Public Health Agency of Canada
Agence de la santé publique du Canada

Canada

The Past, Present and the Future of Mathematical Modeling Supporting Public Health

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What is a model?

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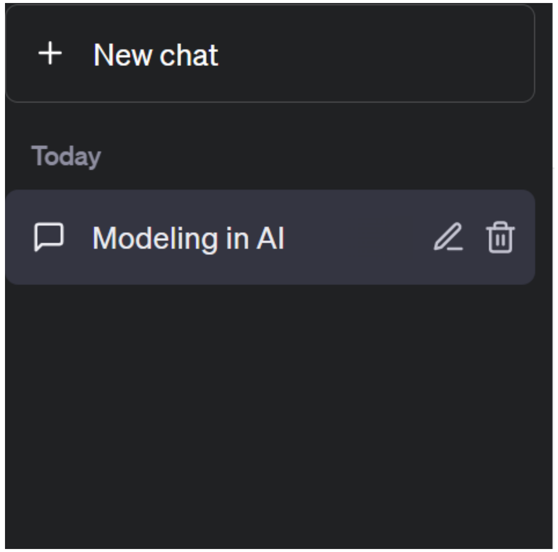

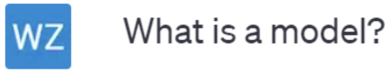

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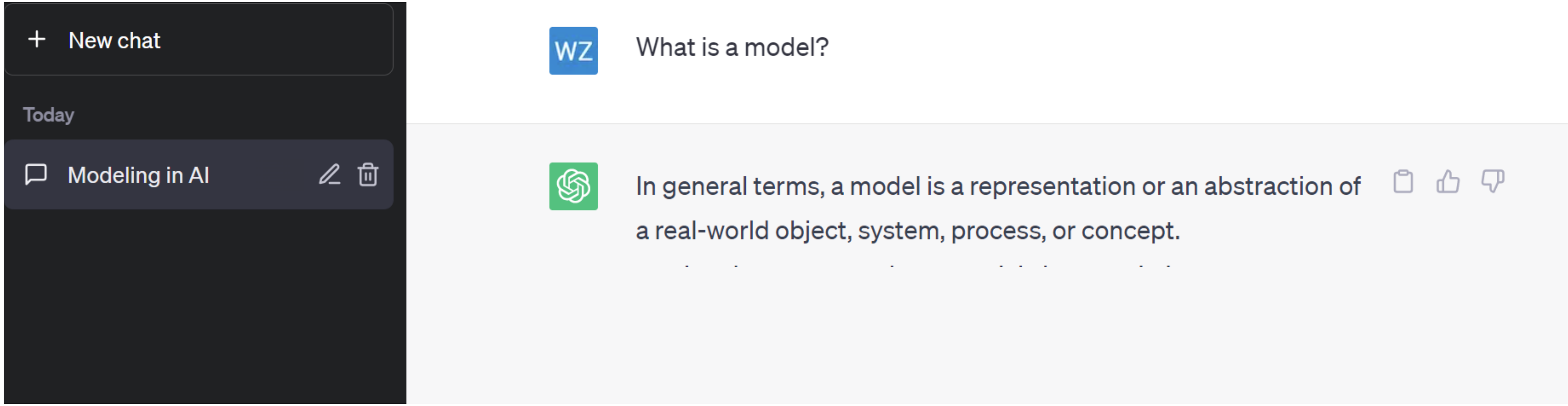

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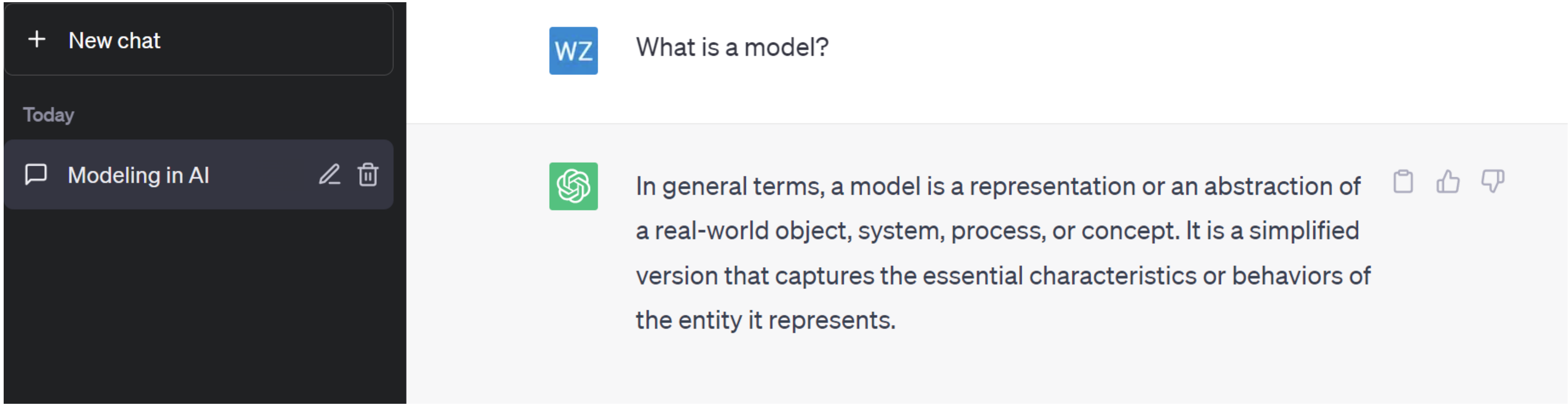

