

# Using statistical methods and reproducible tools to gain new insights from biomedical and public health data

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**MfPH Next Generation Seminar Series**

3/15/23



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- This is specially true in the case of health research: public health, or biomedical data can be complex, and decisions along the analysis can result in different interpretations.
- In this talk I will focus on two examples that showcase how we can get more insight from looking at data from a different perspective.

# The Case of Public Health Data: COVID-19 Vaccination

## COVID-19: Why?

- The pandemic is still ongoing

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- Individuals with lower income, and those belonging to a racial/ethnic minority have had lower vaccination uptake<sup>1,2</sup>.
- This is important because these differences in vaccination uptake have implications on virus transmission.

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- The Fields Institute collected some very nice data regarding COVID-19 vaccination in Ontario: the *Survey of COVID-19 related Behaviours and Attitudes*.
  - The survey ran between late 2021 and early 2022 and collected socio-demographic information along with self-reported vaccination status (“Have you received the first dose of the Covid vaccine?”)

## COVID-19: The Case of Ontario

Table 1: Selected socio-economic factors from the survey

Variable	Levels
Age group	16-34, 35-54, 55 and over
Income bracket (CAD)	under 25,000, 25,000-59,999, 60,000 and above
Race/ethnicity	Arab/Middle Eastern, Black, East Asian/Pacific Islander, Indigenous, Latin American, Mixed, South Asian, White Caucasian, Other

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- We could do the same, but what else can we get from this data?
  - There have been some interesting changes in Ontario with regard to healthcare.

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- LHINs were essentially geographic intra-provincial divisions that determined where you could get health care.
- There were 14 LHINs, with additional subdivisions.

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- Problems with the LHINs:
- In multiple cases, the boundary of a LHIN did not match a municipal boundary.
  - One part of a city would be in a LHIN whereas another part of it would be in another LHIN.
  - Weakness in this approach due to complexity, lack of funding and bureaucracy were identified<sup>3</sup>.

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- In late 2019, Ontario adopted the Health Regions approach for healthcare and phased out the Local Health Integration Network (LHIN) approach.
- The change is relatively new. Multiple challenges:
  - Data for the Health Regions is not available from the Census.
  - **Have the Health Regions helped in reducing disparities in healthcare in the province?**

## COVID-19: The Case of Ontario

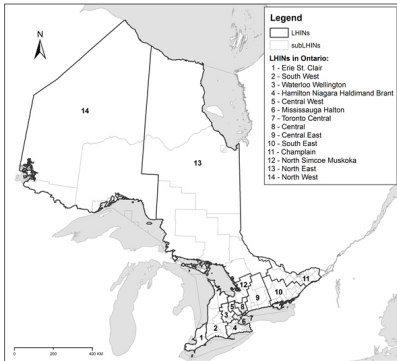


Figure 1: Ontario LHINs (Crighton et al. 2015)

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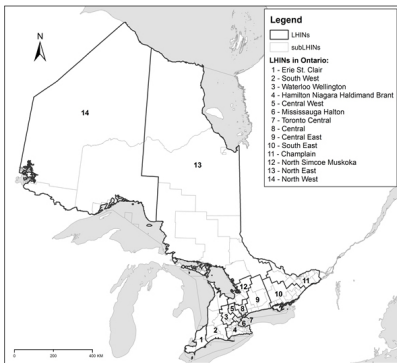


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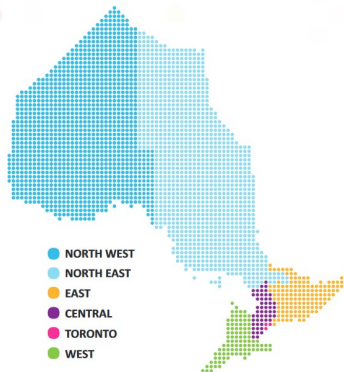


Figure 2: Ontario Health Regions (Ontario Business Health Plan 2022-2023)

## COVID-19: The Case of Ontario

- Where in Ontario did responses come from?

