Challenges in Modeling SARS-CoV-2: Bridging the Best of Both Worlds Between Models and Reality

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McMaster University

Background

Math and Statistics

MacTheoBio

Theoretical, statistical and computational approaches to study biology

Infectious diseases

Spatial ecology

Evolution

Background

Math and Statistics

MacTheoBio

Theoretical, statistical and computational approaches to study biology

Infectious diseases

- Malaria
- Ebola
- Influenza
- Canine Rabies
- HIV
- etc..

Background

Math and Statistics

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Theoretical, statistical and computational approaches to study biology

Infectious diseases

- Malaria
- Ebola
- Influenza
- Canine Rabies
- HIV
- etc..

I can read Chinese!

Part 1

2019–2020

WuHan Novel Corona Virus Outbreak

Background

2019–2020 WuHan Novel Corona Virus Outbreak

- Late December 2019, several suspicious cases of pneumonia in Wuhan City, Hubei Province of China.
- Unknown virus
- Early January 2020, Chinese authorities confirmed that they had identified a new virus.

Data collection

湖北省卫生健康委员会
Health Commission of Hubei Province
首 页 发布解读 互动交流 办事服务 部门动态

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湖北省卫生健康委员会关于新型冠状病毒感染的肺炎情况通报

2020-01-22 21:54 | 湖北省卫生健康委员会

2020年1月21日0时—24时，湖北省武汉市报告新增新型冠状病毒感染的肺炎病例105例，死亡3例，出院3例。其他市州无新增病例报告。

截至1月21日24时，湖北省累计报告新型冠状病毒感染的肺炎病例375例，已治愈出院28例，死亡9例。目前仍在院治疗338例，其中重症65例，危重症23例，均在定点医疗机构接受隔离治疗。累计追踪密切接触者1181人，已解除医学观察755人，尚在接受医学观察426人。

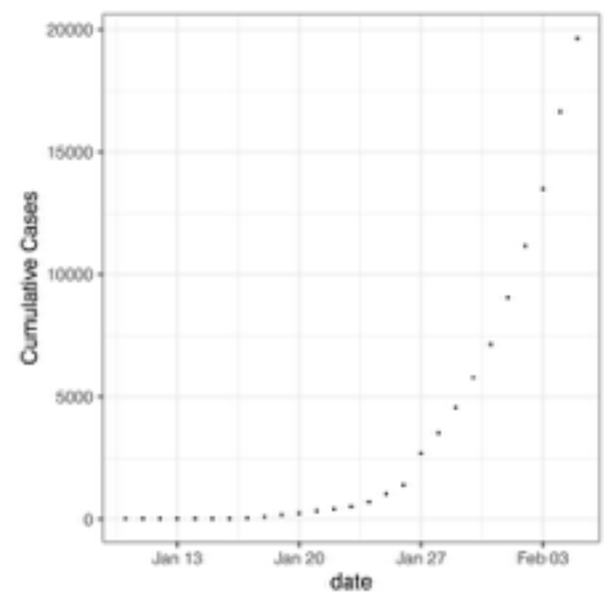
王某，男，75岁，2020年1月11日收治入院，因患者病情加重，1月15日转入ICU，行机械通气，于2020年1月20日11时25分，因呼吸循环衰竭抢救无效死亡。死者生前曾进行髋关节置换，同时患有高血压病3级（极高危）。

罗某，男，66岁，2019年12月23日发病，12月31日出现胸闷前往医院就诊，2020年1月2日转入武汉市金银潭医院救治。入院时即出现严重呼吸窘迫、多脏器功能损害，于2020年1月21日09时50分因病情恶化抢救无效死亡。死者生前有高血压、胆结石等基础疾病。

Jan 21st 24:00

105 new cases,
3 discharge and 3 death

375 Cumulative cases
28 Discharged
9 death



The Basic Reproductive Number/Ratio (R_0)

- Expected number of new cases per case
- Good index of risk at the population level

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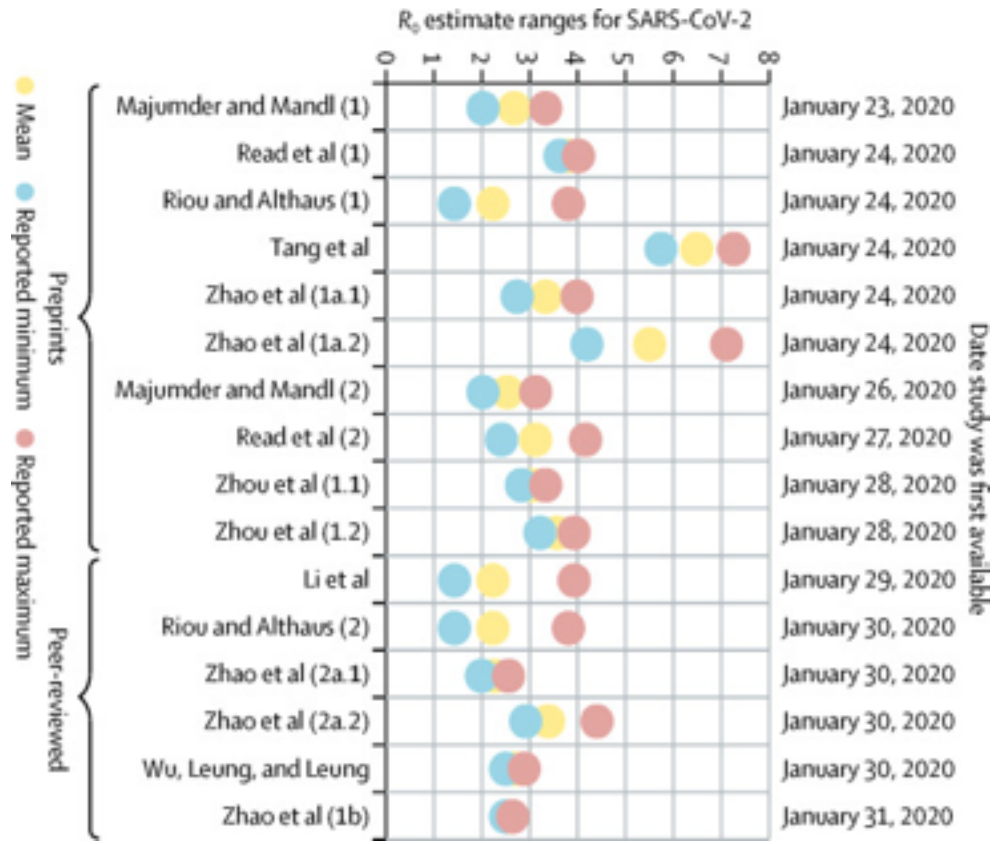
Most **V**aluable **P**iece
of information in disease modelling

WH outbreak R_0 Estimates



Majumder, M.S. and Mandl, K.D., 2020. Early in the epidemic: impact of preprints on global discourse about COVID-19 transmissibility. The Lancet Global Health, 8(5), pp.e627-e630.

Exponential Fitting Framework

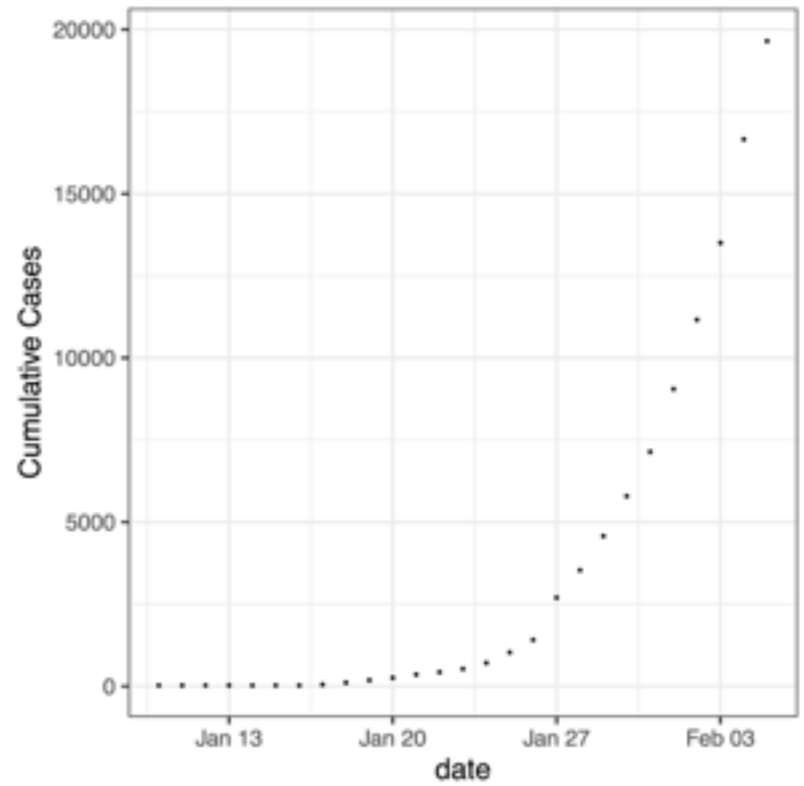
- Exponential growth rate (r)
- Generation Interval

Exponential Fitting Framework

- **Exponential growth rate (r)**
- Generation Interval

Exponential growth rate (r)

- Estimate from time series data



Exponential growth rate (r)

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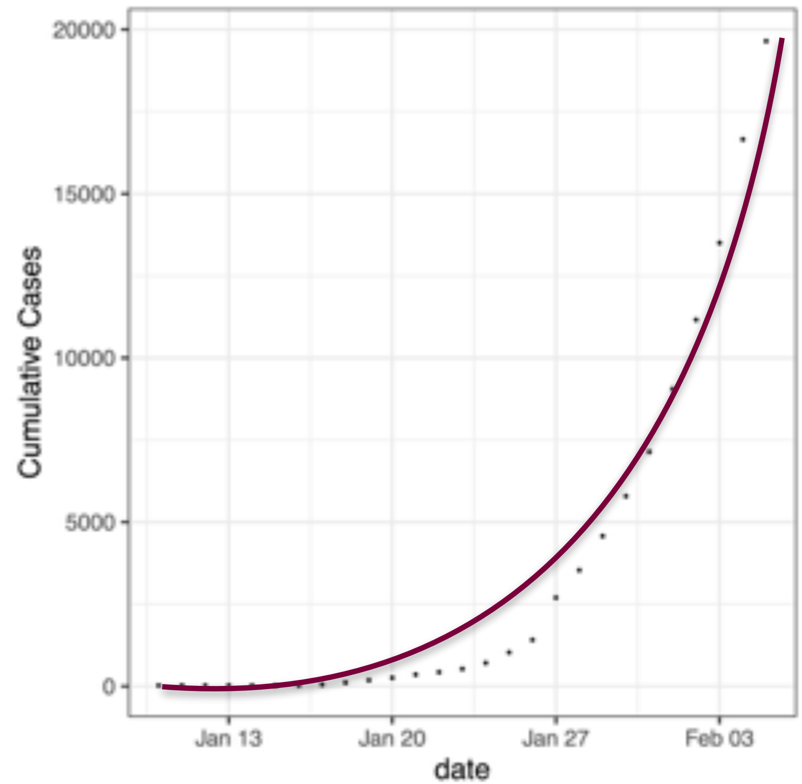

Exponential growth rate (r)

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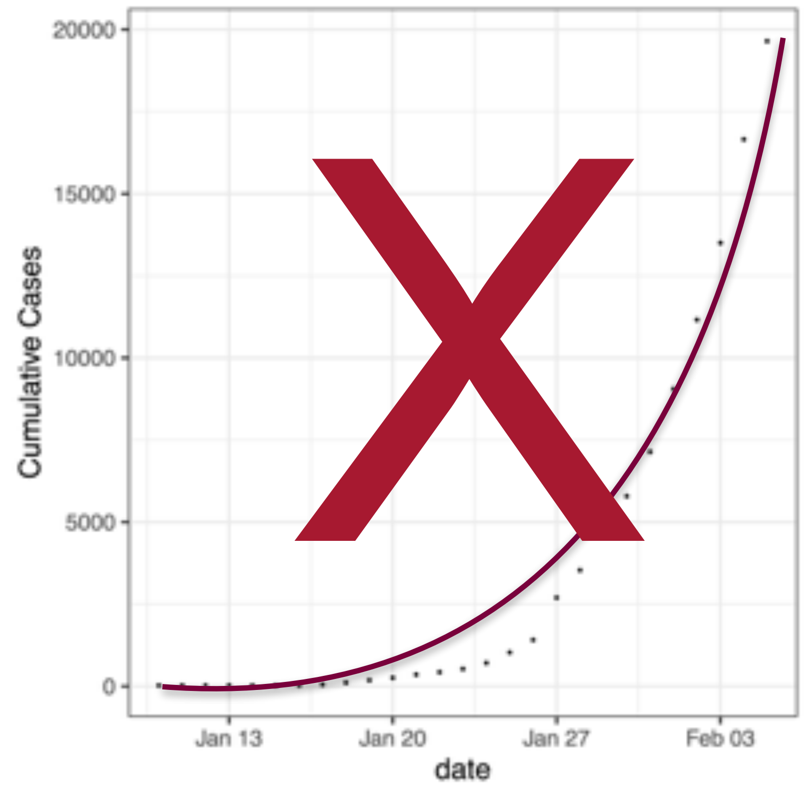
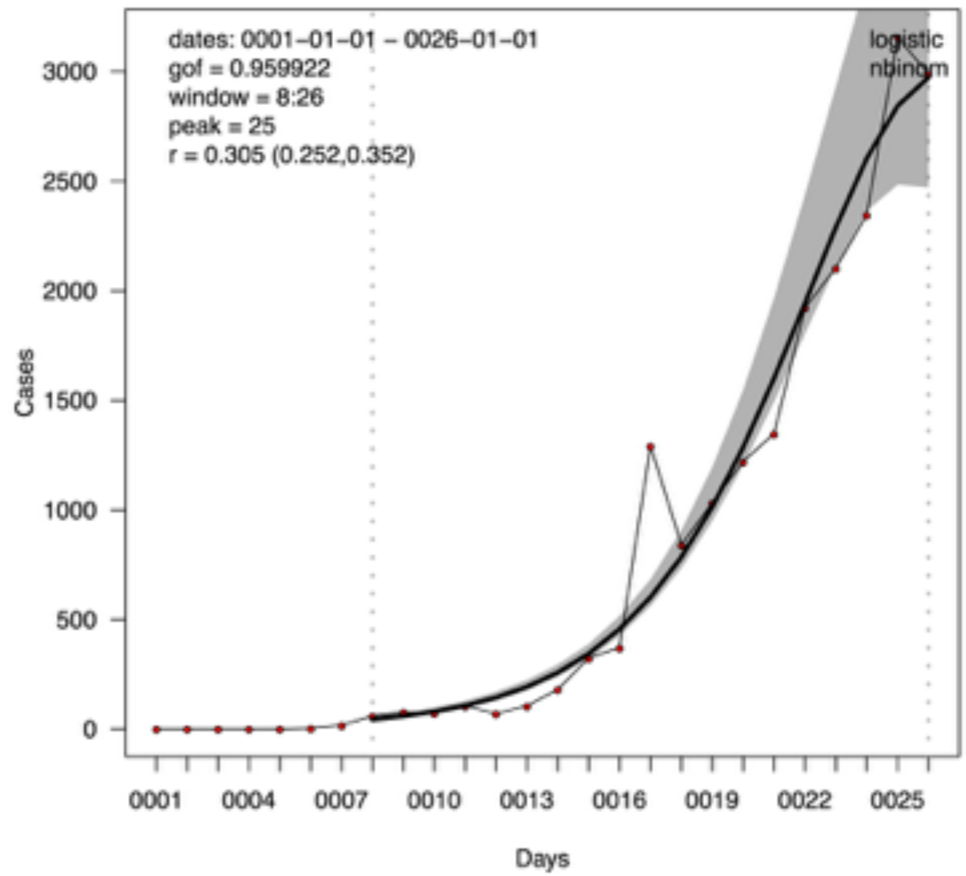


Exponential growth rate (r)

- Estimate from time series data
- Fitting to incidence data
- Logistic model with negative binomial noise
- epigrowthfit package in R



Ma, J., Dushoff, J., Bolker, B.M. and Earn, D.J., 2014. Estimating initial epidemic growth rates. Bulletin of mathematical biology, 76(1), pp.245-260.