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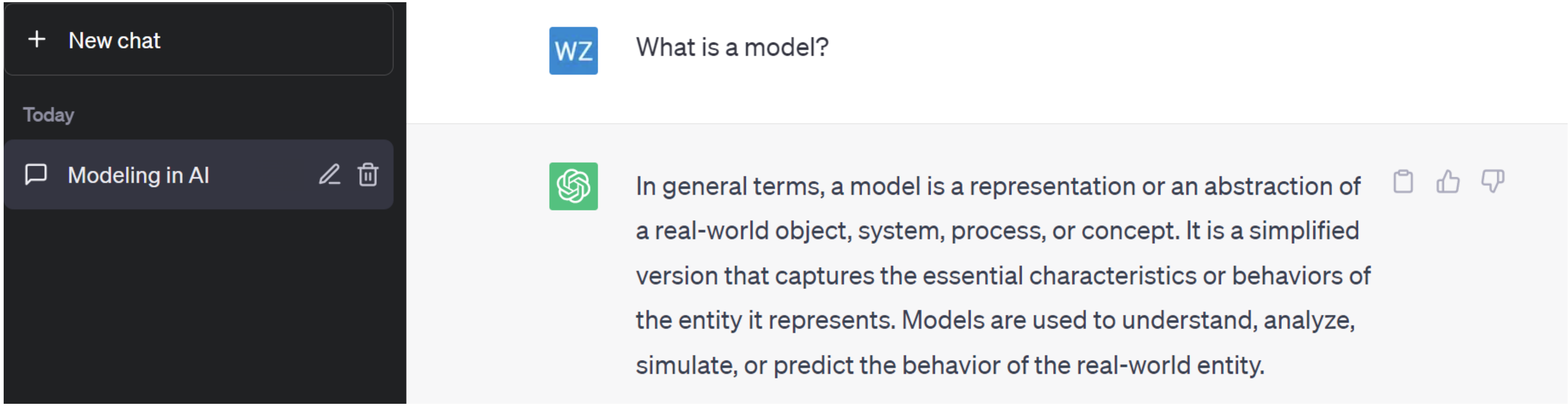


What is a model?

New chat

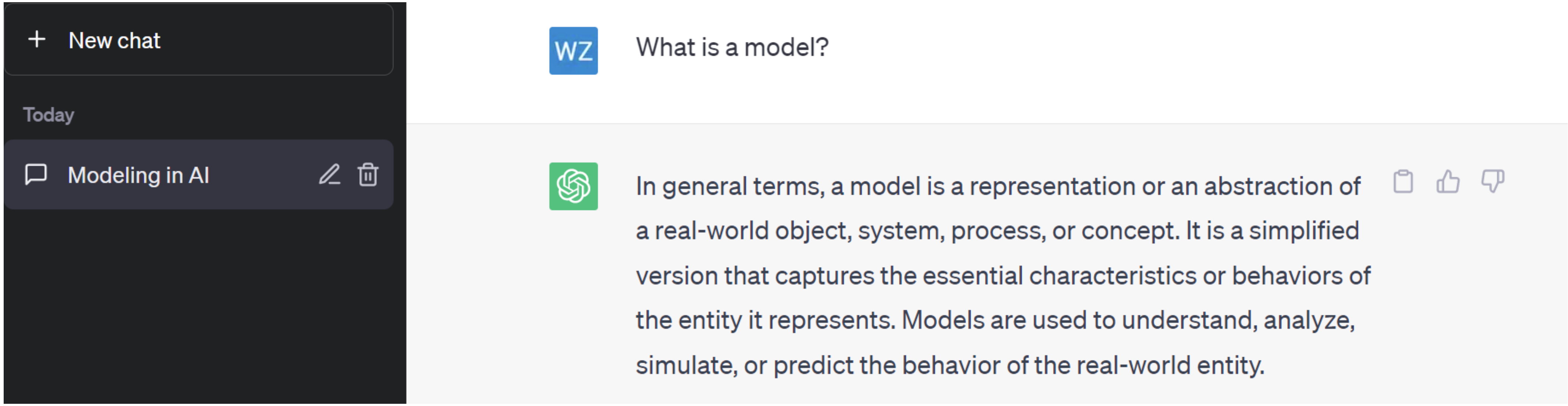
Today

Modeling in AI

WZ What is a model?

