiology

Completed students:
8 MSc in Biostatistics and 1 MPH thesis and 1PhD in Epidemiology

Selected Peer-Reviewed Paper (Last 6 years: 50; Lifetime: 63) *denotes trainee

1. **Feng, C. X.** (2019). Zero-Augmented Accelerated Spatial Failure Model for Modeling Hospital Length of Stay Data. *Spatial and Spatio-temporal Epidemiology*, 29, 121-137.
2. **Feng, C. X.** and Piesse, A. (2018) On Correcting Measurement Error in the Persistence Rate Estimator. *Communication in Statistics -Simulation and Computation*, 47(4)
3. Ahmed, A.*, **Feng, C. X.,** Bowen A., Muhajarine, N. (2018). Latent trajectory groups of perinatal depressive and anxiety symptoms from pregnancy to early postpartum and their antenatal risk factors. *Archives of Women's Mental Health*. 21(6):689-698
4. **Feng, C. X.**, Osgood, N. D. and Dyck, R. F. (2018) Low Birth Weight, Cumulative Obesity Dose, and the Risk of Incident Type 2 Diabetes, *Journal of Diabetes Research*, 2018
5. Essien, S. K.*, **Feng, C. X.**, Sun, W.J., Farag, M., Li, L.H. and Gao, Y.Q. (2018). Sleep Duration and Sleep Disturbances in Association with Falls among the Middle-Aged and Older Adults in China: A Population-based Nationwide Study. *BMC Geriatrics*, 18(1), 196.
6. **Feng, C.X.**, Rostami, M.* and Li, L. (2017) Impact of misspecified residual correlation structure on the parameter estimates in a shared spatial frailty model. *Journal of Statistical Computation and Simulation.* 87(12). 2384–2410.
7. Li, L., **Feng, C.X**., Qiu, S.* (2017). Estimating Cross-validatory Predictive P-values with Integrated Importance Sampling for Disease Mapping Models. *Statistics in* Medicine, 36 (14), 2220-2236
8. Mobin, A.*, **Feng, C.X.** and Neudorf, C. (2017). Cyberbullying victimization among the elementary school children in a community-based sample in Canada: prevalence and risk factors. *Canadian Journal of Public Health*, 108(5-6), 475–e481.
9. **Feng, C.X.**, Li, J., Sun, W.J., Zhang, Y. and Wang, Q.Y. (2016). Impact of Ambient Fine Particulate Matter (PM2.5) Exposure on the Risk of Influenza-Like-Illness: A Time-Series Analysis in Beijing, China. *Environmental Health*, 15:17.
10. Li, L., Qiu, S. *, Zhang, B., and Feng, C.X. (2016). Approximating Cross-validatory Predictive Evaluationin Bayesian Latent Variables Models with Integrated IS and WAIC. *Statistics and Computing*, 26(4), 881-897.
11. **Feng, C.X**., Waldner, C. Cushon, J., Davy, K., Neudorf, C. (2016). Suicidal Ideation in a Community Based Sample of Elementary School Children: a Multilevel and Spatial Analysis. *Canadian Journal of Public Health*, 107(1) 100-5.

12. **Feng, C.X.** (2015). Bayesian joint modeling of correlated counts data with application to adverse birth outcomes. *Journal of Applied Statistics*, 42(6), 1206-1222.
13. Zhang, Y. +, **Feng, C.X.** +, Ma, C.N., Yang, P., Tang, S., Lau, A., Sun, W.J. and Wang, Q.Y. (2015). The impact of temperature and humidity measures on H7N9 outbreak - evidence from China. *International Journal of Infectious Diseases*, 30:122-124. +Equally contributed.
14. **Feng, C.X.,** Dean, C.B. and Richard R. (2013). Impact of misspecifying spatial exposures in a generalized additive model framework: with application to the study of the dynamics of Comandra Blister rust in BC. *Environmetrics*, 24(2), 63-80.
15. **Feng, C.X.** and Dean, C.B. (2012). Joint analysis of multivariate spatial count and zero-heavy count outcomes using common spatial factor models. *Environmetrics*, 23(6), 493-508.
16. **Feng, C.X.,** Debeck, K., Kerr, T., Mathias, S., Montaner, J. and Wood, E. (2012). Homelessness independently predicts injection drug use initiation among street-involved youth in a Canadian setting. *Journal of Adolescent Health*, 52(4), 499-501.
17. **Feng, C.X.,** Cao, J. and Bendell-Young, L. (2011). Exploring spatial and temporal variations of Cadmium concentrations in Pacific oysters from British Columbia. *Biometrics*, 67, 1142-1152.