Exponential Fitting Framework

- Exponential growth rate (r)
- **Generation Interval**

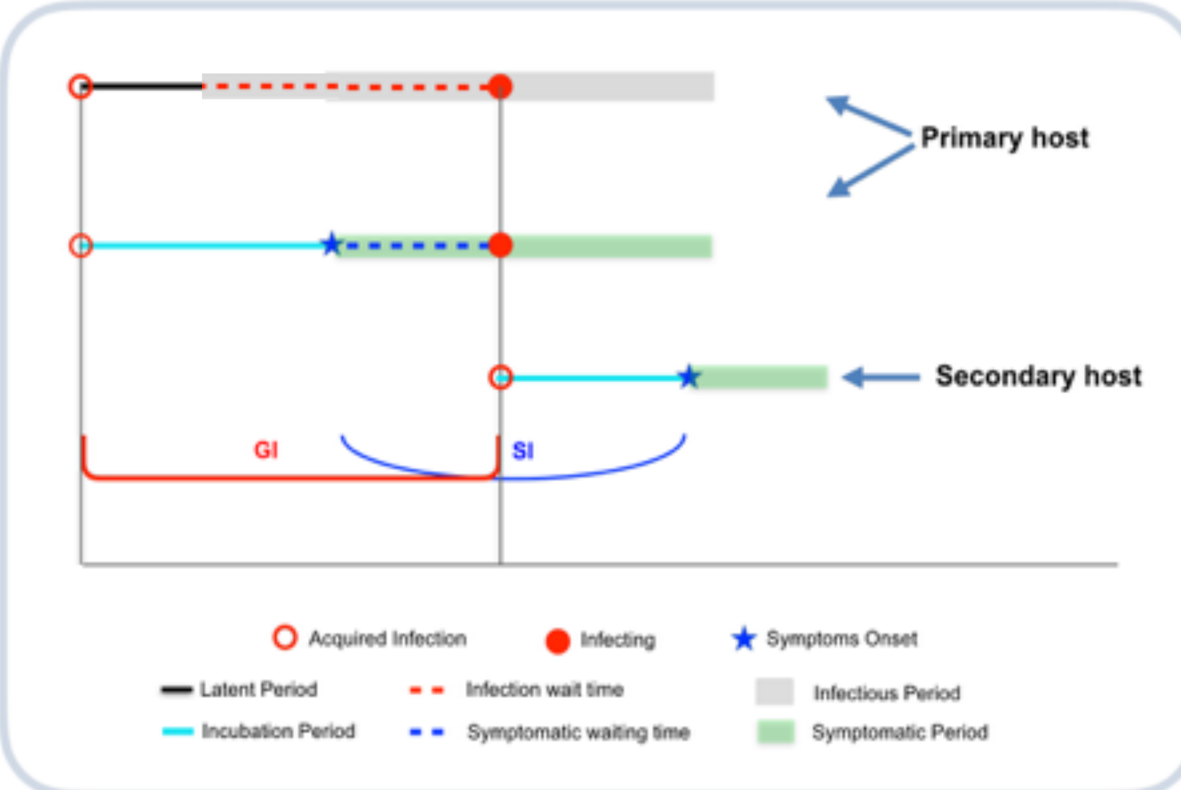
Generation interval

- Time between infections

- Focal individual

Generation interval

- Time between infections
- Focal individual
- Infection are hard to observe
- Serial intervals
- Time between symptom onsets



Exponential Fitting Framework

- Exponential growth rate (r)
- Generation Interval

Exponential Fitting Framework

- Exponential growth rate (r)
- Generation Interval

$$1/\mathcal{R}_0 = \int \exp(-r\tau) g(\tau)\, d\tau.$$

Euler-Lotka equation

Wallinga, J. and Lipsitch, M., 2007. How generation intervals shape the relationship between growth rates and reproductive numbers. Proceedings of the Royal Society B: Biological Sciences, 274(1609), pp.599-604.

Gamma approximation framework

- Exponential growth rate (r)

- **Generation Interval (GI)**
  - Mean GI ($\bar{G}$)
  - Dispersion (κ)

$$\mathcal{R}_0 = \left(1 + \kappa r \bar{G}\right)^{1/\kappa}$$

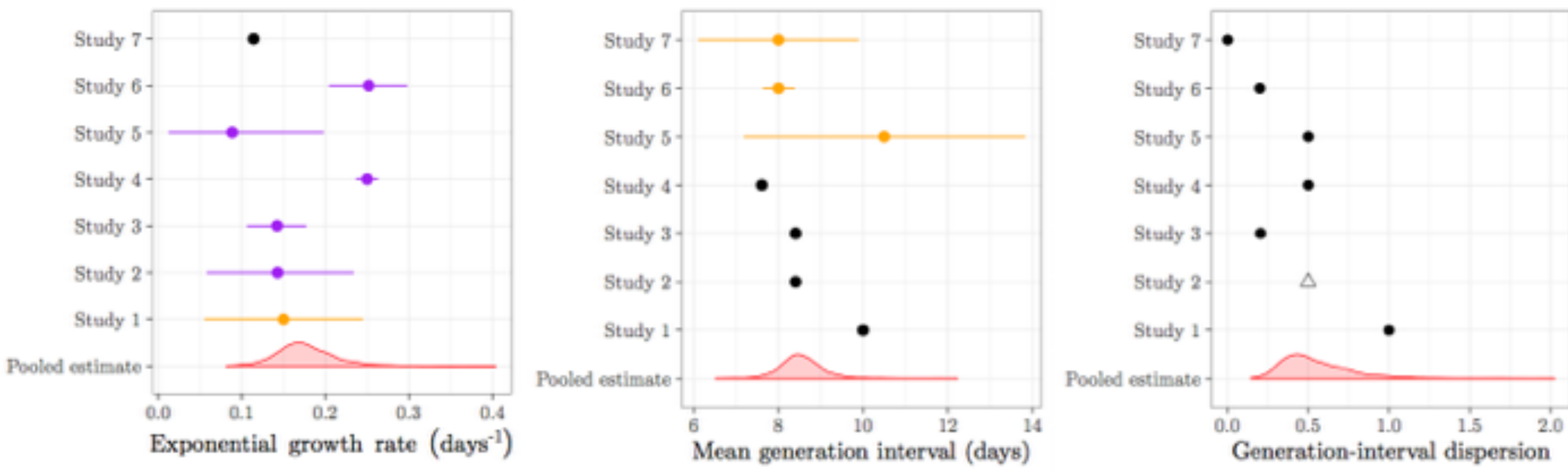
Park, S.W., Champredon, D., Weitz, J.S. and Dushoff, J., 2019. A practical generation-interval-based approach to inferring the strength of epidemics from their speed. Epidemics, 27, pp.12-18.

R_0 estimates

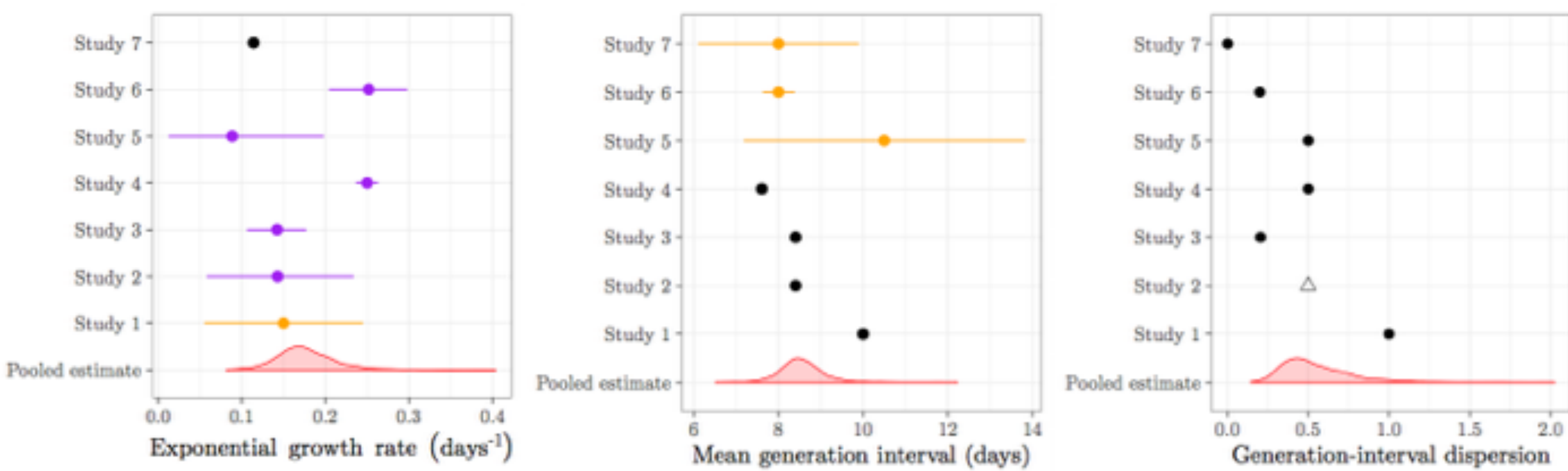
	Model	Data (study period)	Data source	Basic reproductive number $\mathcal{R}_0$	Mean generation interval $\bar{G}$ (days)	Generation-interval dispersion κ	Reference
Study 1	Deterministic branching process model	Total number of cases in Wuhan City, China (Jan 18, 2020)	Estimated by Imai et al. (2020)	1.5–3.5	10	1	Bedford et al. (2020)
Study 2	Stochastic branching process model	Total number of cases in Wuhan City, China (Jan 18, 2020)	Estimated by Imai et al. (2020)	2.6 (1.5–3.5)*	8.4	Not reported†	Imai et al. (2020)
Study 3	Poisson offspring distribution model	Confirmed cases from China and other countries (Dec 29, 2019–Jan 23, 2020)	Medical records and epidemiological investigations from Guangdong Province, China, and official websites of other regions in China	2.92 (95% CI: 2.28–3.67)	8.4	0.2	Liu et al. (2020)
Study 4	Deterministic Metapopulation Susceptible-Exposed-Infected-Recovered (SEIR) model	Confirmed cases from China and other countries (Jan 1–21, 2020)	Not reported	3.8 (95% CI: 3.6–4.0)	7.6	0.5	Read et al. (2020a)
Study 5	Stochastic branching process model	Total number of cases in Wuhan City, China (Jan 18, 2020)	Estimated by Imai et al. (2020)	2.2 (90% CI: 1.4–3.8)	7–14	0.5	Riou and Althaus (2020a)
Study 6	Exponential growth model	Confirmed cases from China (Jan 10–22, 2020)	Wuhan Municipal Health Commission, China and National Health Commission of China	5.47 (95% CI: 4.16–7.10)‡	7.6–8.4	0.2	Zhao et al. (2020)
Study 7	Incidence Decay and Exponential Adjustment (IDEA) model	Reported cases from Wuhan City, China (Dec 1, 2019–Jan 26, 2020)	World Health Organization, National Health Commission of China, Wuhan Municipal Health Commission, and Huang et al. (2020)	2.0–3.1	6–10	0	Majumder and Mandl (2020a)

Park, S.W., Bolker, B.M., Champredon, D., Earn, D.J., Li, M., Weitz, J.S., Grenfell, B.T. and Dushoff, J., 2020. Reconciling early-outbreak estimates of the basic reproductive number and its uncertainty: framework and applications to the novel coronavirus (SARS-CoV-2) outbreak. (In press)

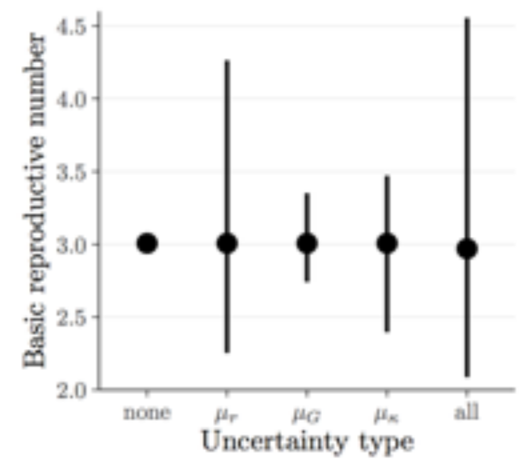
Parameter Uncertainties



Parameter Uncertainties

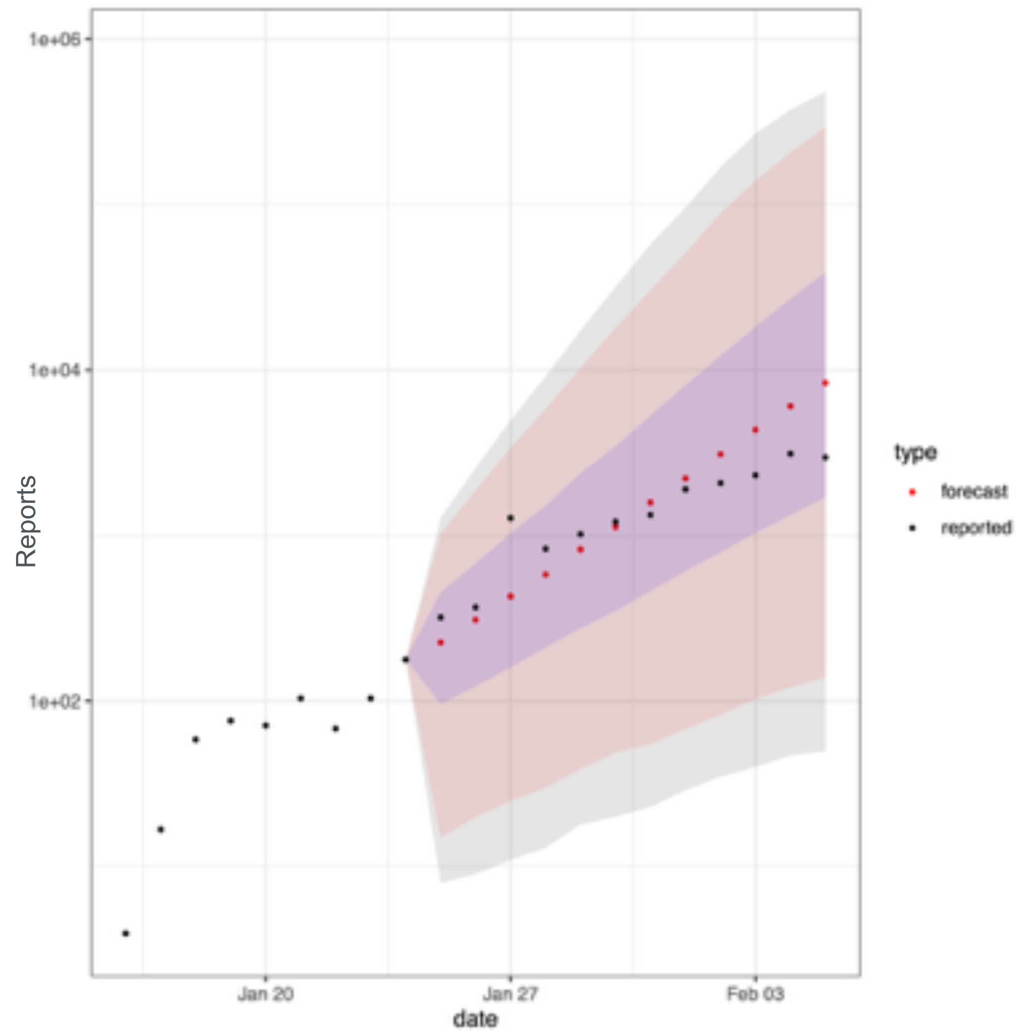


- Uncertain of R_0 comes from these parameters
- Important to propagate uncertainties from all the parameters



Forecasting

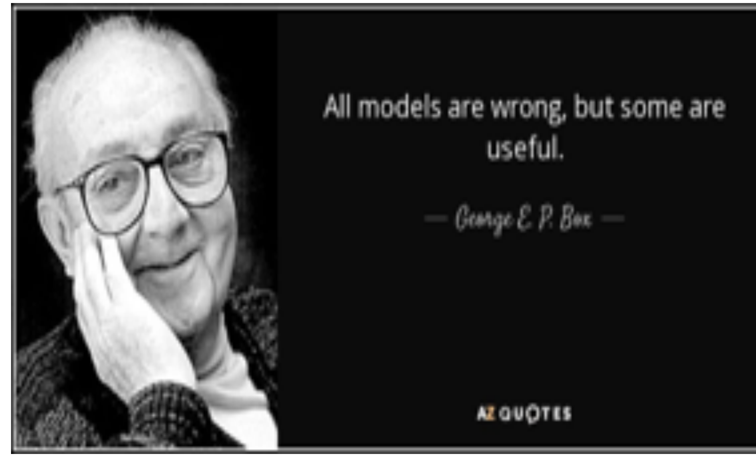
- Bayesian Discrete-time SIR
  - Dual beta-binomial process
  - Transmission and observation
- 2 week projection



Li, M., Dushoff, J. and Bolker, B.M., 2018. Fitting mechanistic epidemic models to data: A comparison of simple Markov chain Monte Carlo approaches. Statistical methods in medical research, 27(7), pp. 1956-1967.