In general terms, a model is a representation or an abstraction of a real-world object, system, process, or concept. It is a simplified version that captures the essential characteristics or behaviors of the entity it represents. Models are used to understand, analyze, simulate, or predict the behavior of the real-world entity.

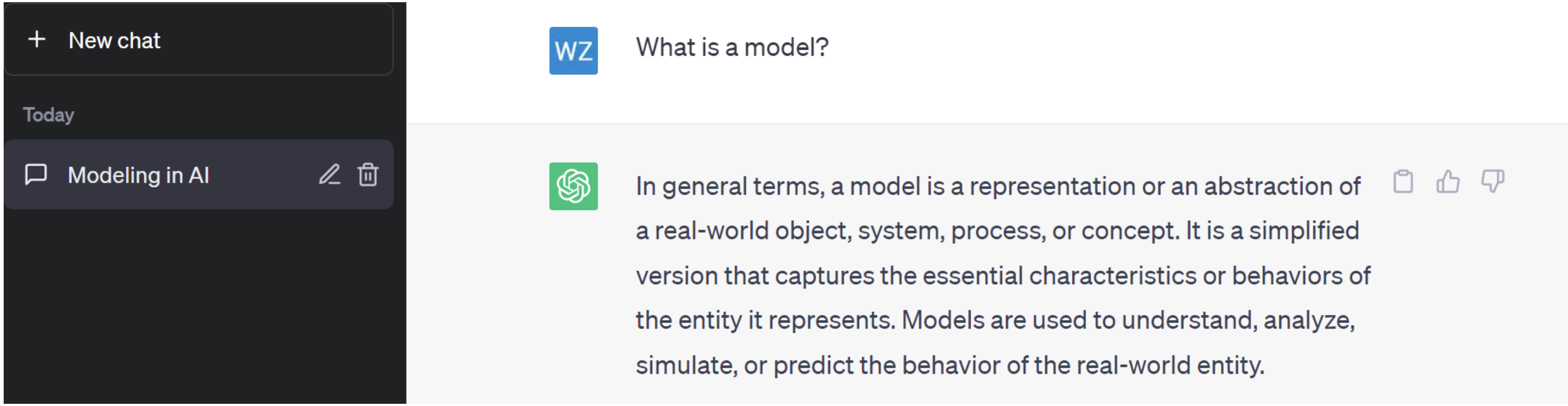
What is a model?



Knowledge
Experience
Lesson

Past

What is a model?



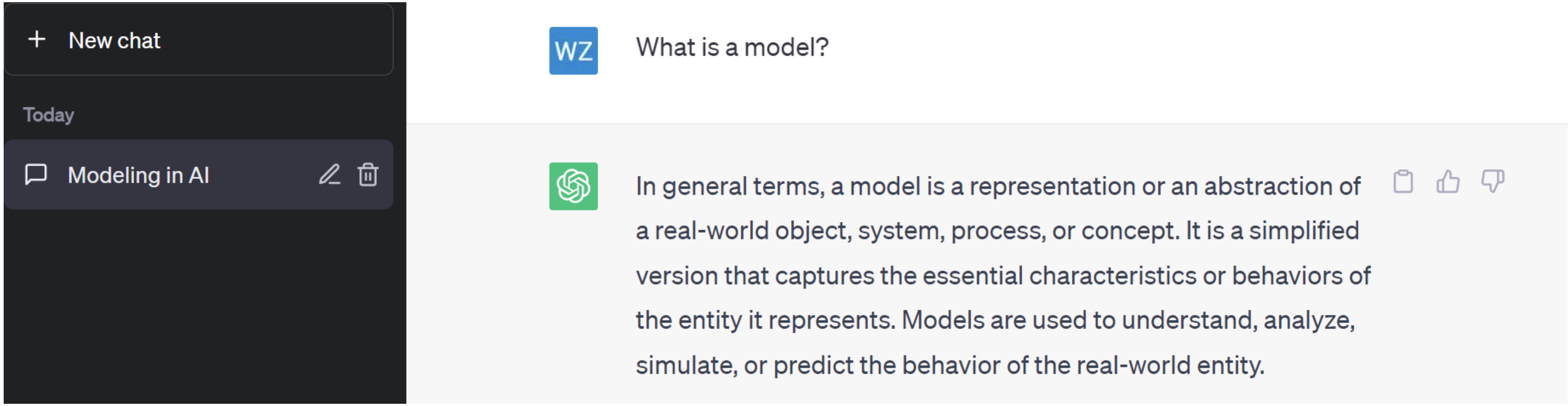
Present

To face the challenges we encounter

Knowledge
Experience
Lesson

Past

What is a model?