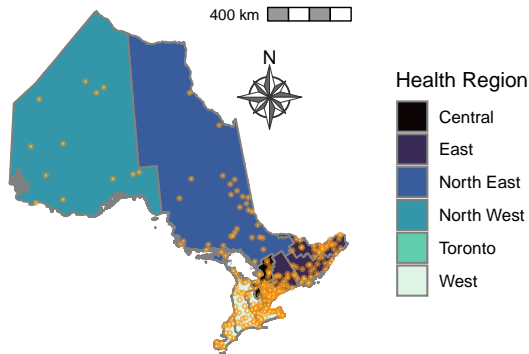


Figure 3: Geographic representation of the survey data collected by the Fields Institute

## COVID-19: The Case of Ontario

- Therefore, we decided to integrate the different Health Regions in our analysis to determine the odds of vaccination.

$$\log \left( \frac{p(\text{vac})}{1 - p(\text{vac})} \right) = \beta_0 + \beta_1(\text{Age group}) + \beta_2 \text{ Race} + \beta_3 \text{ Health Region} + \beta_4 \text{ Income} + \quad (1)$$

$$\beta_5(\text{Health Region} \times \text{Race}) + \beta_6 (\text{Income} \times \text{Race})$$



## Results

Table 2: **Selected** Multivariable Regression Results

Characteristic	OR	95% CI	p-value
<b>Income (CAD)</b>			
60000 and above	—	—	
25000-59999	0.59	0.39, 0.89	0.011
under 25000	0.37	0.25, 0.56	<0.001
<b>Race</b>			
White/Caucasian	—	—	
Arab/Middle Eastern	0.31	0.14, 0.69	0.004
Black	0.32	0.17, 0.60	<0.001
East Asian/Pacific Islander	1.15	0.50, 2.66	0.7
Indigenous	0.44	0.19, 1.02	0.056
Latin Aamerican	0.28	0.11, 0.67	0.004
Mixed	0.64	0.25, 1.65	0.4
Other	0.22	0.12, 0.41	<0.001
South Asian	0.91	0.49, 1.69	0.8
<b>Health Region</b>			
Toronto	—	—	
Central	1.47	0.92, 2.35	0.11
East	1.42	0.90, 2.23	0.13
West	1.55	1.05, 2.30	0.029
<b>Income and Race</b>			
25000-59999 * Arab/Middle Eastern	1.79	0.67, 4.83	0.2
under 25000 * Arab/Middle Eastern	3.05	1.26, 7.39	0.013
25000-59999 * Black	1.34	0.59, 3.05	0.5
under 25000 * Black	3.19	1.45, 6.99	0.004
25000-59999 * East Asian/Pacific Islander	0.42	0.17, 1.05	0.062
under 25000 * East Asian/Pacific Islander	1.16	0.47, 2.86	0.8
25000-59999 * Indigenous	1.36	0.48, 3.89	0.6
under 25000 * Indigenous	1.45	0.55, 3.80	0.5
25000-59999 * Latin American	1.24	0.45, 3.43	0.7

# Results

Characteristic	OR	95% CI	p-value
under 25000 * Latin American	2.80	1.04, 7.51	0.041
25000-59999 * Mixed	0.85	0.32, 2.26	0.7
under 25000 * Mixed	1.10	0.37, 3.27	0.9
25000-59999 * Other	6.93	2.65, 18.1	<0.001
under 25000 * Other	4.59	2.33, 9.05	<0.001
25000-59999 * South Asian	1.20	0.51, 2.85	0.7
under 25000 * South Asian	2.00	0.93, 4.30	0.077
<b>Race and Health Region</b>			
Arab/Middle Eastern * Central	0.66	0.26, 1.70	0.4
Black * Central	0.44	0.19, 0.98	0.046
East Asian/Pacific Islander * Central	0.98	0.38, 2.53	>0.9
Mixed * East	0.91	0.28, 3.03	0.9
other * East	1.05	0.39, 2.83	>0.9
South Asian * East	0.52	0.19, 1.45	0.2
Arab/Middle Eastern * West	1.00	0.37, 2.73	>0.9
Black * West	0.76	0.32, 1.80	0.5
East Asian/Pacific Islander * West	0.52	0.20, 1.34	0.2
Indigenous * West	0.39	0.14, 1.09	0.073
Latin American * West	0.94	0.32, 2.72	>0.9
Mixed * West	0.37	0.12, 1.16	0.089
Other * West	0.41	0.18, 0.93	0.032
South Asian * West	0.41	0.18, 0.95	0.037

<sup>1</sup> OR = Odds Ratio, CI = Confidence Interval

## How do we interpret this?

- Our results show that there were disparities in vaccination uptake in Ontario.