Summary

- Easy to make a model
- Extremely hard to make models that:
  - are informative
  - predict well
  - work in real time
- Discrepancies between R_0 estimates is hard to understand
  - Method
  - Data
- Hard to communicate clearly.
  - E.g. $R_0 \sim 3$ (2,4)



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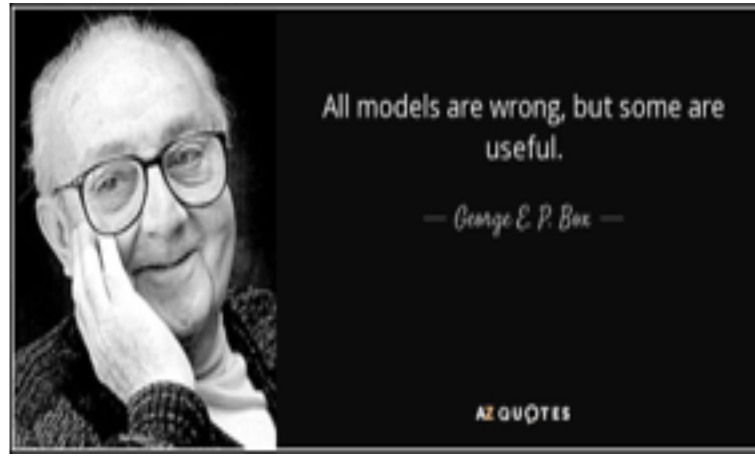


- Predictions of the short-term trajectories are useful

Moving forward and preparing for the global pandemic

- Interesting and important to figure out the discrepancies

- What else? What do people want to know?

Preparing for the global pandemic

Public Health

Questions:
Is the outbreak taking off?
How many cases are we going to see in a week? a month?

Transmission route?

What do we want to tell the public?

Who's at risk?

Biology

Questions:
What kind of virus is it and what is its natural history?

What is the pathogenesis of the disease?

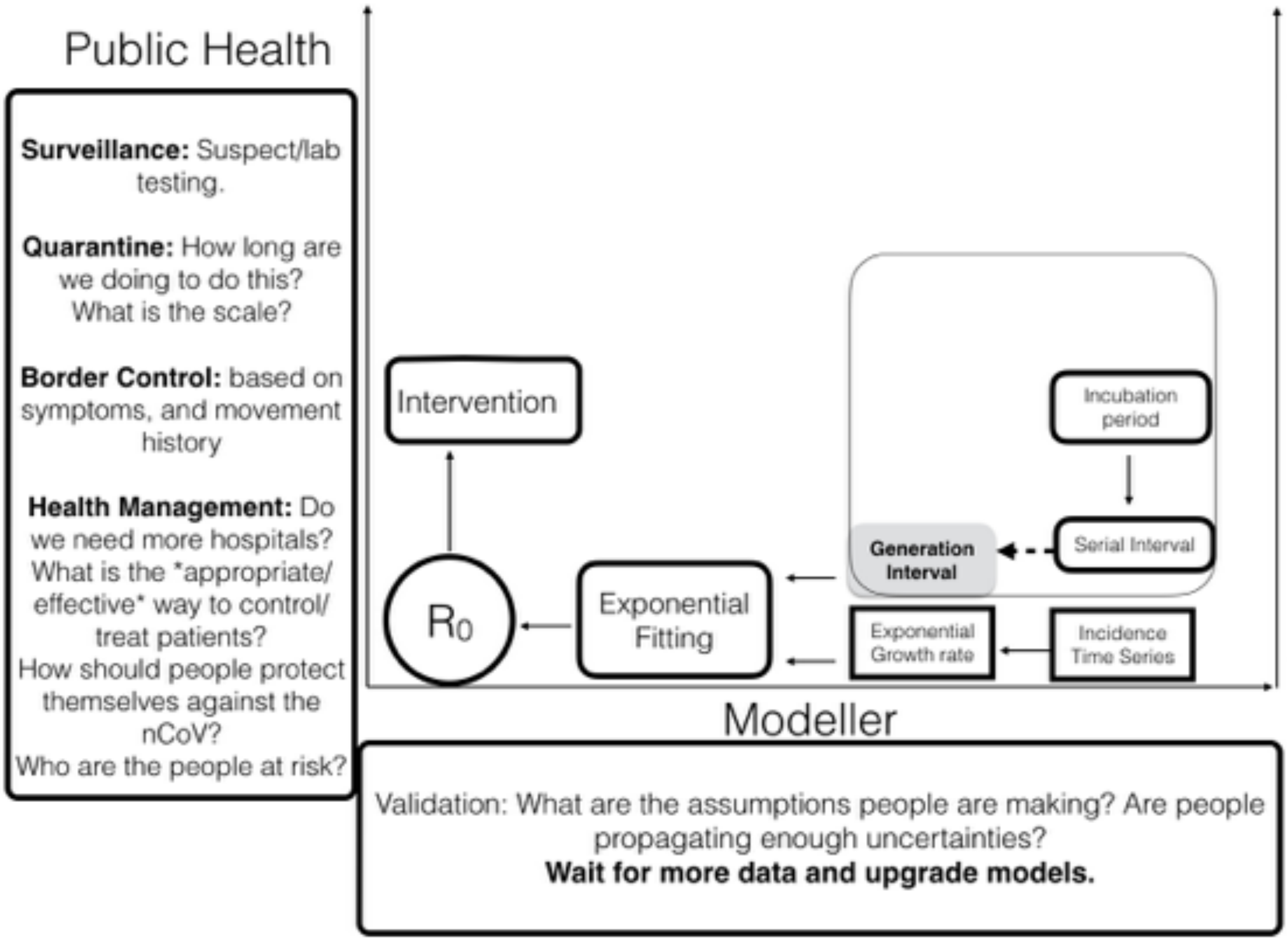
Do we know anything phylogenetically about the disease?

R_0

Modeller

Questions:
What is its R_0?
What kind of data are available and what assumptions do we have to make to estimate R_0?