Present

To face the challenges we encounter

Knowledge
Experience
Lesson

Past

Future

Improve
Support

What is Public Health?

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The focus of the talk will be modelling for infectious disease and public health, but there are also important aspects (E.g. climate change, chronic diseases etc.)

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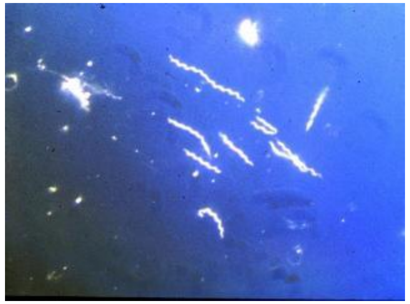
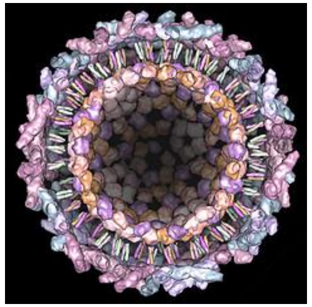
Old Chinese quote: “To defeat your enemy, you must know your enemy.”

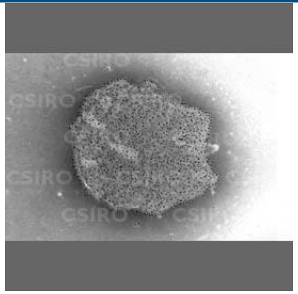
The history of our invisible enemy



Lyme

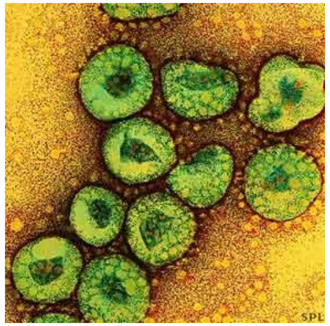


Chikungunya



Hendra

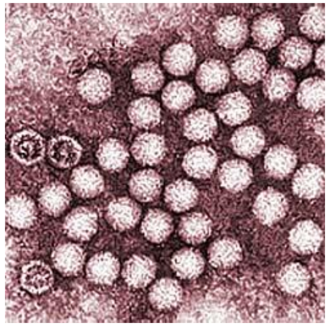
HIV



SARS

Using modern day techniques in the field of molecular and evolutionary biology, many pathogens exist on this planet millions of years ago.

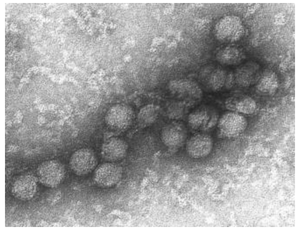
They have been persisting and evolving in harsh environments and times throughout history, infecting different host species.