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- People in certain racial minority groups had lower odds of vaccination than White/Caucasian individuals.
- However, individuals that identified with a racial/ethnic minority and that were in a low household income bracket (<60k CAD) had higher odds of vaccination than individuals with a high household income.

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- Our results show that there were disparities in vaccination uptake in Ontario.
- People in certain racial minority groups had lower odds of vaccination than White/Caucasian individuals.
- However, individuals that identified with a racial/ethnic minority and that were in a low household income bracket (<60k CAD) had higher odds of vaccination than individuals with a high household income.
- This is likely caused by the type of occupation: people in racial minorities, and those with a low household income work in essential occupations (gas station workers, grocery store workers, agricultural workers)<sup>4</sup>, and thus potentially got the vaccine to be able to work.

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- But there are also intra-provincial differences in vaccine uptake within the Health Regions:
  - For example, South Asian individuals in the West Health Region had lower odds of vaccination than in other Health Regions.
  - These results provide a more comprehensive assessment of COVID-19 vaccination rates within Ontario, as they showed that certain minority groups within specific income brackets and certain Health Regions had differences in vaccination.

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- A more granular view of data (in this case, examining differences within Health Region, Income and Race) can provide insight for public policy development.

## Conclusions

- Data cleaning is **important**
  - Unifying geographical data can be challenging
  - Specially because most data relies on legacy information from the LHINs
- A more granular view of data (in this case, examining differences within Health Region, Income and Race) can provide insight for public policy development.
- There is a need for future studies that examine more in detail these differences and can provide a rationale.

## The Case of Biomedical Data

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- Biomedical studies often collect longitudinal data to see the effect of an intervention over time:
  - How a chemotherapy treatment changes the metabolism of a tumor
  - How the concentration of a drug changes over time in the blood
- How is this data typically analyzed?

## Linear Models

$$y_{ijt} = \beta_0 + \beta_1 \times treatment_j + \beta_2 \times time_t + \beta_3 \times time_t \times treatment_j + \varepsilon_{ijt} \quad (2)$$

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A LMEM follows the same exact structure, only incorporates a random effect  $\alpha_{ij}$ , which allows for different intercepts.

## Trends Over Time

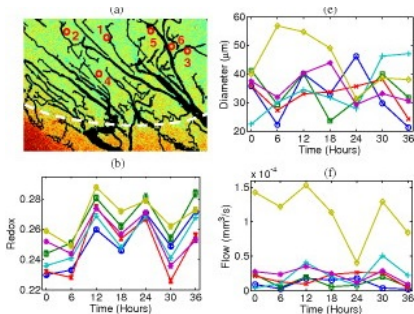


Figure 4: Tumor imaging data  
(Skala et al. 2010)

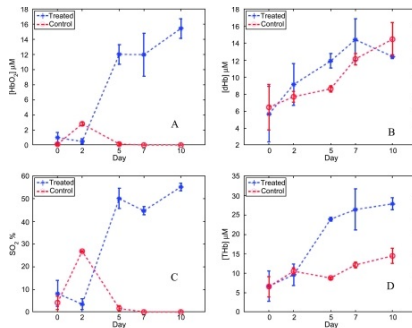


Figure 5: Tumor oxygenation data  
(Vishwanath et al. 2009)

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- The issue in those data is that the trends are not linear, and therefore, a linear model will miss changes in the signal where some metabolic or physiological relevant change is taking place.

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- Polynomial effects can be used, but they create biases at the boundaries of the covariates<sup>5</sup>.

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## Generalized Additive Models (GAMs)

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- We can use a *basis function* to estimate the smooth function.
- Splines are helpful as basis functions: Thin plate regression splines (TPRS) are computationally efficient, and the underlying principle is that of polynomial pieces “joined” together

# How GAMs work

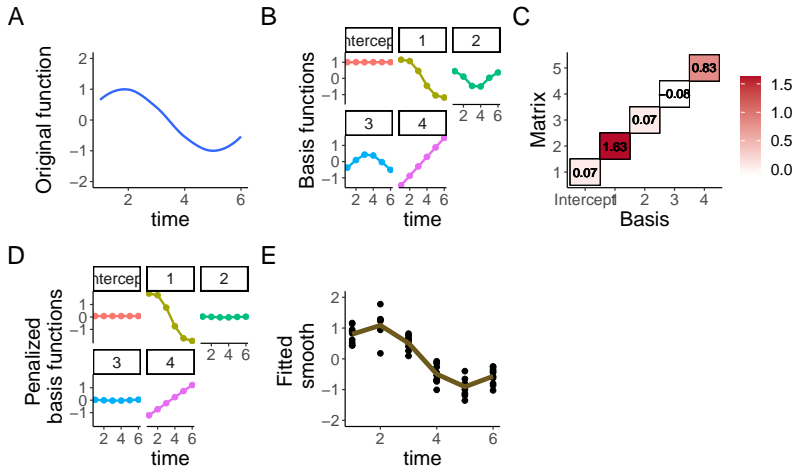


Figure 6: Fitting process of a GAM.