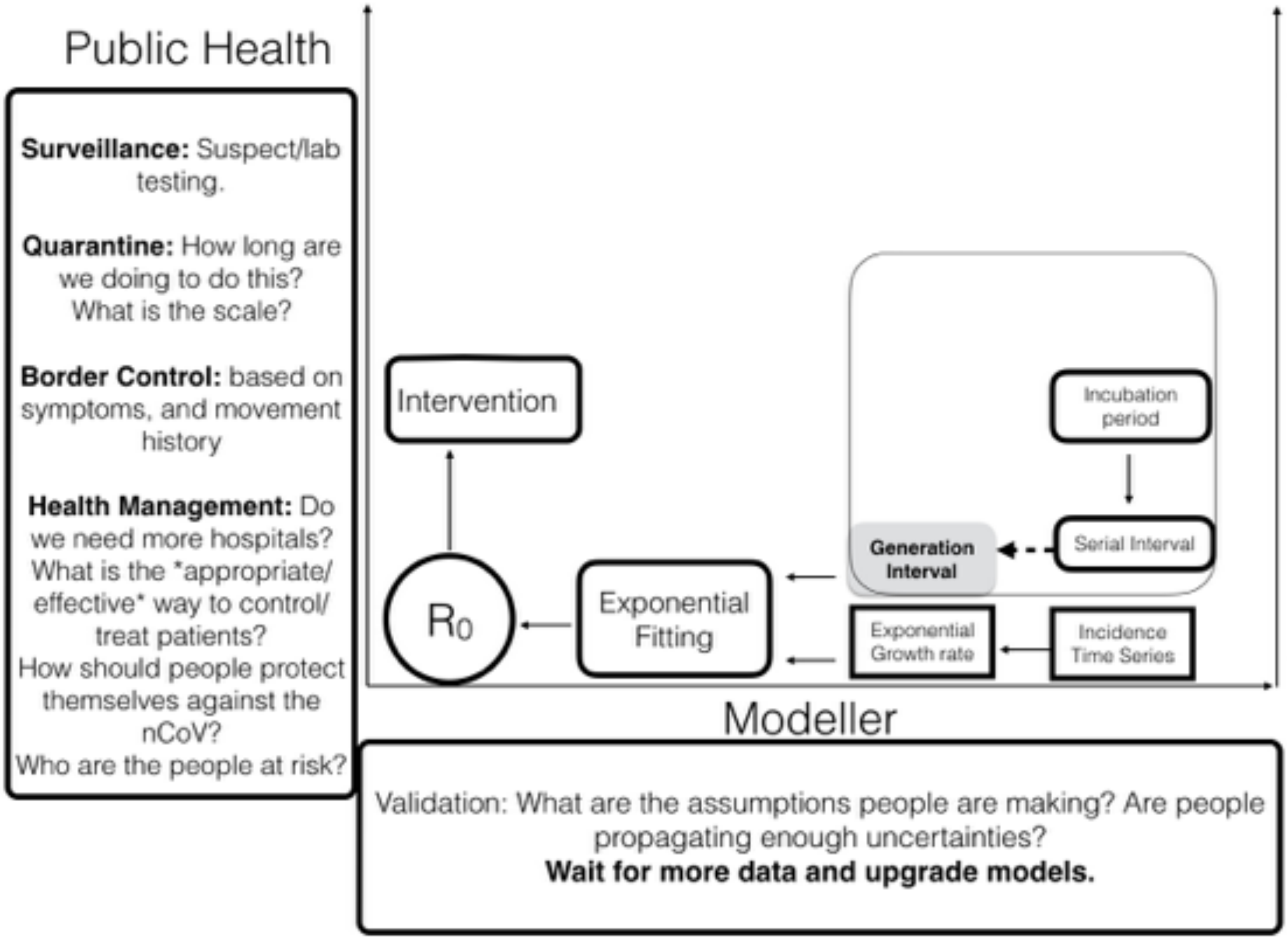
Preparing for the global pandemic



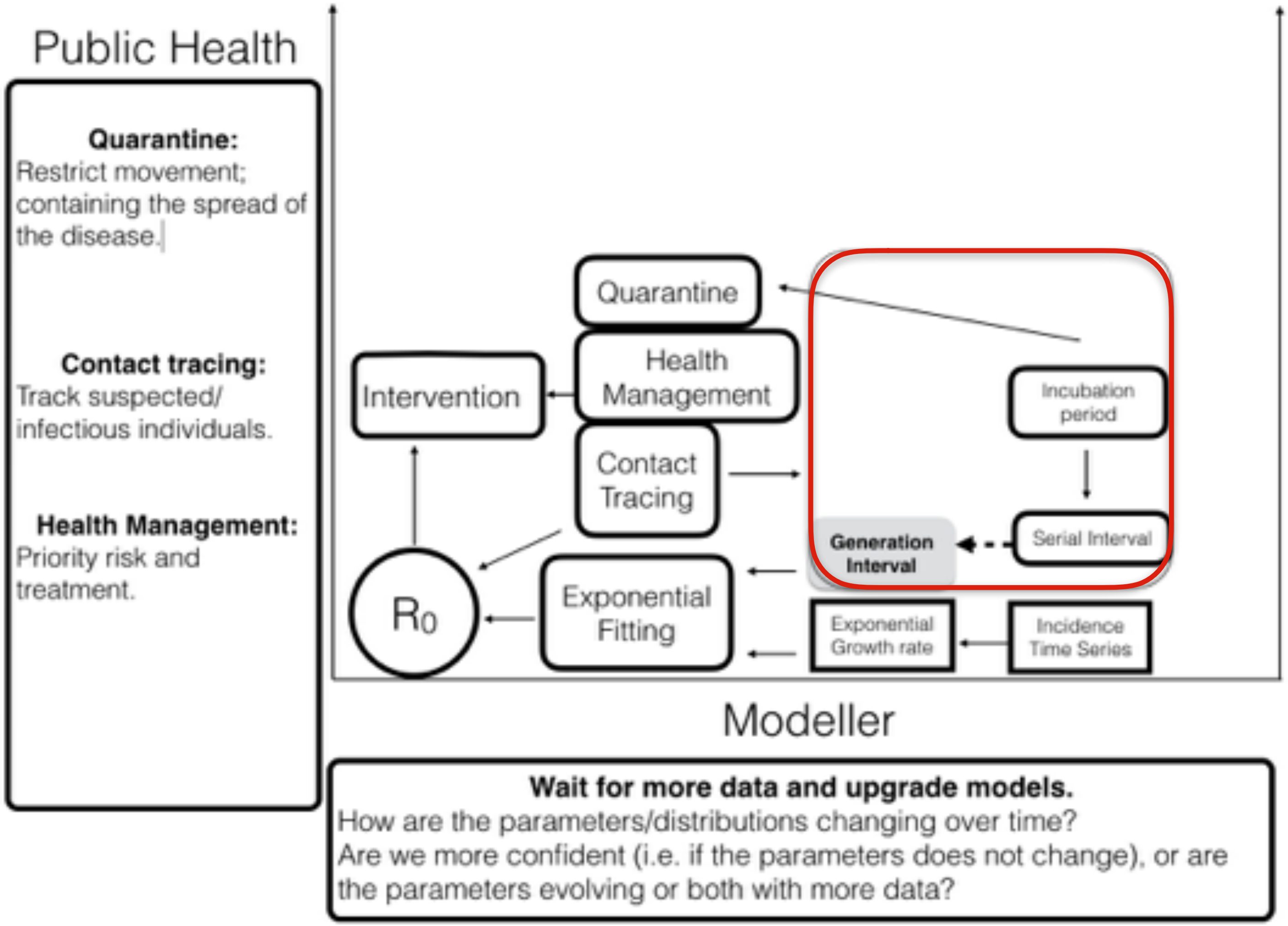
Part 2

Distributions of delays associated with COVID-19 healthcare in Ontario, Canada

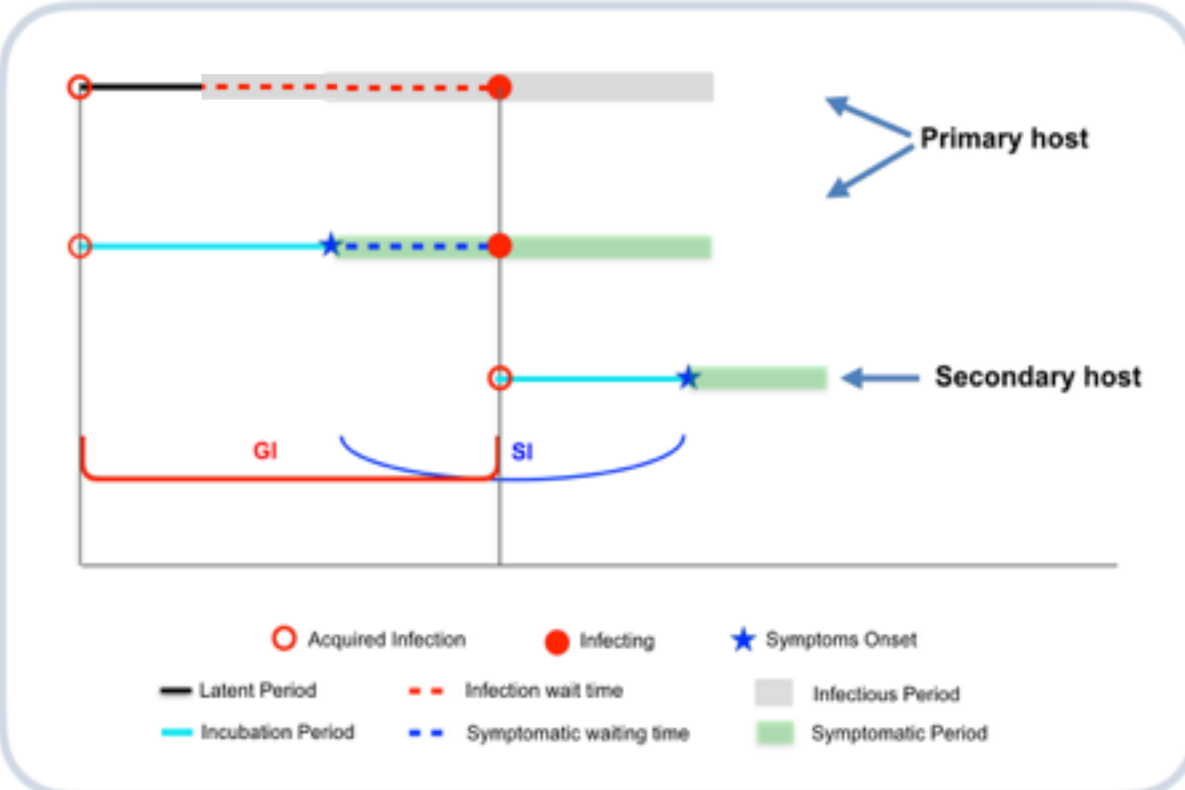
Preparing for the global pandemic



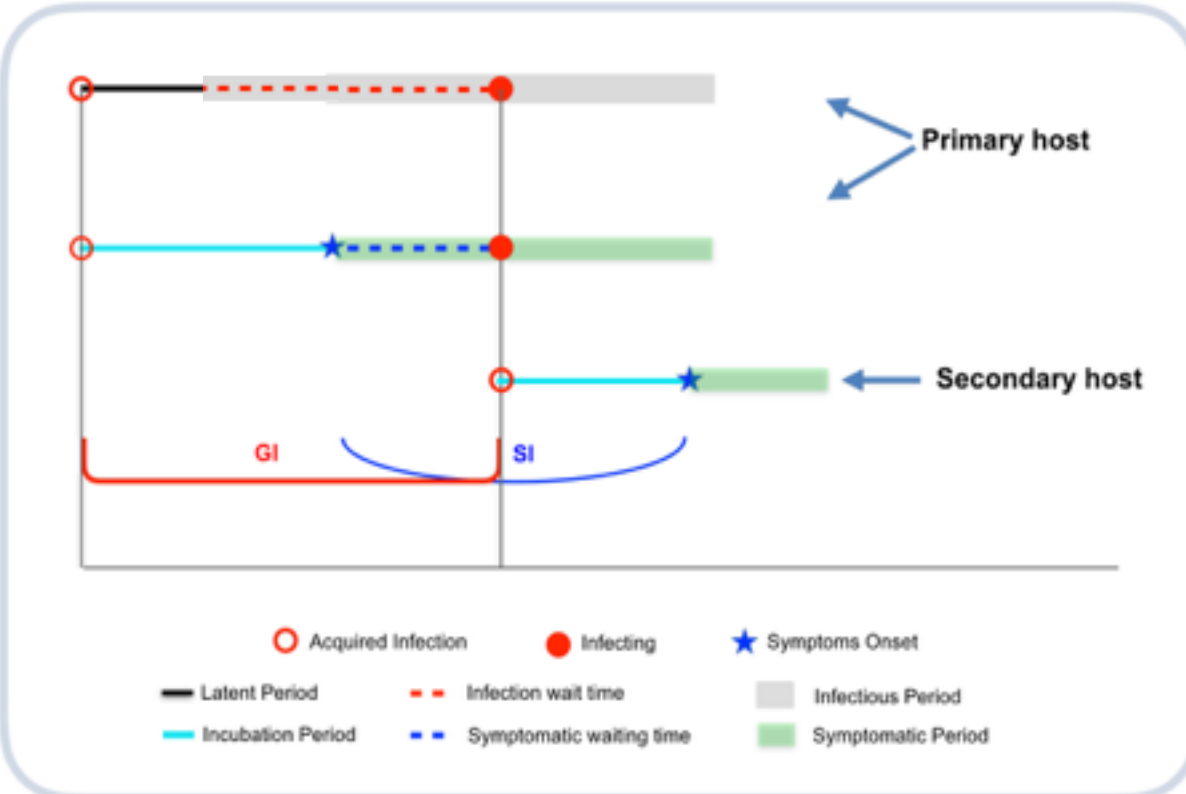
Distributions of delays associated with COVID-19 healthcare in Ontario, Canada



Time intervals



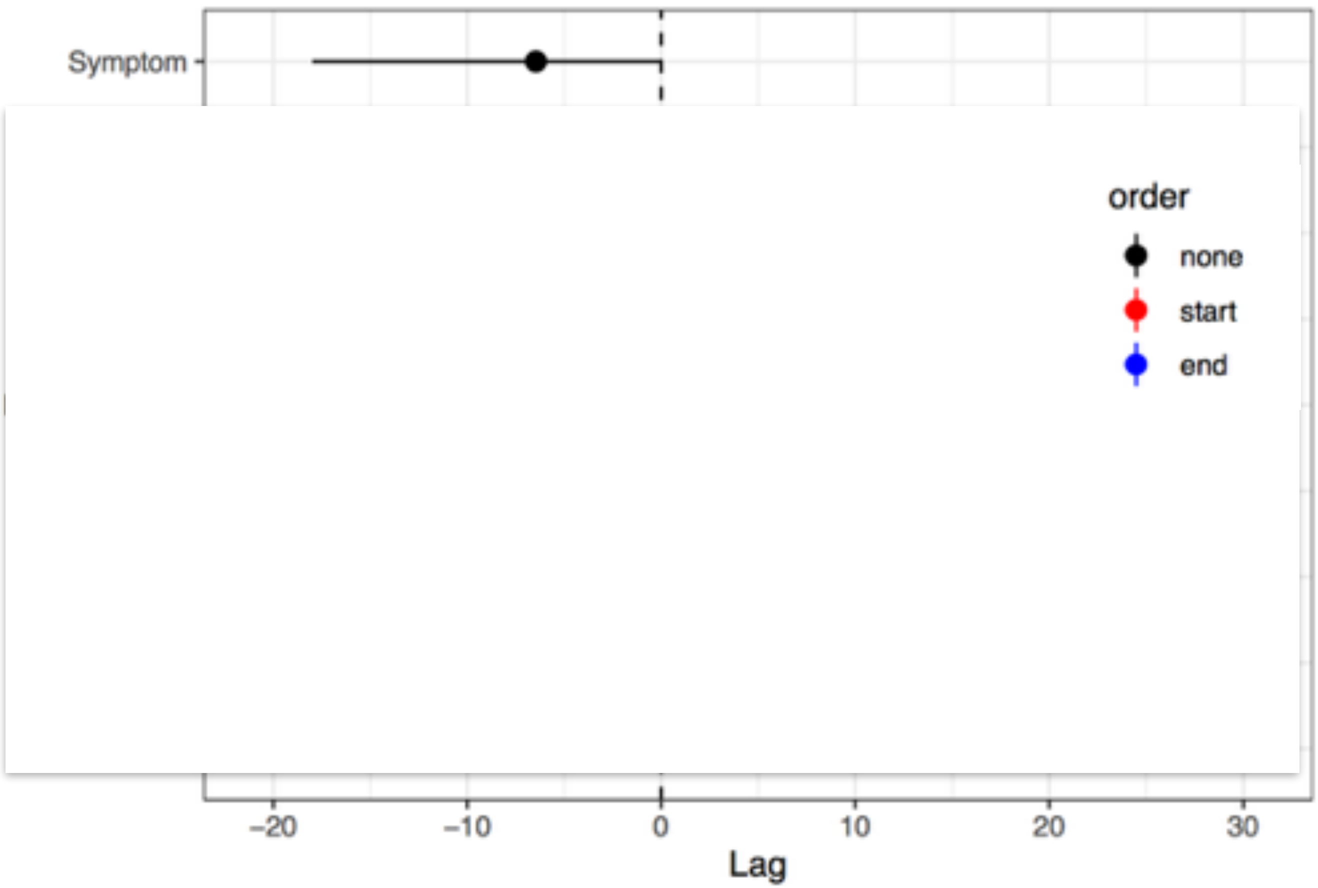
Time intervals

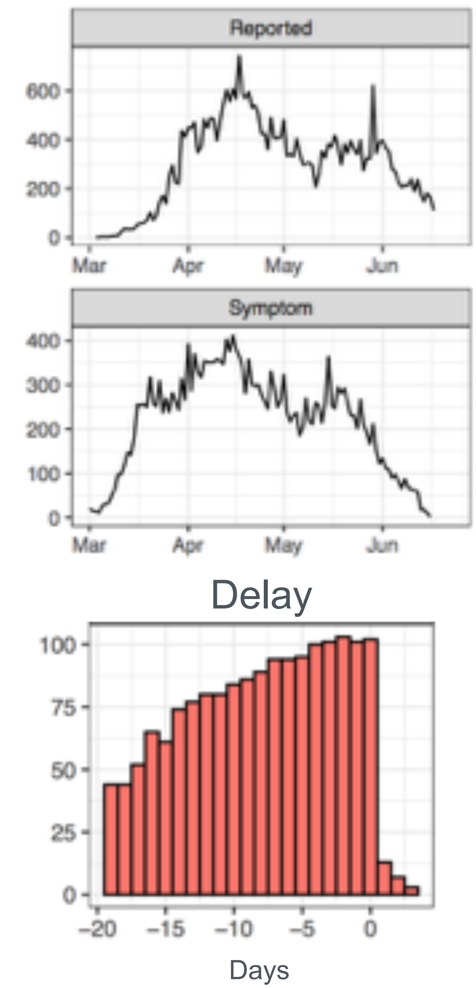


Isolation time
Specimen collection time
Reporting time

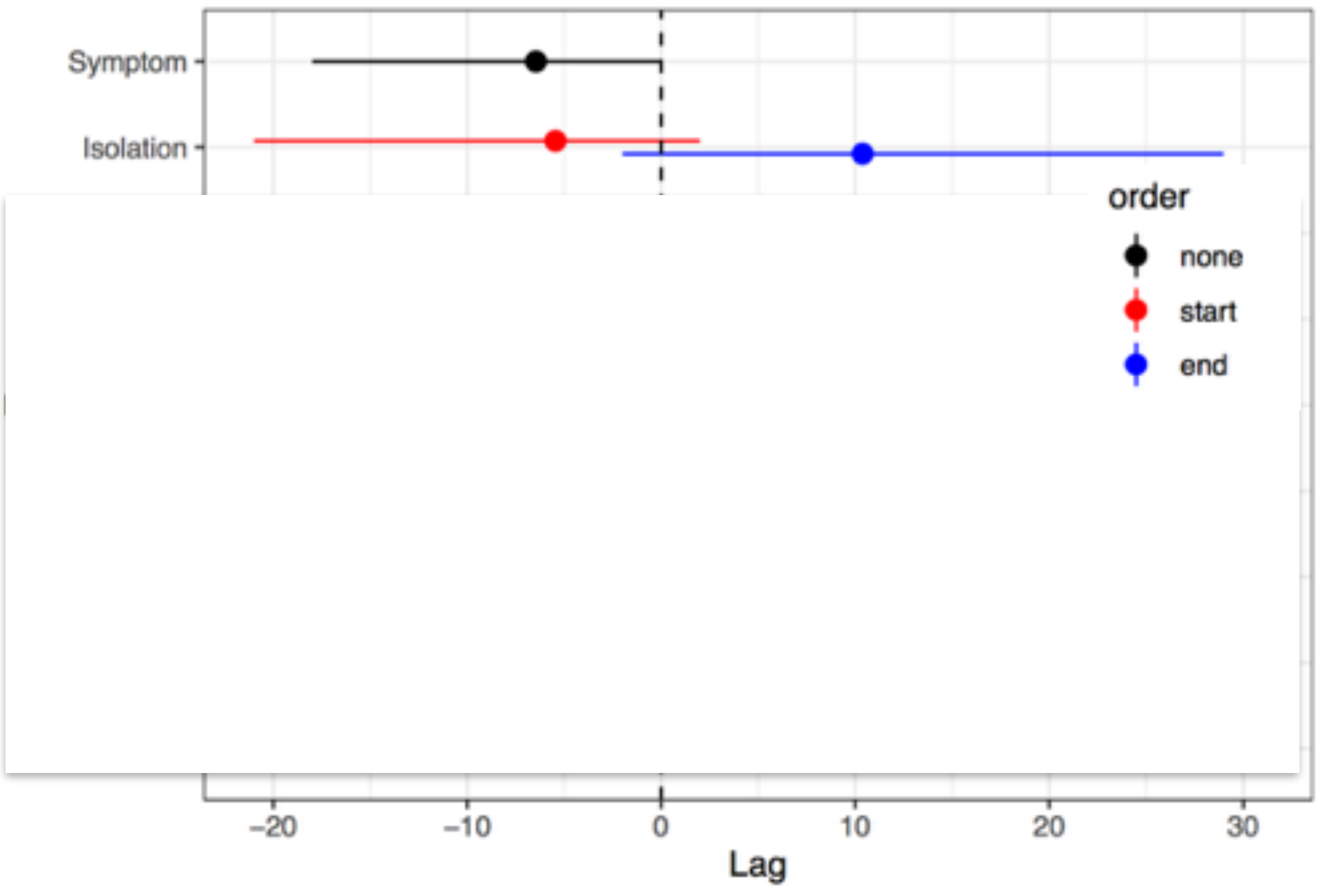
ER time
Hospital admission time
ICU time

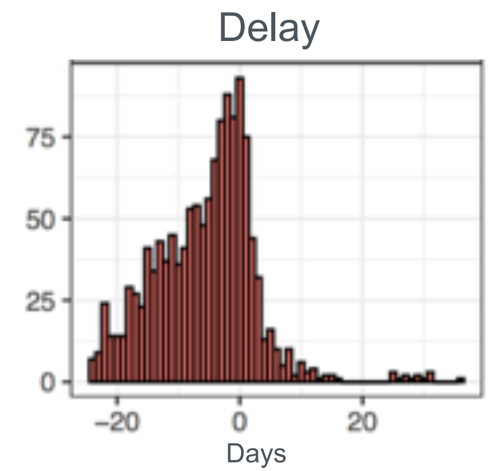
Chronological Episodes (Symptom onset)

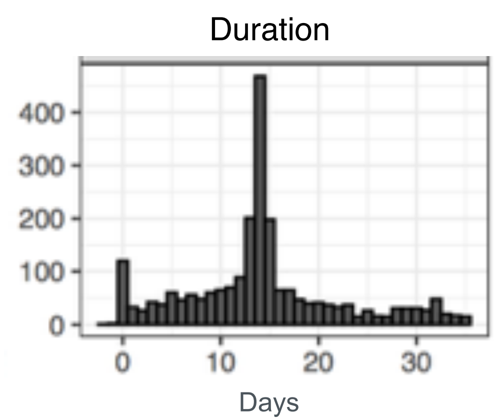




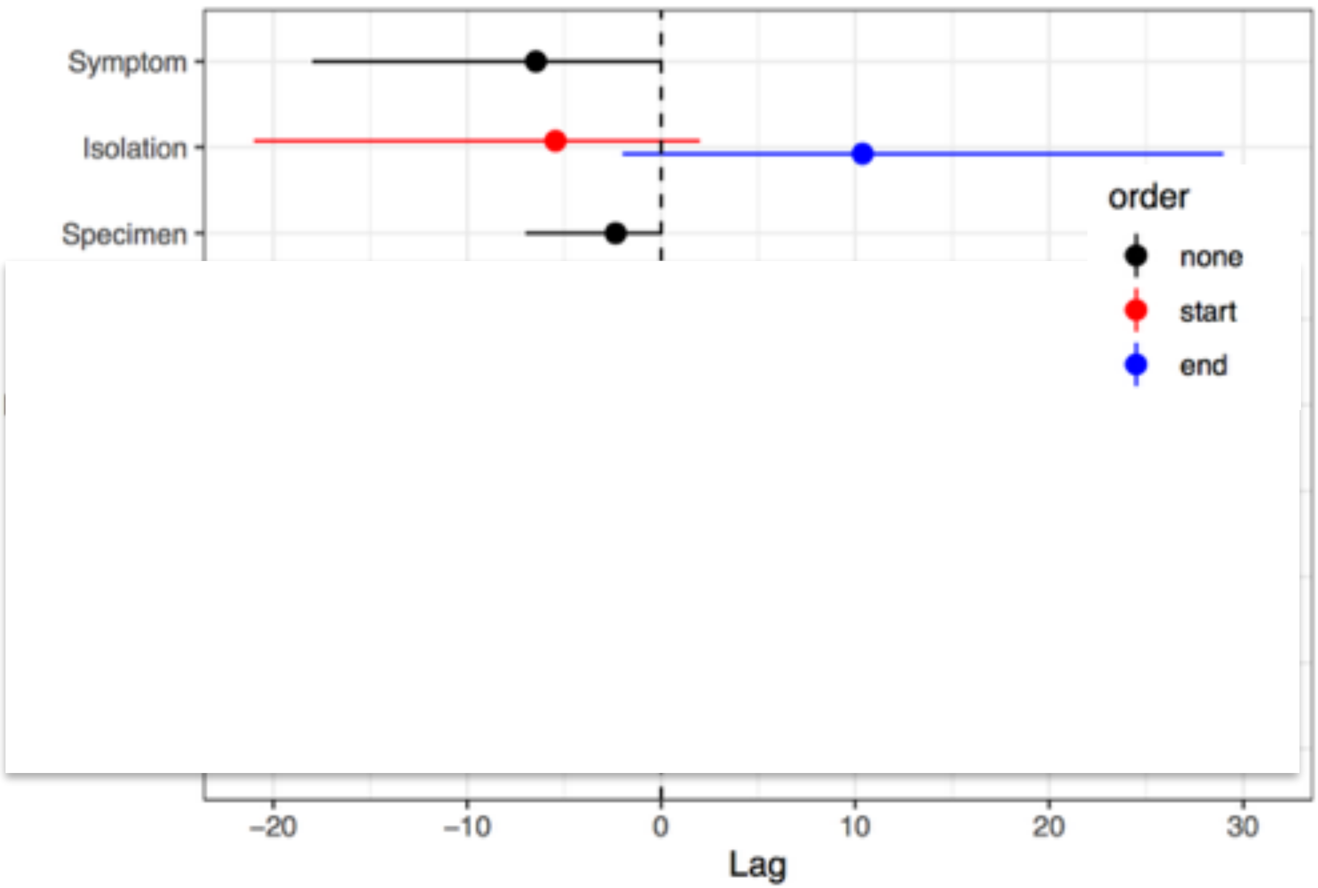
Chronological Episodes (Isolation)