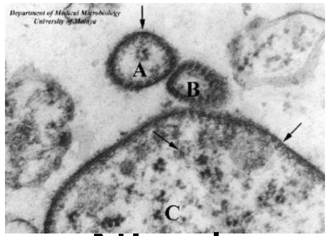
RVF

Chikungunya vector

Lyme vector

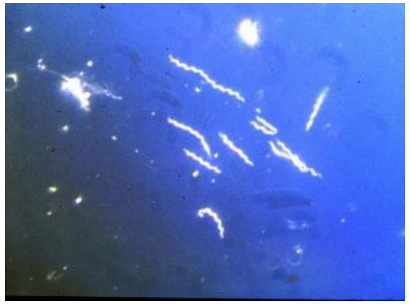


WNV

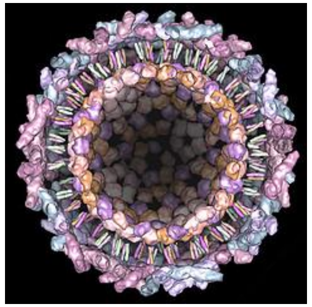


Nipah

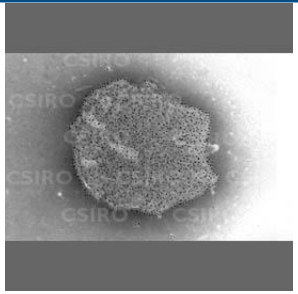
The history of our invisible enemy



Lyme

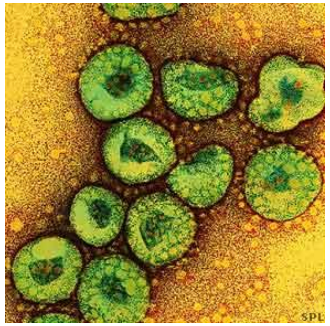


Chikungunya



Hendra

HIV

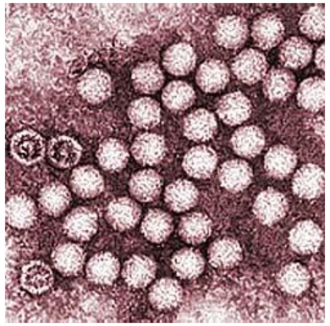


SARS

Most (73%) emerging infectious diseases are zoonoses

Woolhouse ME, Gowtage-Sequeria S. 2005 EID

Most affecting Canada have been zoonoses that emerged elsewhere in the world (HIV, SARS, WNv, pH1N1, Lyme)



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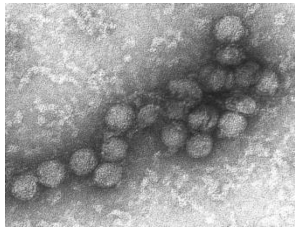
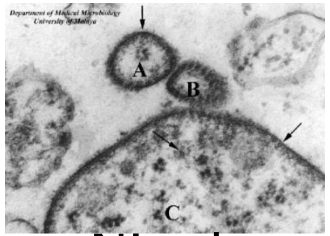


WNV



Nipah

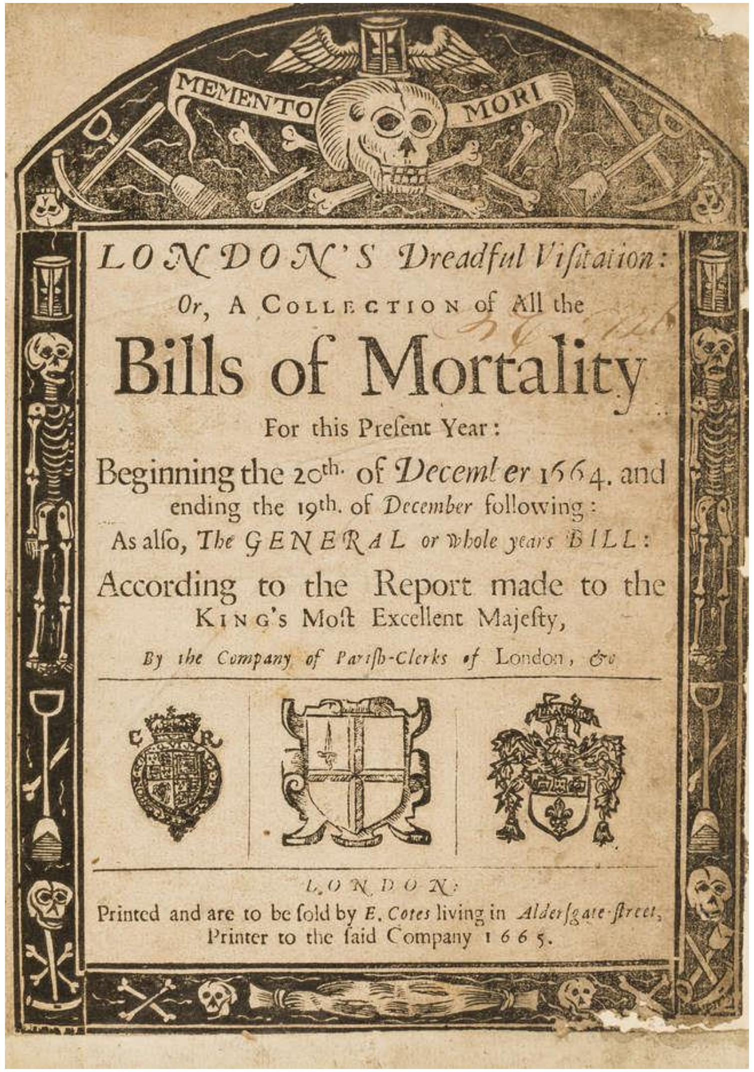
Historical records of infectious diseases (Rabies; 2000 BC)

Laws of Eshnunna (dated back to 2000 BC)