Book Chapters:

- **Feng, C.** and Li, L. (2016). Modeling Zero Inflation and Overdispersion in the Length of Hospital Stay for Patients with Ischaemic Heart Disease. In D. Chen, J. Chen J, X. Lu, G. Yi and H. Yu (Eds.), *Advanced Statistical Methods in Big-Data Sciences* (pp. 50-65). United States: Springer. pp 35-53
- **Feng, C.X.** and Dean, C.B. (2015). Spatial Pattern Analysis of Multivariate Disease Data. In Dongmei Chen, Bernard Moulin, Jianhong Wu (Eds.), *Analyzing and Modeling Spatial and Temporal Dynamics of Infectious Diseases* (pp. 1-30). United States: Wiley.

Research Grants:

- Principal Investigator, Discovery grant, Natural Sciences and Engineering Research Council Canada (NSERC). 2019-2023, $80,000. Title: Statistical Models and Diagnostics Tools for Spatially Correlated Skewed and Heterogeneous Data.
- Principal Investigator, Discovery grant, Natural Sciences and Engineering Research Council Canada (NSERC). 2013-2019, $90,000. Title: Joint Modeling of Multivariate Spatial and Temporal Outcomes.
- Co-Principal Investigator, Occupational health in Saskatchewan, MITACS. 2016-2019, $45,000. Co-PI: Dr. Catherine Trask
- Co-Principal Investigator, Occupational health in Saskatchewan, Saskatchewan Worker's Compensation Board. 2016-2019, $65,000. Co-PI: Dr. Catherine Trask
- Co-Investigator, Collaborative Research Team (CANSSI-CRT). Spatial Modeling of Infectious Diseases: Environment and Health. PI: Mahmoud Torabi, 2017-2020, $180,000
- Co-Investigator, Targeted Collaborative Innovation Development Grant on studying HIV in Southern Saskatchewan, Saskatchewan Health Research Foundation, 2016-2018, $73,182. PI: Dr. Alex Wong.
- Co-Investigator, Safe Water for Health Research Team, Saskatchewan Health Research Foundation, 2012-2016, $300,000 PIs: Cheryl Waldner and Lalita Bharadwaj.

Other Evidence of Impact and Contributions

- Guest editor for the *Spatial and Spatial-Temporal Epidemiology*.
- Reviewed more than 30 papers for statistical, public health or epidemiological journals.
- Reviewed research grants for the NSERC, CIHR, MITACS, CHRIM, etc.
- Advisory committee member for more than 20 thesis-based PhD or MSc students.
- Gave more than 20 invited presentations at the provincial, national, and international conferences.
- Organized and chaired multiple sessions for the Statistical Society of Canada annual meetings.
- Statistical Society of Canada regional representative.

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Education

09/2007	Harvard University, Cambridge, MA, Ph.D. Concentrations: Statistics and Environmental Health
06/2003	Ottawa-Carleton Institute for Mathematics and Statistics, Ottawa, Canada, M.Sc. Statistics
11/2001	McGill University, Montreal, Québec, Canada, B.Sc. Mathematics

Post-Graduate Training

10/2007-03/2010	Post-Doctoral Researcher, University of Chicago Department of Statistics and Argonne National Laboratory, Chicago, IL.