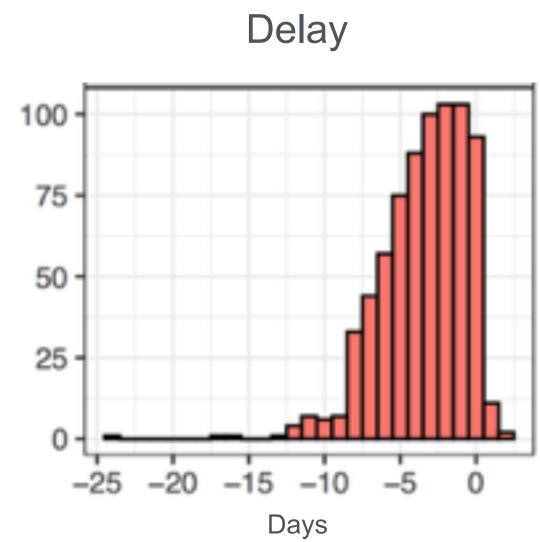




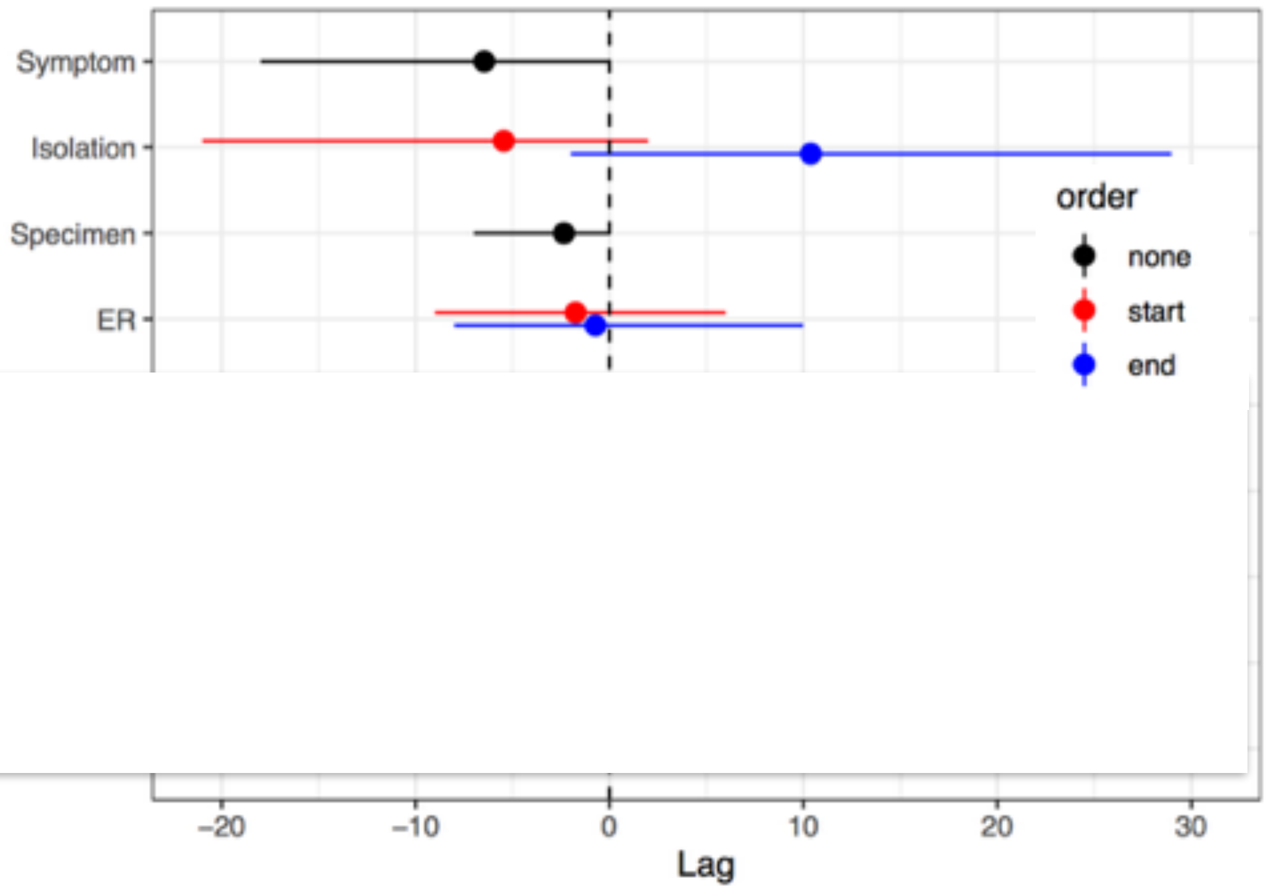


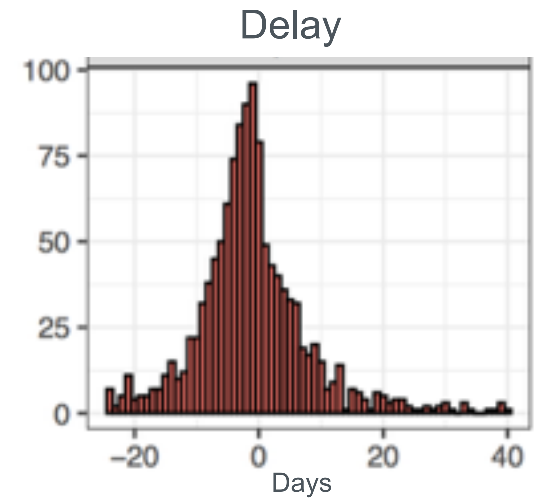
Chronological Episodes (Specimen collection)

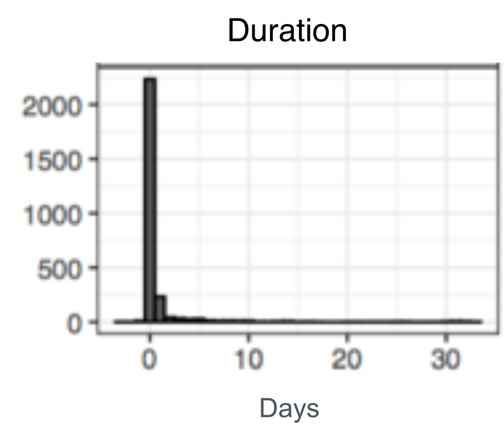




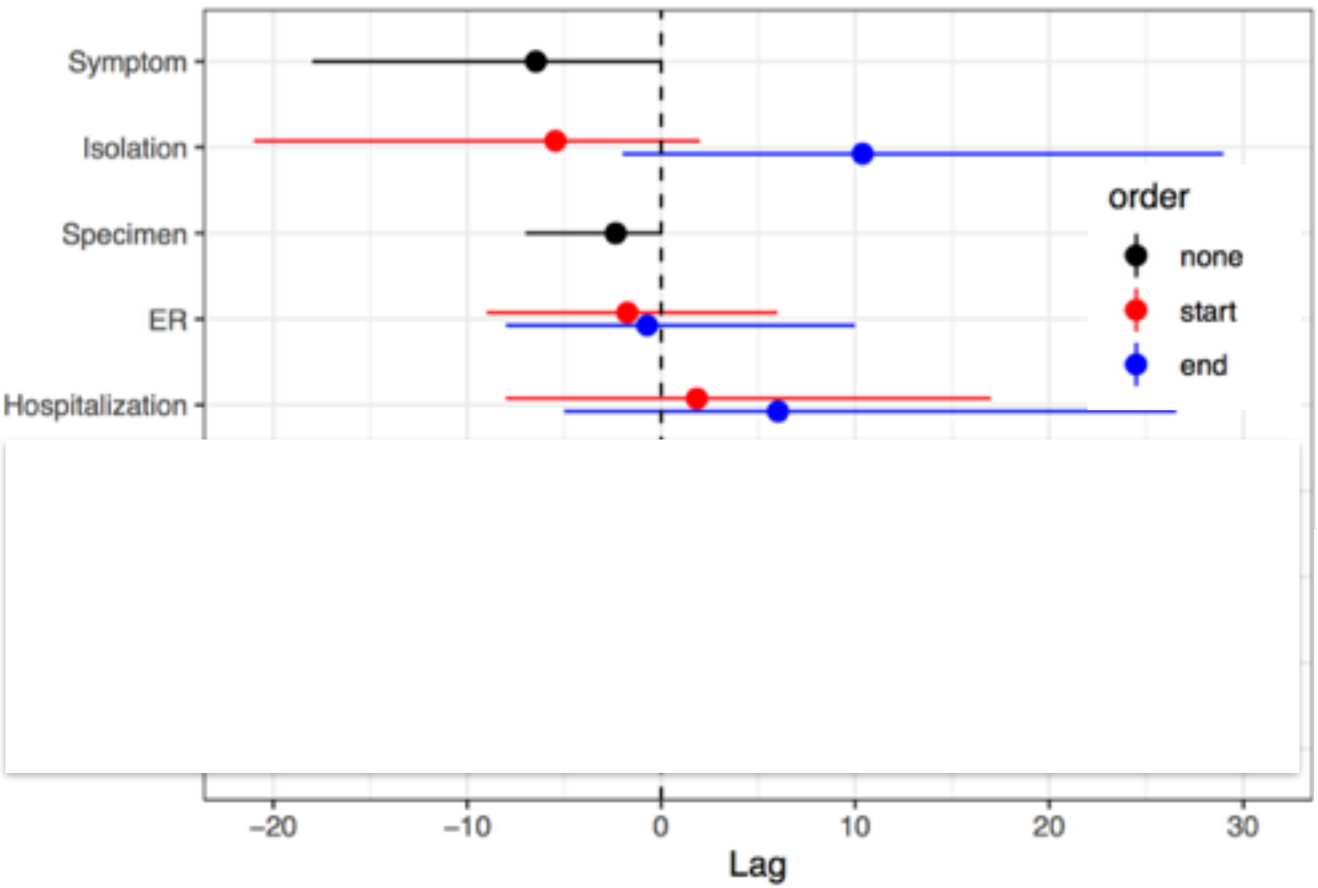
Chronological Episodes (ER)

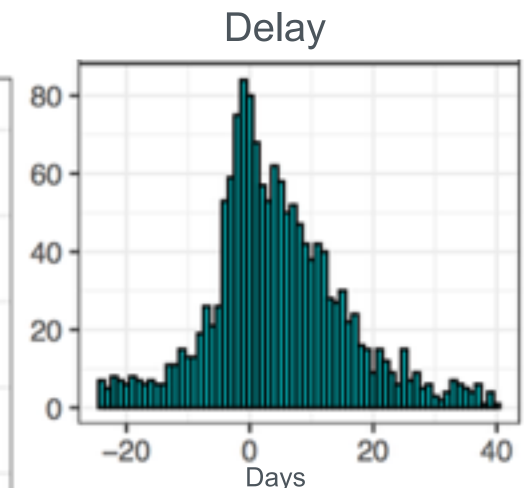


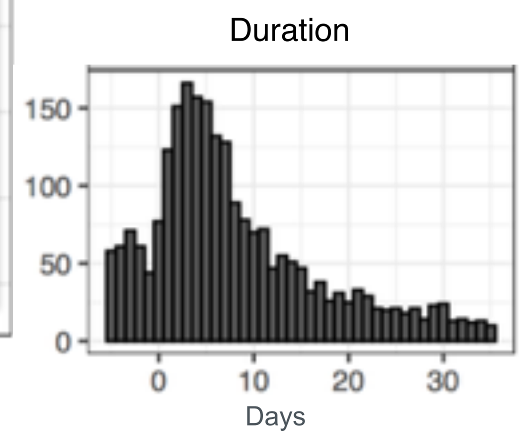




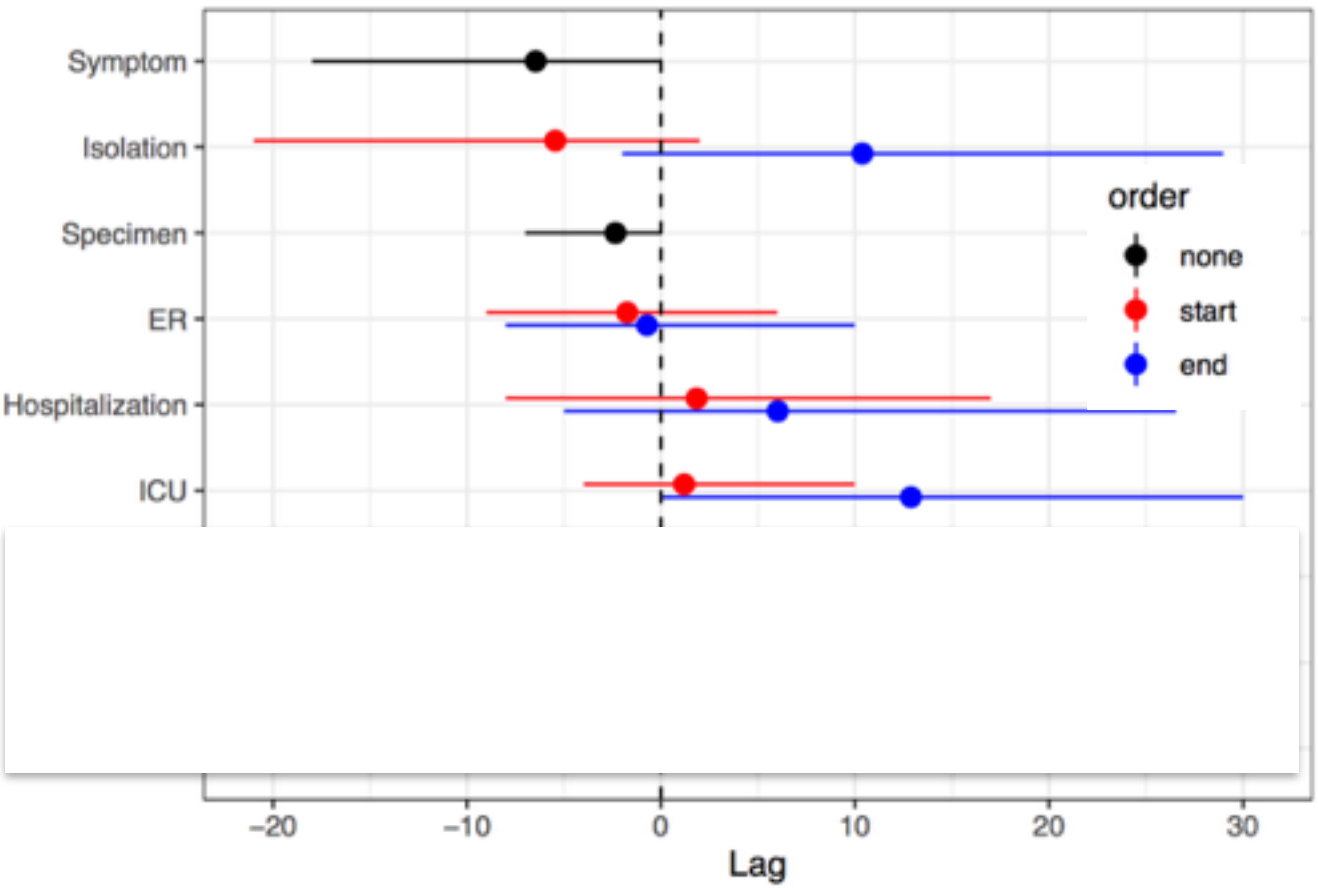
Chronological Episodes (Hospitalization)