• Owners of dogs showing symptoms should take preventive measures

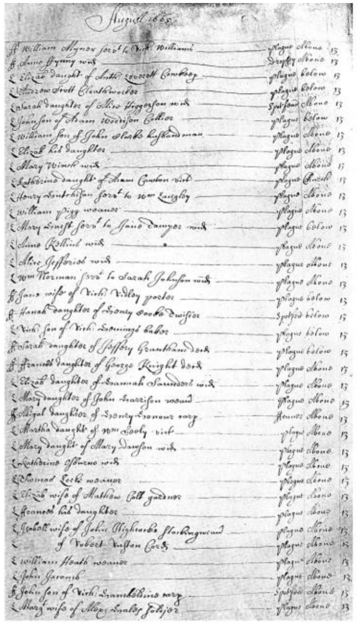
• Responsible for rabid dog attacks

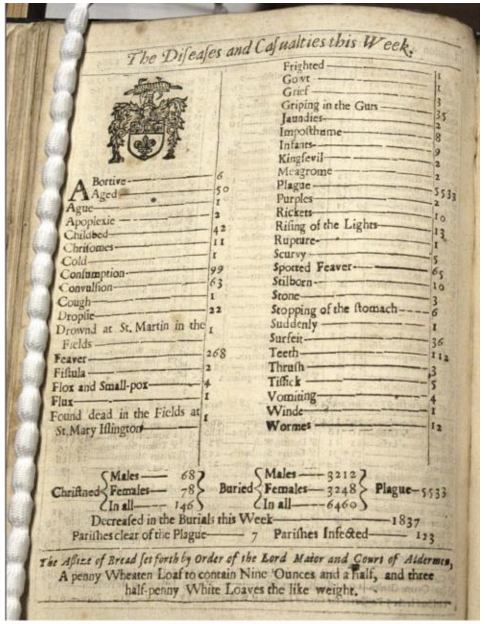
Historical records of infectious diseases (Plague; 16-17th c.)

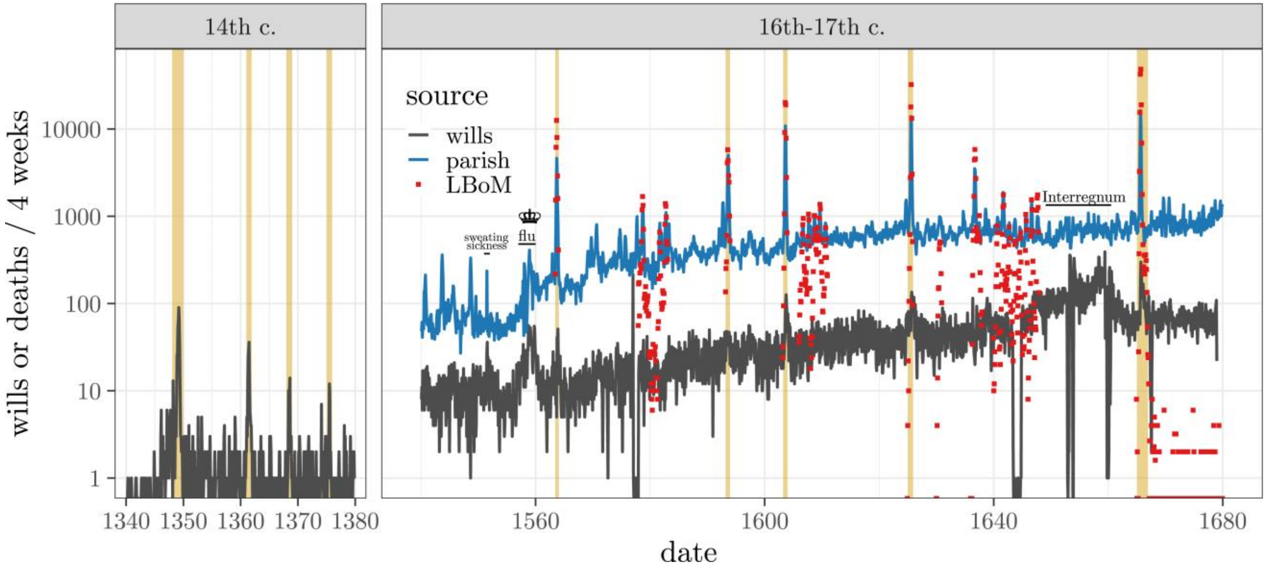

MEMENTO MORI

LONDON'S Dreadful Visitation:
Or, A COLLECTION of All the
Bills of Mortality
For this Present Year:
Beginning the 20th. of December 1664. and
ending the 19th. of December following:
As also, The GENERAL or whole years BILL:
According to the Report made to the
KING's Most Excellent Majesty,
By the Company of Parish-Clerks of London, &c.