Professional Experience

07/2021–present	**Associate Professor, University of Toronto** Department of Statistical Sciences and School of the Environment, Toronto, ON
09/2018–07/2021	**Associate Professor, University of Southern California** Keck School of Medicine, Division of Biostatistics, Los Angeles, CA Dornsife College of Letters, Arts and Sciences, Spatial Sciences Institute
07/2017–07/2021	**Director of MS programs in Biostatistics, Health Data Science, and Epidemiology, University of Southern California** Keck School of Medicine, Department of Preventive Medicine, Los Angeles, CA
06/2010–09/2018	**Assistant Professor, University of Southern California** Keck School of Medicine, Division of Biostatistics, Los Angeles, CA
09/2005–06/2007	**Teaching Fellow, Harvard University** Faculty of Arts and Science & Harvard School of Public Health, Cambridge, MA
01/2002–10/2003	**Statistician, Federal Government of Canada** Health Canada, Biostatistics and Air Health Effects Directorates, Ottawa, ON

Selected Publications

[1] Cushing, L., Vavra-Musser, K., Chau, K., **Franklin, M.**, Johnston, J. Flaring from unconventional oil and gas development and increased risk of adverse birth outcomes in the Eagle Ford Shale in South Texas. *Environmental Health Perspectives*, 2020 doi:10.1289/EHP6394.

[2] Johnston, J., Chau, K., **Franklin, M.**, Cushing, L. Environmental Justice Dimensions of Oil and Gas Flaring in South Texas: Disproportionate Exposure among Hispanic communities. *Environmental Science & Technology*, 54(10):6289-6298, 2020.

[3] Sorek-Hamer, M., **Franklin, M.**, Chau, K., Garay, M., Kalashnikova, O. Spatiotemporal characteristics of the association between AOD and PM over the California Central Valley. *Remote Sensing*, 12(4), 2020.

[4] Chau, K., **Franklin, M.***, Gauderman, W. J. Satellite-Derived $PM_{2.5}$ Composition and Its Differential Effect on Children's Lung Function. *Remote Sensing*, 12(1028), 2020.
**co-first author*

[5] Li, L., **Franklin, M.**, Girguis, M., Lurmann, F., Wu, J., Pavlovic, N., Breton, C., Gilliland, F. Habre, R. Spatiotemporal Imputation of MAIAC AOD Using Deep Learning with Downscaling. *Remote Sensing of Environment*, 111584, 2020.

[6] **Franklin, M.**, Chau, K., Cushing, L., Johnston, J. Characterizing flaring from unconventional oil and gas operations in south Texas using satellite observations. *Environmental Science & Technology*, 53, 2220-2228, 2019.

[7] Johnston, J., **Franklin, M.**, Roh, H., Austin, C., Arora, M. Lead and Arsenic in Shed Deciduous Teeth of Children Living Near a Lead-Acid Battery Smelter. *Environment Science & Technology*,53(10): 6000-6006, 2019.

[8] **Franklin, M.**, Chau, K., Kalashnikova, O.V., Garay, M.J, Enebish, T., Sorek-Hamer, M. Using Multi-Angle Imaging SpectroRadiometer Aerosol Mixture Properties for Air Quality Assessment in Mongolia. *Remote Sensing* 10(8),1317, 2018.

[9] **Franklin, M.**, Kalashnikova, O., Garay, M., Fruin, S. Characterization of subgrid scale variability in particulate matter with respect to satellite aerosol observations. *Remote Sensing*, 10(4),623, 2018.

[10] Chen, W., Qian, L., Shi, J., **Franklin, M.** Comparing Performance between Log- Binomial and Robust Poisson Regression Models for Estimating Risk Ratios under Model Misspecification. *BMC Medical Research Methodology*, 18(63):1-12, 2018.

[11] **Franklin M.**, Fruin S. The role of traffic noise on the association between air pollution and children's lung function. *Environmental Research*, 157:153-159, 2017.

[12] **Franklin M.**, Kalashnikova O.V., Garay M.J. Size-resolved particulate matter concentrations derived from 4.4 km resolution size-fractionated Multi-angle Imaging SpectroRadiometer (MISR) aerosol optical depth over Southern California. *Remote Sensing of Environment*, 196:312-323, 2017.

[13] **Franklin M.**, Vora H., Avol E., McConnell R.S., Lurmann F., Liu F., Penfold B., Berhane K., Gilliland F., Gauderman W.J Predictors of intra-community variation in air quality. *Journal of Exposure Science and Environmental Epidemiology*, 22(2):135-47, 2012.

[14] Zanobetti A., **Franklin M.**, Koutrakis P., Schwartz J. Fine particulate air pollution and its components in association with cause-specific emergency admissions in 26 U.S. cities. *Environmental Health*, 8(58), 2009.