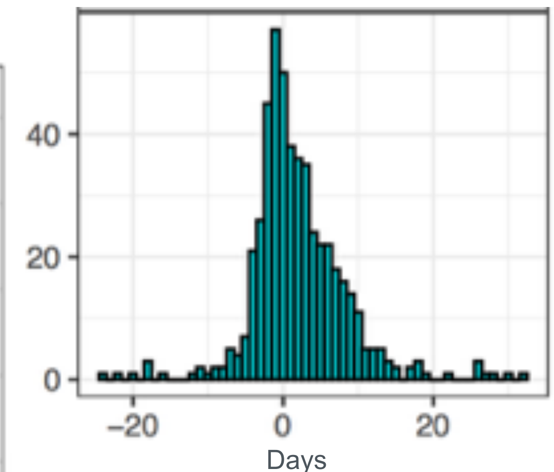




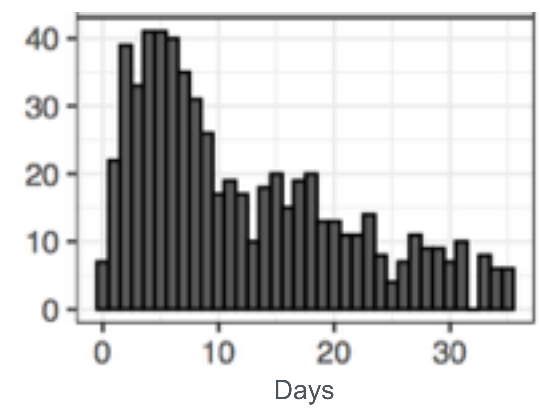
Chronological Episodes (ICU)



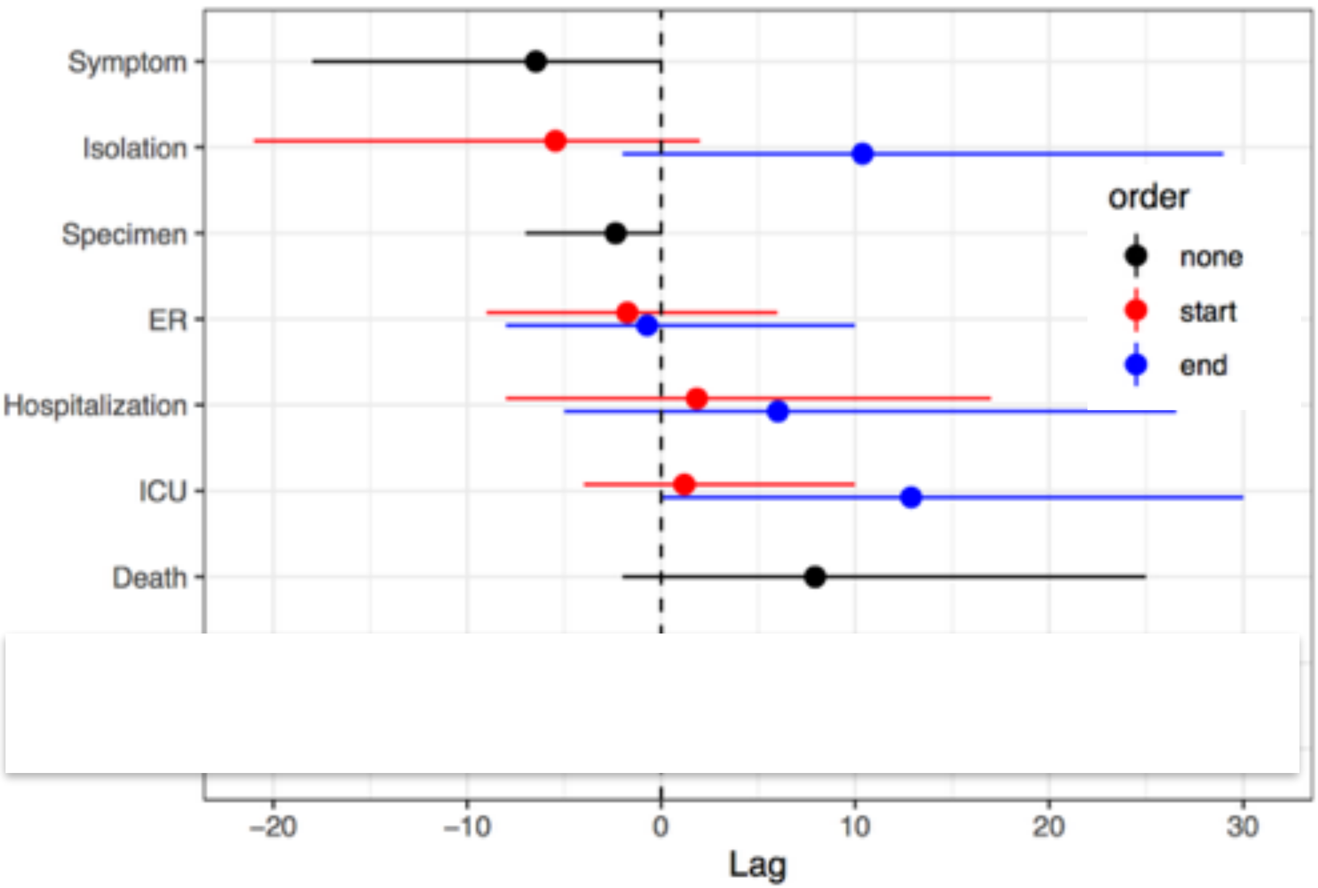
Delay

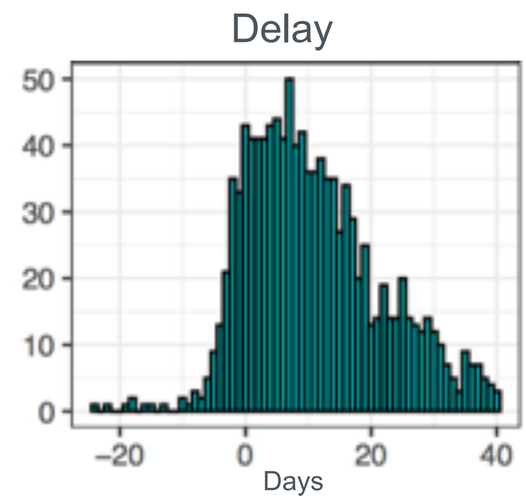


Duration

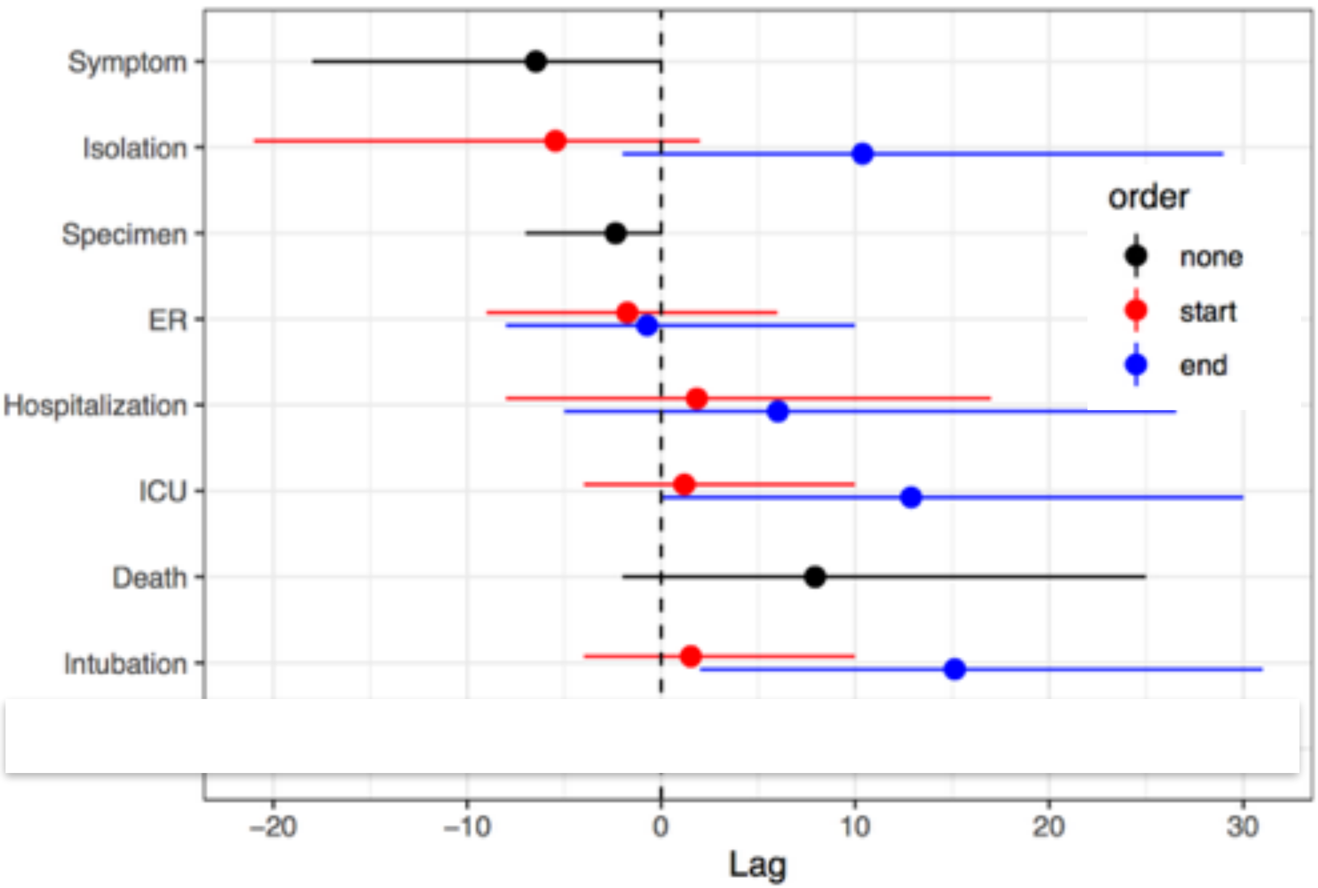


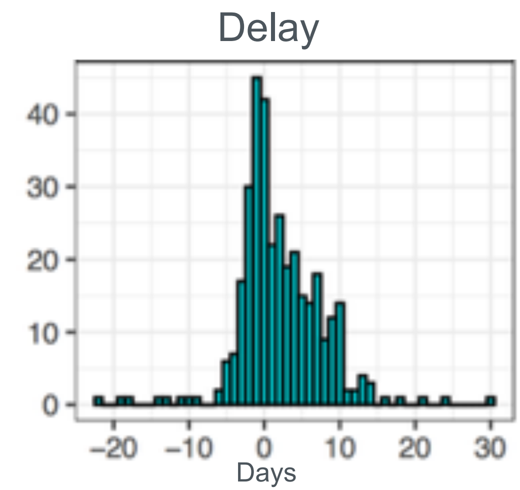
Chronological Episodes (Death)

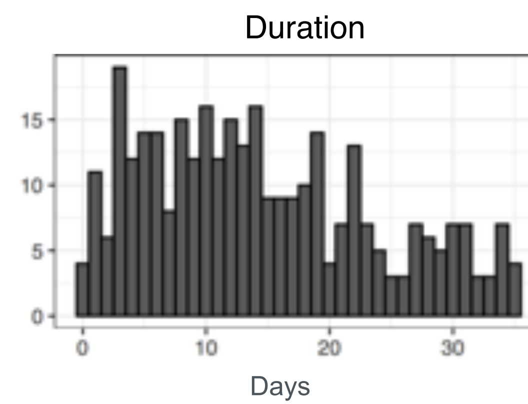




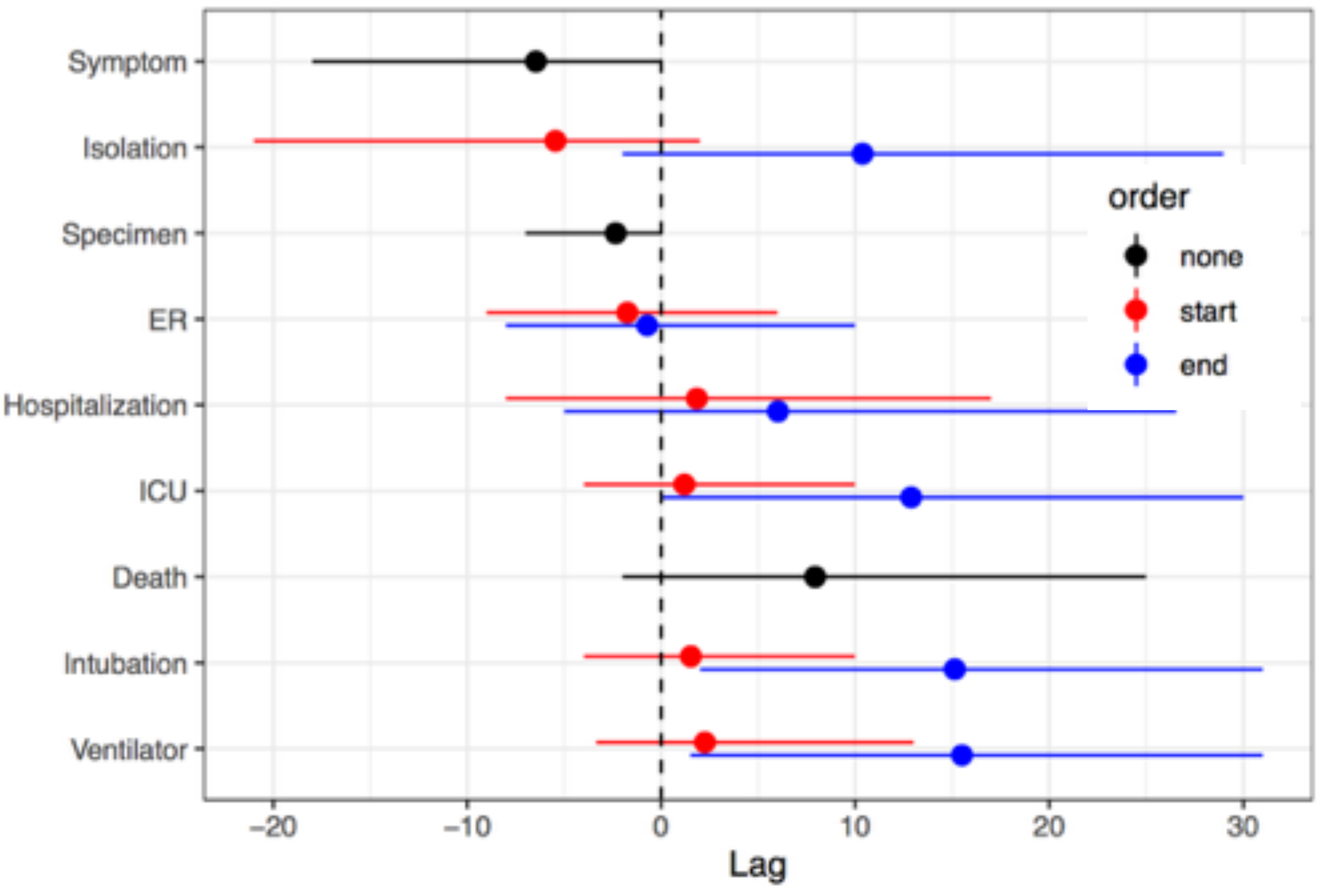
Chronological Episodes (Intubation)