LONDON:
Printed and are to be sold by E. Cotes living in Aldersgate-street,
Printer to the said Company 1665.

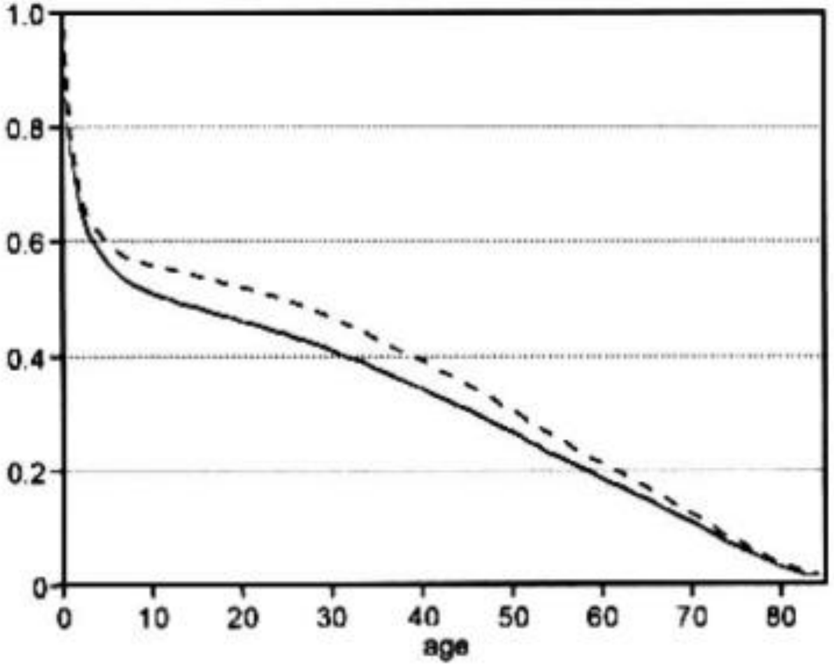






Earn et al. 2020, PNAS

Disease patterns and questions (Smallpox, 1766)



Ages by years	Natural state with smallpox	State without smallpox	Difference or gain
0	1,300	1.300	0
1	1,000	1,017.1	17.1
2	855	881.8	26.8
3	798	833.3	35.3
4	760	802.0	42.0
5	732	779.8	47.8
6	710	762.8	52.8
7	692	749.1	57.2
8	680	740.9	60.9
9	670	734.4	64.4
10	661	728.4	67.4
11	653	722.9	69.9
12	646	718.2	72.2
13	640	741.1*	74.1
14	634	709.7	75.7
15	628	705.0	77.0
16	622	700.1	78.1
17	616	695.0	79.0
18	610	689.6	79.6
19	604	684.0	80.0
20	598	678.2	80.2
21	592	672.3	80.3
22	586	666.3	80.3
23	579	659.0	80.0
24	572	651.7	79.7
25	565	644.3	79.3