[15] **Franklin, M.**, Koutrakis, P., Schwartz, J The role of particle composition on the association between $PM_{2.5}$ and mortality. *Epidemiology*, 19(5):680–689, 2008.

[16] **Franklin, M.**, Schwartz, J. The impact of secondary particles on the association between ambient ozone and mortality. *Environmental Health Perspectives*, 116(4):453–458, 2008.

[17] **Franklin, M.**, Zeka A., Schwartz, J. Association between $PM_{2.5}$ and all-cause and specific-cause mortality in 27 US communities. *Journal of Exposure Science and Environmental Epidemiology*,17:279–287, 2007.

Curriculum Vitae

Personal Information

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Education

- *Postdoctoral Researcher:* Department of Mathematics and Statistics, Queen's University, 1999-2001.
- *Ph.D.*: Department of Mathematics and Statistics, Queen's University, 1996-1999.
- *M.Sc.* : Department of Mathematics and Statistics, Queen's University, 1995-1996.
- *B.Sc.* : Department of Mathematics Education, Seoul National University, Republic of Korea, 1978-1982.

Current Position

- Research Scientist (https://profils-profiles.science.gc.ca/en/profile/hwashin-hyun-shin)
  Air Health Science Division, Health Canada, 2006-Present.
- Adjunct Associate Professor (https://www.queensu.ca/mathstat/people/faculty/profiles/hwashin)
  Department of Mathematics and Statistics, Queen's University, 2017-Present.

Research Project & Funding (Principal Investigator)

1. Air Health Trend Indicator (AHTI) Project: On-going $300K/Y funded under the CESI of Environment and Climate Change Canada, 20016-Present.
2. Autism in children in Ontario project: 70K/Y for 3 years, 2019-2022, funded under the Addressing Air Pollution Horizontal Initiative (AAPHI) Program of Health Canada.
3. Air Quality Health Index (AQHI) project: 85K/Y for 3 years, 2019-2022, funded under the AAPHI.
4. Air Quality Health Index (AQHI) project: 5K for 1 year, 2018-2019, funded by Water and Air Quality Bureau (WAQB) of Health Canada.
5. PM Component Project: $60K/Y for 3 years, 2016-2019, funded under the Clean Air Regulatory Agenda (CARA) Program of Health Canada.
6. 3-Pollutant Model Project: $60K/Y for 3 years, 2016-2019, funded under the CARA Program.
7. Ozone Risk Project: $68K/Y for 2 years, 2014-2016, funded under the CARA Program.
8. Ozone Risk Project: $35K/Y for 1 year, 2014-2015, funded under the Canadian Environmental Sustainability Indicators (CESI) program of Environment and Climate Change Canada (ECCC).
9. Oil Refinery Closure Project: $60K/Y for 2 years, for 2013-2015, funded under the CARA program.
10. Air Health Indicator (AHI) Project: $300K/Y for 5 years, 2010-2015 funded under the CESI of ECCC.

Contributions

1. Canada government web report, 2017, 2014, & 2011:
   Canadian Environmental Sustainability Indicators. *Air Health Indicator Updates.*
   (http://www.ec.gc.ca/indicateurs-indicators/default.asp?lang=en&n=CB7B92BA-1).
2. National Academies of Sciences Committee, 2015-2017:
   "Assessing Toxicologic Risks to Human Subjects Used in Controlled Exposure Studies of Environmental Pollutants".
3. External advisor of the Research Support Center for Korean Children's Environmental Health, 2017-2021:
   Department of Occupational and Environmental Medicine, School of Medicine, Ewha Womans University, Seoul, Korea.
4. Outdoor Air Pollution Committee of Global Burden Disease (GBD), 2011-2016.
5. CCHO climate change and health intradepartmental committee, 2013-2015.