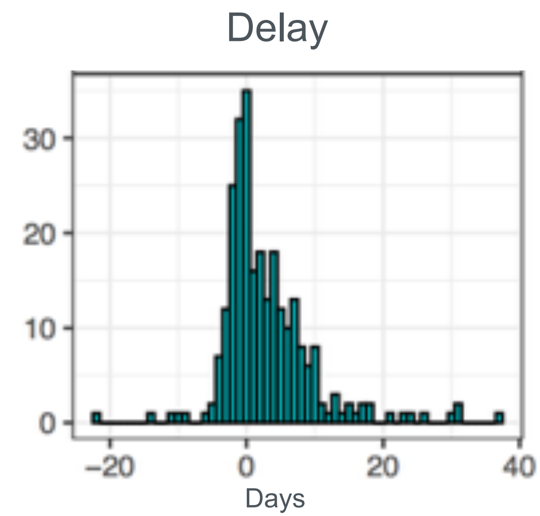


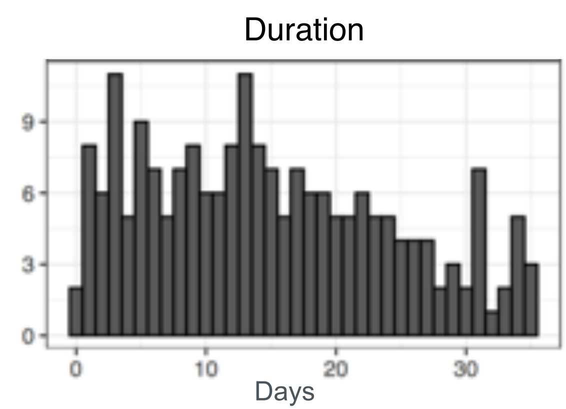




Chronological Episodes (Ventilator)

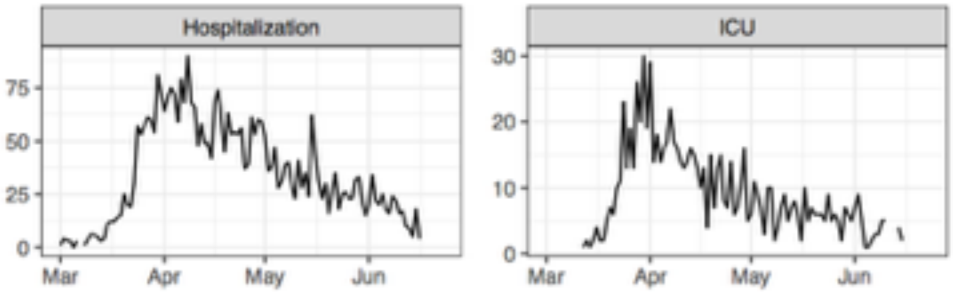






Admissions, Durations and Occupancies

Daily Admissions



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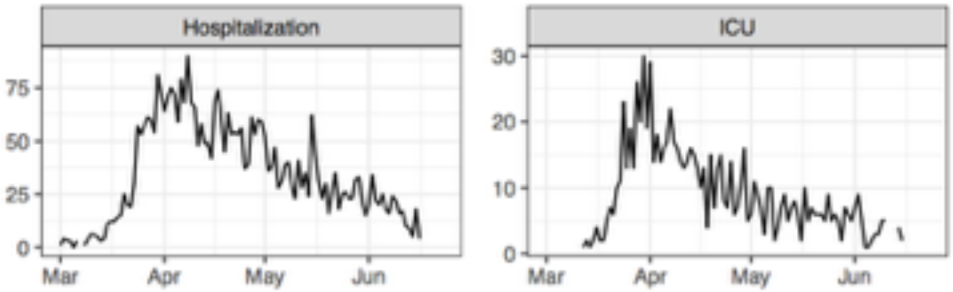
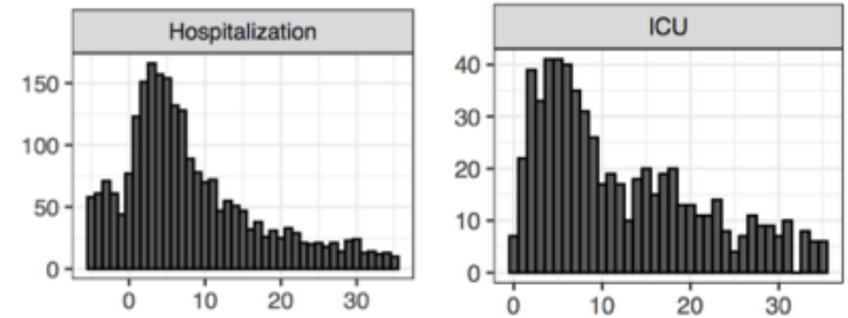


Durations



Admissions, Durations and Occupancies

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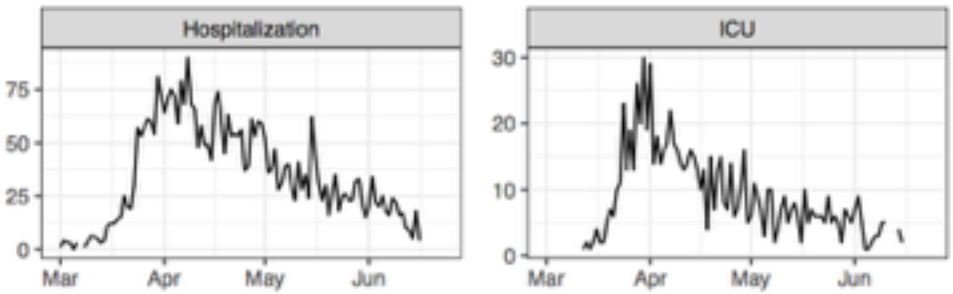
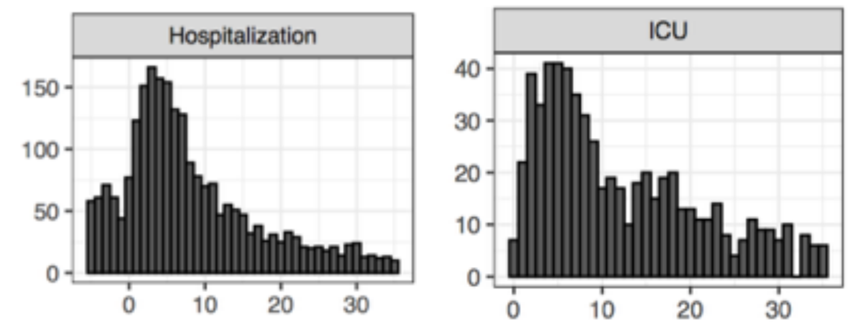
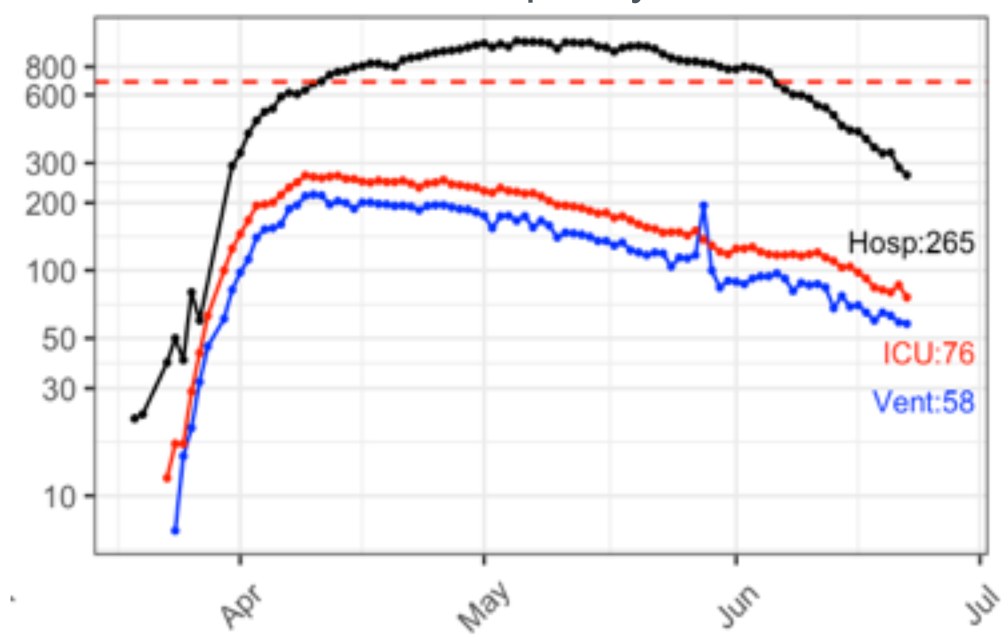


Durations



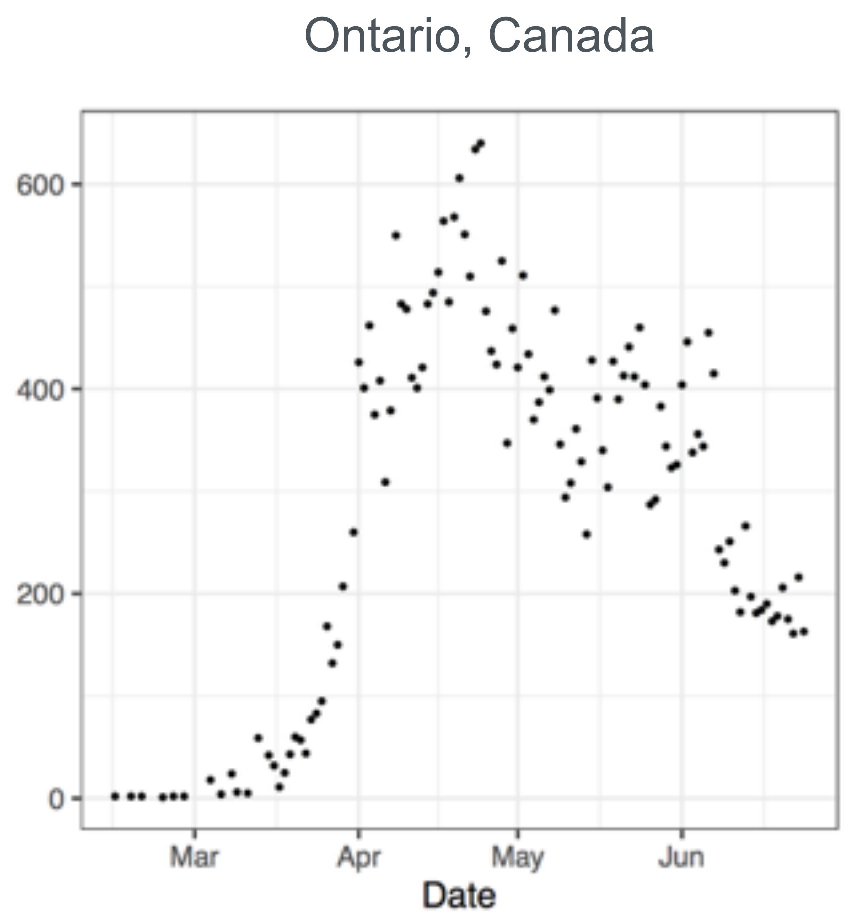
Occupancy



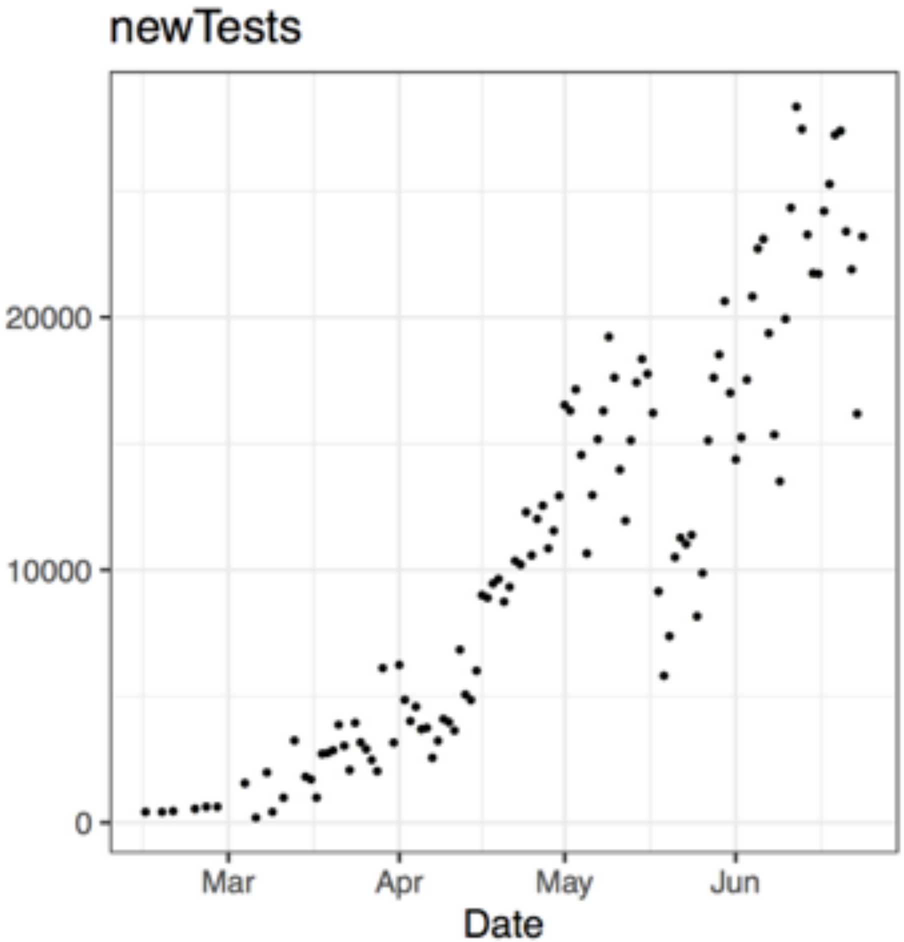
Distributions of delays associated with COVID-19 healthcare in Ontario, Canada