## An Example

- Simulated data from a study on radiotherapy in a mouse model of melanoma<sup>6</sup>.

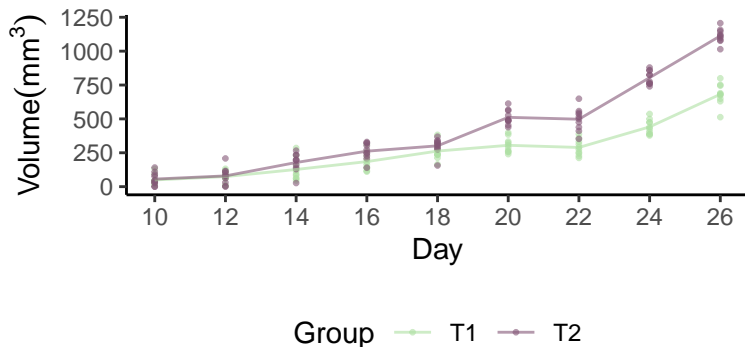


Figure 7: Tumor volume in two groups of tumors under radiotherapy

<sup>6</sup>Sen et al. 2011.

## Fitting a GAM

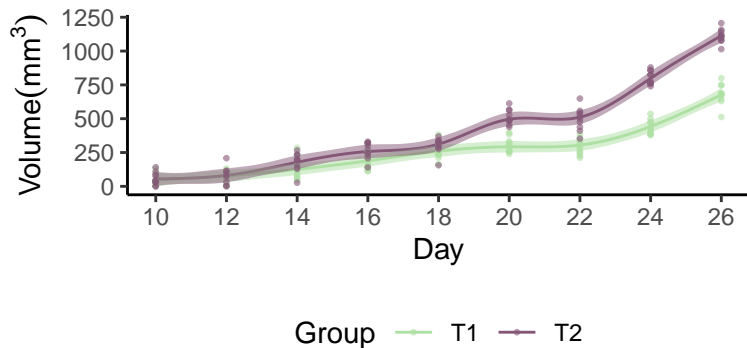


Figure 8: GAM fitted to simulated data

- The model captures the trend of the data

## Fitting a GAM

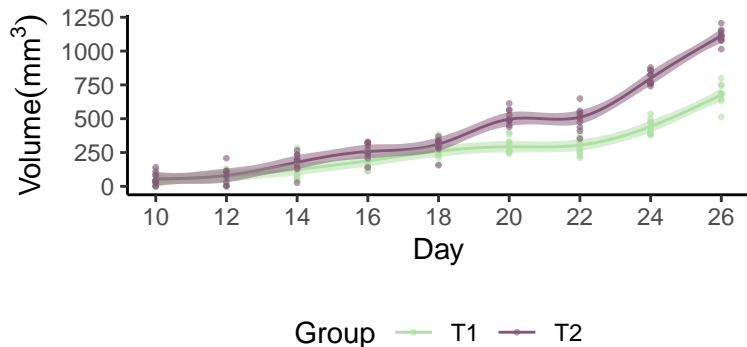


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- The model captures the trend of the data
- We can furthermore compare the trends.

## Differences

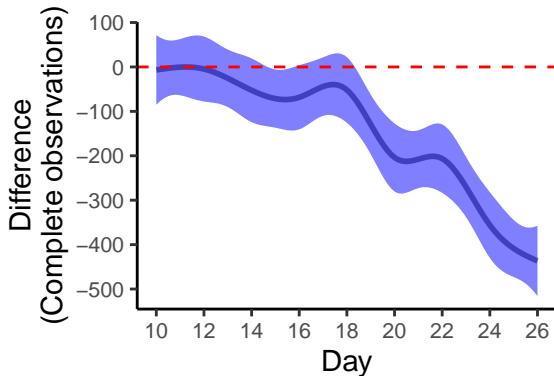


Figure 9: Pairwise comparisons between smooths

- We can compare the smooths for each group. Here, we see that T2 is significantly higher after day 18.