Supervising and training

- Post-doctoral fellow (Natural Sciences and Engineering Research Council of Canada)
  - W. Burr, Queen's Univ (2013-2016).
- Ph.D in Statistics
  - D. Riegert, Queen's Univ (2016-present)
  - K. Rai, Univ of Toronto (2018- present)
  - G. Huang, Univ of Toronto (2018-2019)
- Master degree in Statistics
  - Y. Gao, Queen's University (2013-2014)

Selected peer-reviewed publications since 2014 (*corresponding author)

2020	**HH Shin***, RP Parajuli, A Maquiling and Marc Smith-Doiron. Temporal Trends in Associations between Ozone and Circulatory Mortality in Age and Sex in Canada for 1984-2012. Science of the Total Environment 2020 1;724:137944. doi: 10.1016/j.scitotenv.2020.137944.
2020	Stieb DM*, Zheng C, Salama D, Berjawl R, Emode M, Hocking R, Lyrette N, Matz C, Lavigne E, **Shin HH**. Systematic review and meta-analysis of case-crossover and time-series studies of short term outdoor nitrogen dioxide exposure and ischemic heart disease morbidity. Environmental Health. 1;19(1):47.
2019	H Chun, C Leung, SW Wen, J McDonald, **HH Shin*.** Maternal Exposure to Air Pollution and Risk of Autism in Children: A Systematic Review and Meta-analysis. Environmental Pollution. 016/j.envpol.2019.113307
2018	Burr WS, Dales R, Liu L, Stieb D, Smith-Doiron M, Jovic B, Kauri LM, **Shin HH***. The Oakville Oil Refinery Closure and Its Influence on Local Hospitalizations: A Natural Experiment on Sulfur Dioxide. International Journal of Environmental Research and Public Health. 2018; 15(9):2029.
2018	Wesley Burr*, **Hwashin Shin,** Glen Takahara. *Synthetically Lagged Models.* Statistics and Probability Letters. 2018; 144, 37-43 https://doi.org/10.1016/j.spl.2018.07.008.
2018	**Shin HH***, Burr WS, Stieb D, Haque L, Kalayci H, Jovic B, Smith-Doiron. Air Health Trend Indicator: Association between Short-Term Exposure to Ground Ozone and Circulatory Hospitalizations in Canada for 17 Years, 1996–2012. International Journal of Environmental Research and Public Health. 15(8):1566.
2017	Hiatt R*, et al., **Shin HH**. *Controlled Human Inhalation-Exposure Studies atEPA*. National Academies of Sciences, Engineering, and Medicine. The National Academies Press. doi: 10.17226/24618.
2017	Cohen AJ*, Brauer M, Burnett R, et al., **Shin HH**, et al. *Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015.* Lancet. 2017; 389(10082):1907-1918.
2016	Wang H* et al., **Shin HH,** GBD 2015 Child Mortality Collaborators**.** *Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015***.** Lancet. 2016;388(10053):1725-1774
2016	Wang H* et al., **Shin HH,** GBD 2015 HIV Collaborators**.** *Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2015: the Global Burden of Disease Study 2015***.** Lancet HIV. 2016;3(8):e361-87
2016	Wesley Burr, Glen Takahara, **Hwashin Shin***. *Bias Correction in Estimation of Public Health Risk Atributable to Short-term Air Pollution Exposure.* Environmetrics. Vol26 (4), 298-311. /10.1002/env.2337.
2015	**Shin HH,** Cohen AJ, Pope CA 3rd, et al., Rick Burnett***.** *Meta-Analysis Methods to Estimate the Shape and Uncertainty in the Association between Long-term Exposure to Ambient Fine Particulate Matter and Cause-Specific Mortality over the Global Concentration Range,* Risk Analysis. doi: 10.1111/risa.12421.
2015	**Hwashin H. Shin,** Paul Jones, Robert D. Brook, Robert Bard, Karen Oliver, Ron Williams*. *Associations between personal exposures to VOCs and alterations in cardiovascular physiology: Detroit Exposure and Aerosol Research Study (DEARS).* Atmospheric Environment, Vol 104, 246-255.
2014	**Hwashin H. Shin**, Neal Fann*, Rick Burnett, Aaron Cohen, and Bryan Hubbell. *Outdoor fine particles and nonfatal strokes: systematic review and meta-analysis*. Epidemiology, 25(6):835-42.
2014	**Shin HH***, Cakmak S, Brion O, Villeneuve P, Turner MC, Goldberg MS, Jerrett M, Chen H, Crouse D, Peters P, Pope CA 3rd, Burnett RT. *Indirect Adjustment for Multiple Missing Variables Applicable to Environmental Epidemiology* Environmental research, 134:482-7. doi: 10.1016/j.envres.2014.05.016.