Changes over time

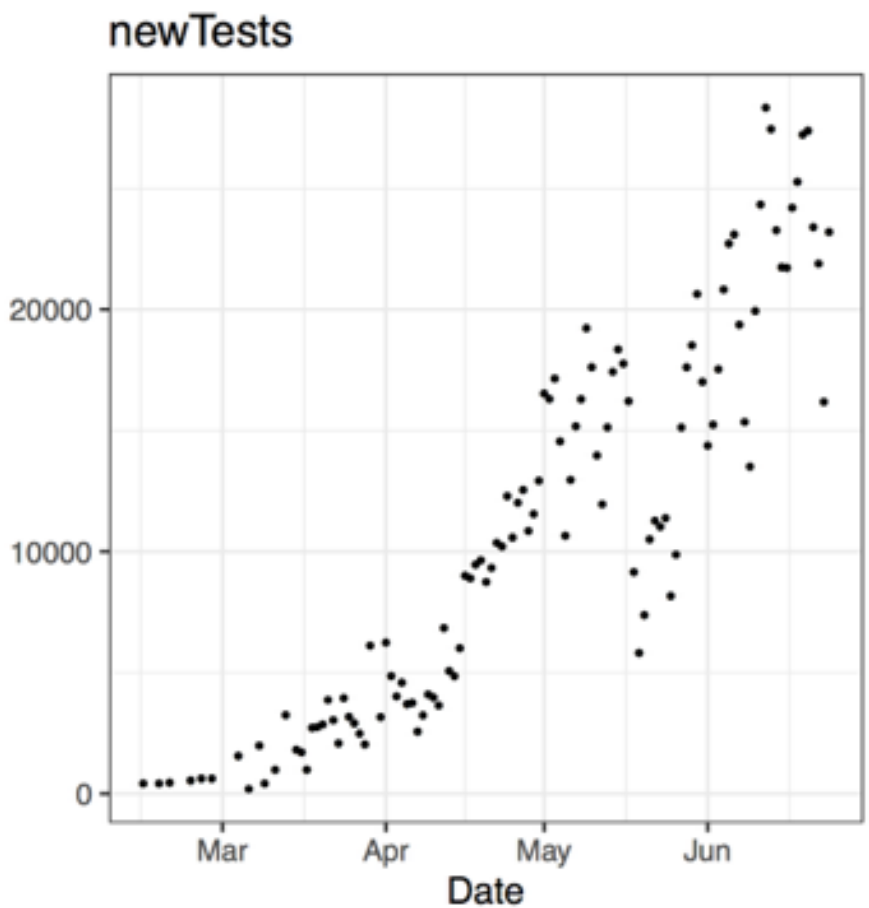
New Confirmations

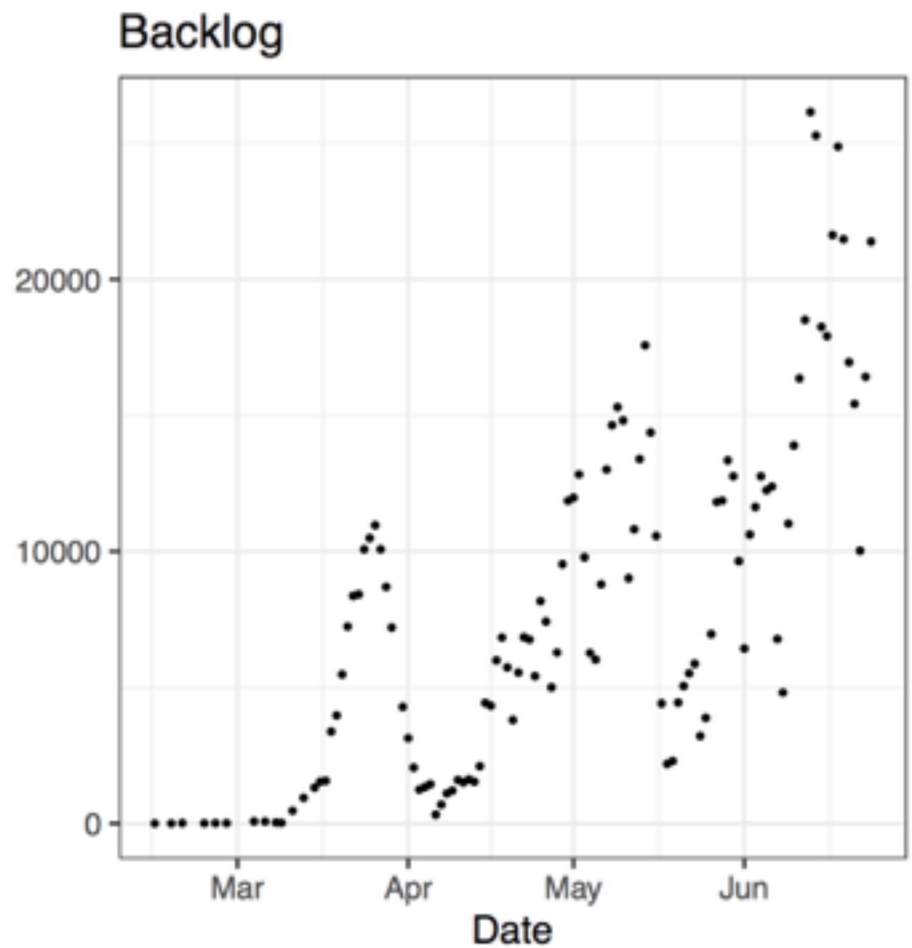


Testing capacity



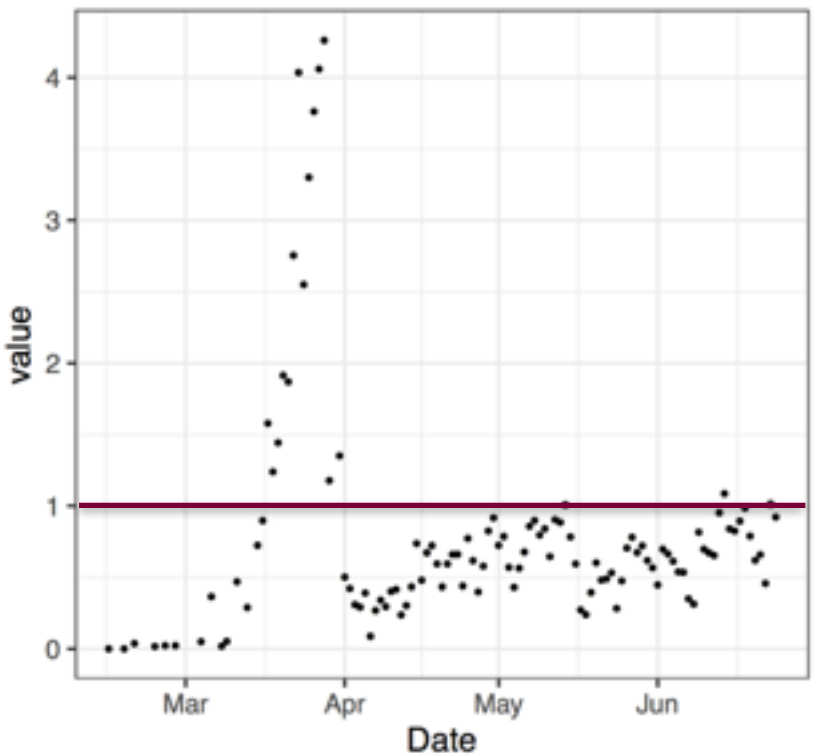
Testing capacity





Backlog ratio

Backlog ratio

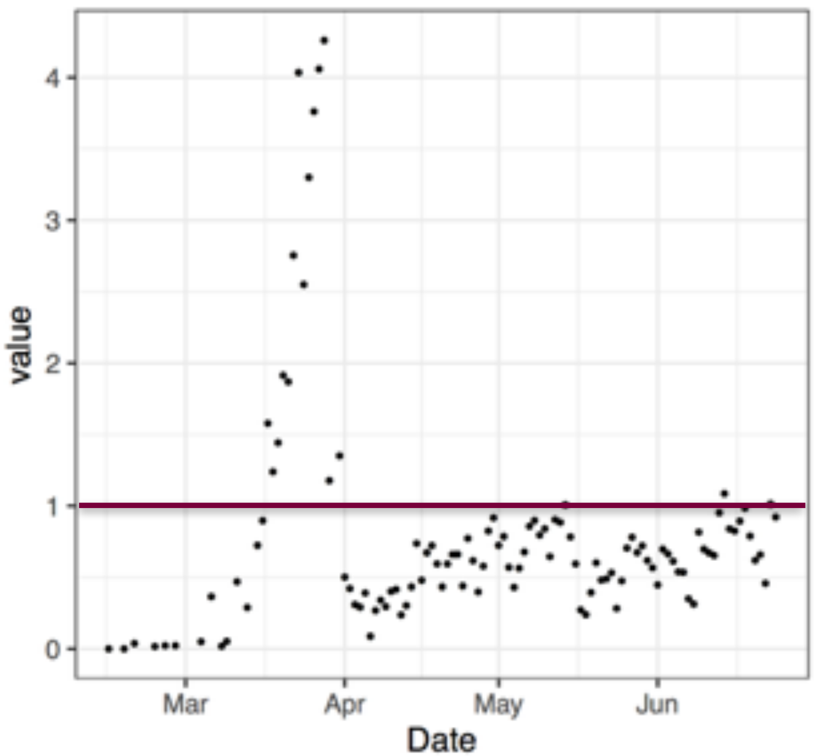


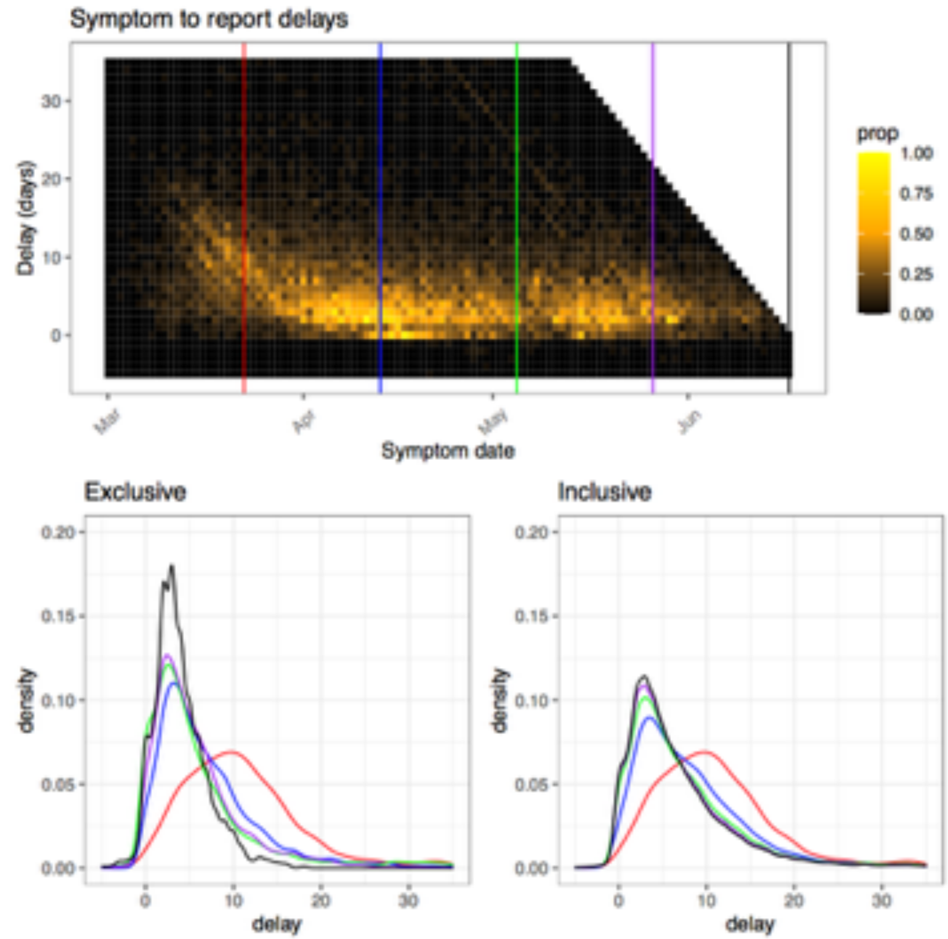
$$\frac{\text{Backlog} \quad (\text{test})}{\text{newTests} \quad (\text{test/day})}$$

~ X days to clear the backlogs

Changes in Delays over time

Backlog ratio






```
#> [1] "2020-03-01" "2020-03-22" "2020-04-13" "2020-05-04" "2020-05-26"
#> [6] "2020-06-17"
```

Summary

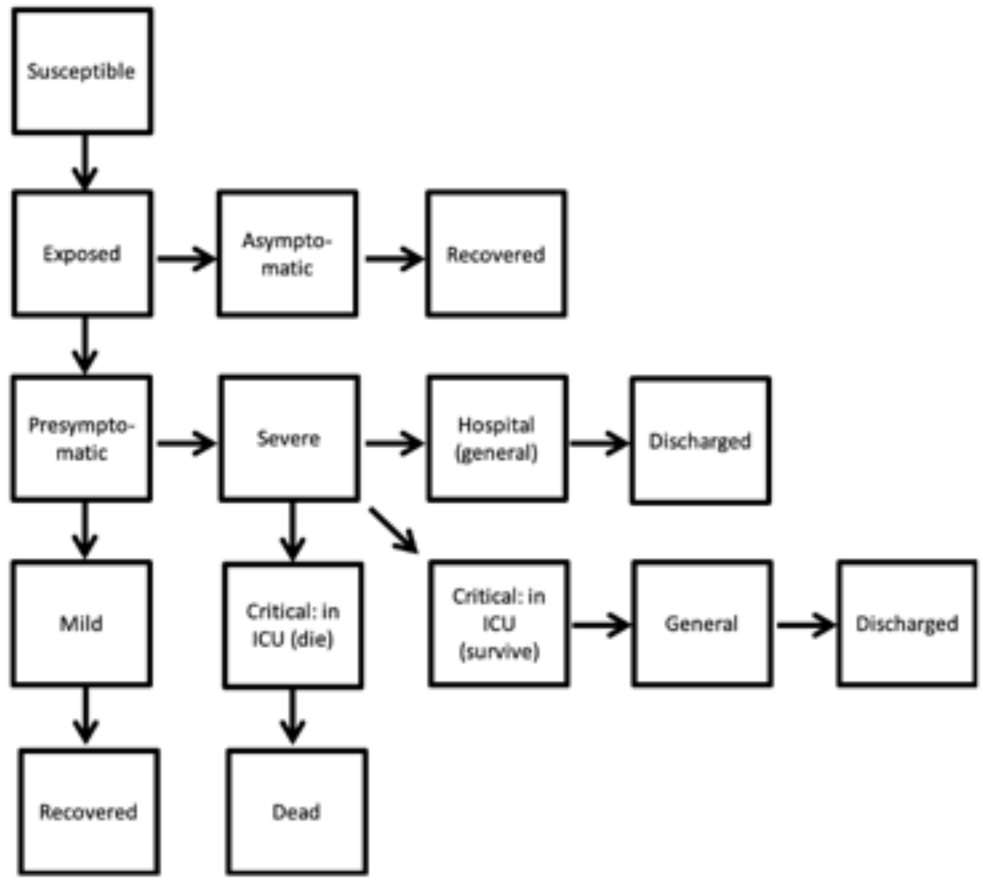
- Early detection is key in controlling the spread of covid
  - Reduce delay -> earlier isolation/treatment
- What components we can take back to the modelling world to improve models
  - e.g. Hospitalization data
  - Duration spent in treatment
- Combining different data streams to model

McMaster Pandemic

- SEIR model
  - Including Hospitalization time series
  - Using empirical delay/ duration distributions to parameterize the flow of the compartments

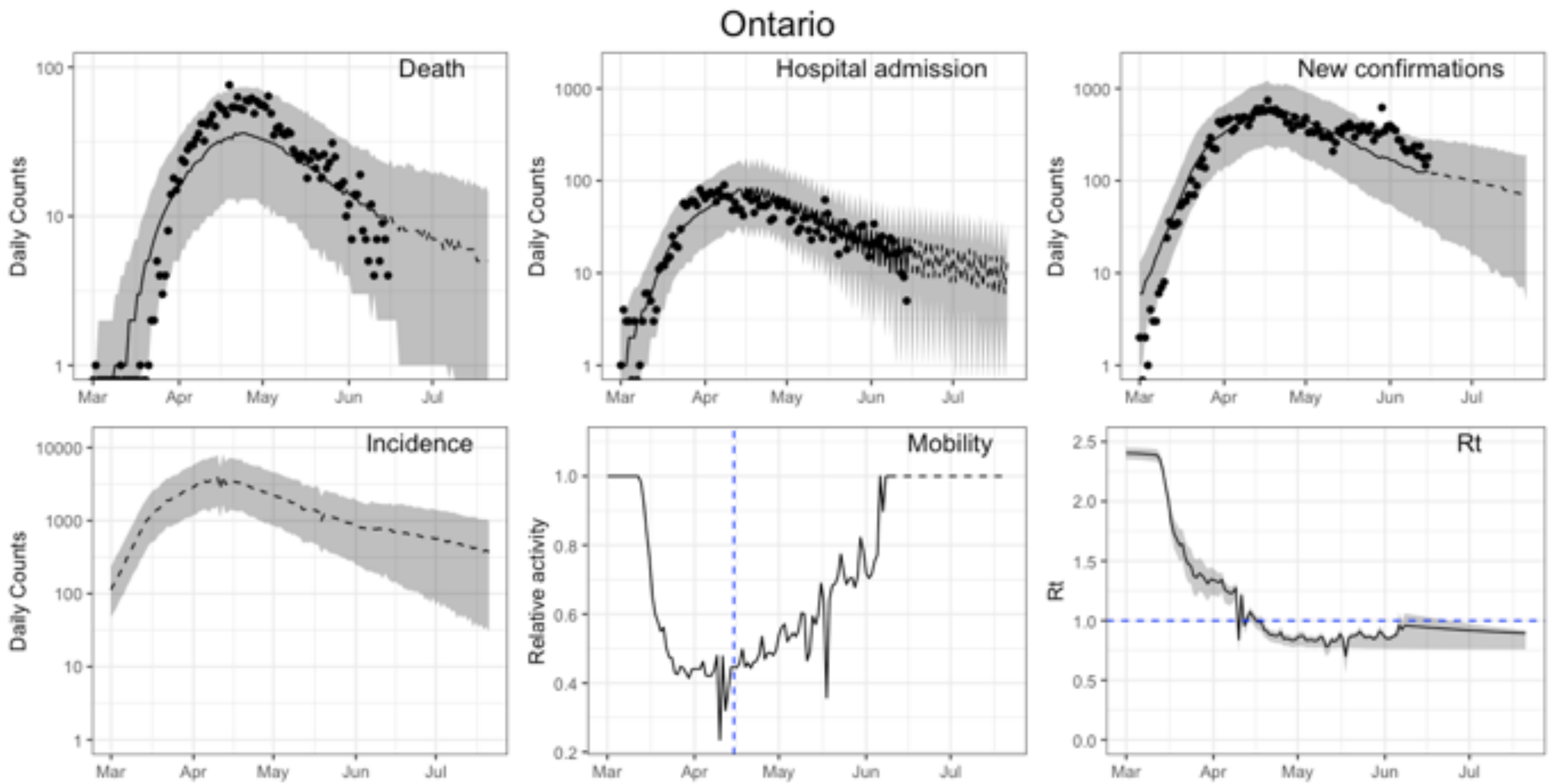
Additional features

- mobility from google and apple



https://github.com/bbolker/McMasterPandemic

Distributions of delays associated with COVID-19 healthcare in Ontario, Canada



Final remarks

- Easy to be tunnel visioned in the model world
- Important to get a sense what is happening in reality
- Bridging the knowledge gap in both directions (Public Health and Modelling)

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- Important to get a sense what is happening in reality
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- Small piece of the pie

Acknowledgments

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