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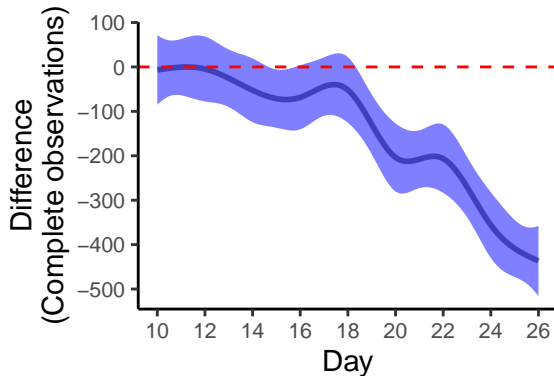


Figure 9: Pairwise comparisons between smooths

- We can compare the smooths for each group. Here, we see that T2 is significantly higher after day 18.
- This can give an idea of further explorations of biological

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  - A model that captures non-linear trends in the data
  - This allows to examine specific time points that might be of interest, where metabolic, or physiological relevant changes might be occurring
  - Lets the data speak for itself

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  - Methods: Sharing the code used for statistical analyses
- In synthesis, sharing all the information used to create a paper such that anyone can re-create the analysis, results, and the paper itself from the files provided.

## Addressing Reproducibility

- For GAMs

<https://github.com/aimundo/GAMs-biomedical-research>

## Addressing Reproducibility

- For GAMs  
<https://github.com/aimundo/GAMs-biomedical-research>
- COVID-19: Work is ongoing, but repository will be ready when paper is submitted

## Conclusion

- There is an ongoing need of analyzing public health data to address important disparities in areas such as vaccination.

## Conclusion

- There is an ongoing need of analyzing public health data to address important disparities in areas such as vaccination.
- Semi-parametric statistical to analyze biomedical/public health longitudinal data, such as GAMs can provide better insight on periods where important biological changes might occur.

## Acknowledgements

- The Nasri Lab (Université de Montréal)
  - Bouchra Nasri, PhD (PI)
  - Idriss Sekkak, PhD
  - Rado Ramasy
  - Fatima El-Mousawi
  - Rawda Berkat
- The Muldoon Lab (University of Arkansas)
  - Timothy J. Muldoon (PI)
- John R. Tipton (Los Alamos National Laboratory)



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-  Beck, Nathaniel and Simon Jackman (Apr. 1998). “Beyond Linearity by Default: Generalized Additive Models”. In: *American Journal of Political Science* 42.2, p. 596. DOI: 10.2307/2991772. URL: <https://doi.org/10.2307/2991772>.
-  Gerretsen, Philip et al. (Nov. 2021). “Individual determinants of COVID-19 vaccine hesitancy”. In: *PLOS ONE* 16.11. Ed. by Leeberk Raja Inbaraj, e0258462. DOI: 10.1371/journal.pone.0258462. URL: <https://doi.org/10.1371/journal.pone.0258462>.
-  Hawkins, Devan (June 2020). “Differential occupational risk for COVID-19 and other infection exposure according to race and ethnicity”. In: *American Journal of Industrial Medicine* 63.9, pp. 817–820. DOI: 10.1002/ajim.23145. URL: <https://doi.org/10.1002/ajim.23145>.

-  Nafilyan, Vahe et al. (July 2021). “Sociodemographic inequality in COVID-19 vaccination coverage among elderly adults in England: a national linked data study”. In: *BMJ Open* 11.7, e053402. DOI: 10.1136/bmjopen-2021-053402. URL: <https://doi.org/10.1136/bmjopen-2021-053402>.
-  Sen, Arindam et al. (May 2011). “Mild Elevation of Body Temperature Reduces Tumor Interstitial Fluid Pressure and Hypoxia and Enhances Efficacy of Radiotherapy in Murine Tumor Models”. In: *Cancer Research* 71.11, pp. 3872–3880. DOI: 10.1158/0008-5472.can-10-4482. URL: <https://doi.org/10.1158/0008-5472.can-10-4482>.
-  Tsasis, Peter, Jenna M. Evans, and Susan Owen (Sept. 2012). “Reframing the challenges to integrated care: a complex-adaptive systems perspective”. In: *International Journal of Integrated Care* 12.5. DOI: 10.5334/ijic.843. URL: <https://doi.org/10.5334/ijic.843>.