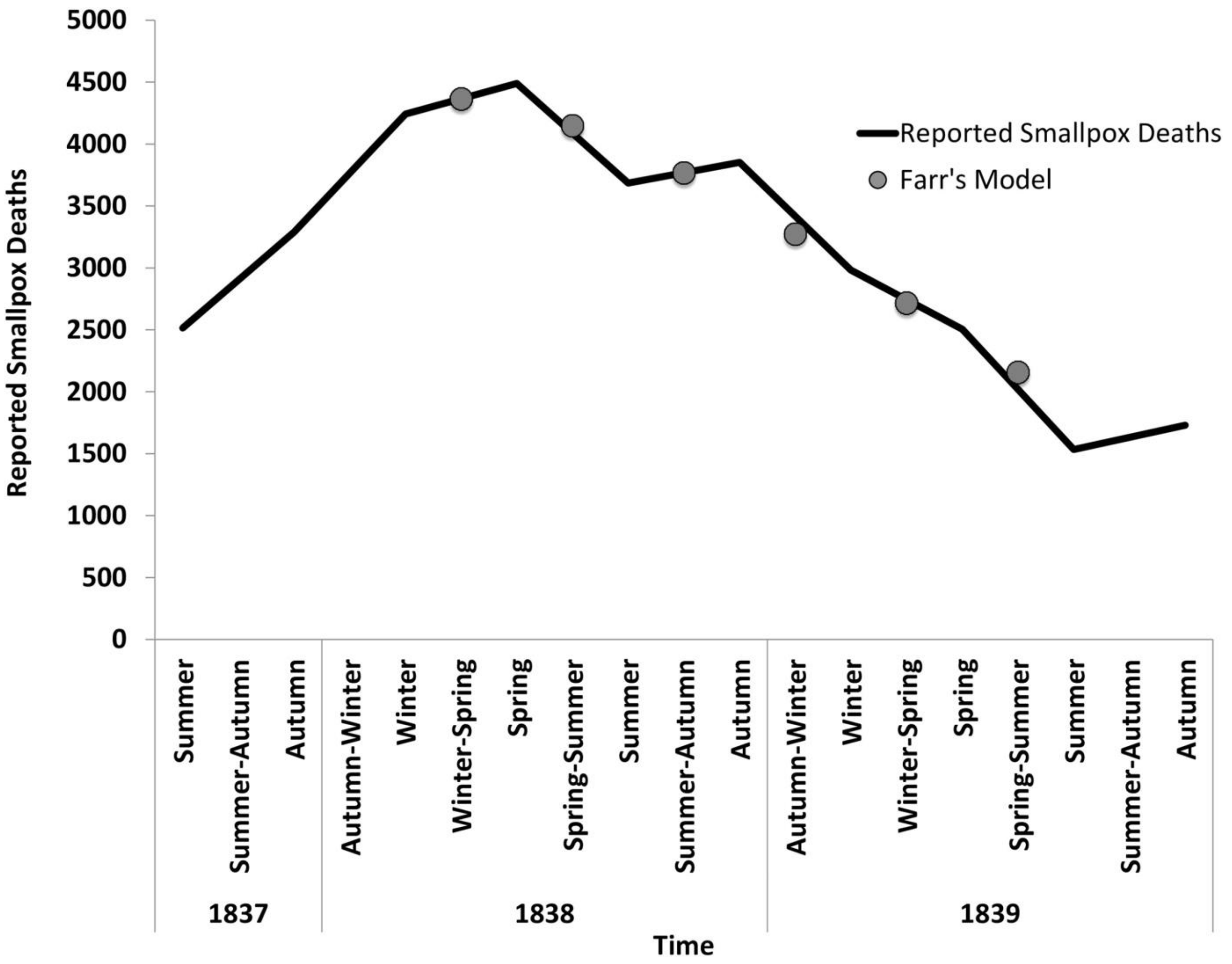
Dietz and Heesterbeek (2002)

Disease patterns and questions (Smallpox, 1800s)

- Farr's law
- Rise and fall of epidemics
- Roughly symmetric
- Bell shape
- I(t) = new cases at time t

$$\frac{\left(\frac{I(t+3)}{I(t+2)}\right)}{\left(\frac{I(t+1)}{I(t)}\right)} = K$$

(Santillana et al. 2018)

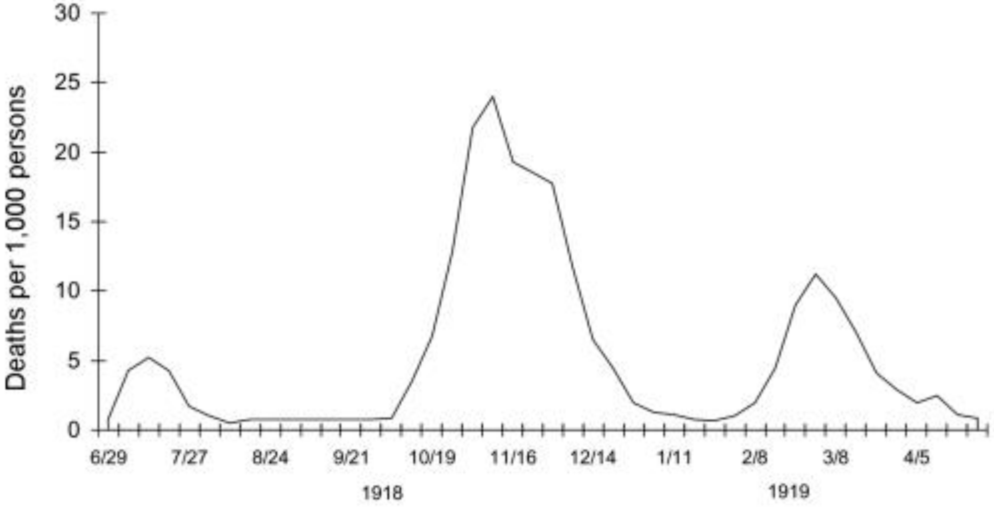


1918 Influenza: the Mother of All Pandemics


ILLUSTRATED CURRENT NEWS

To Prevent Influenza!

Do not take any person's breath.
Keep the mouth and teeth clean.
Avoid those that cough and sneeze.
Don't visit poorly ventilated places.
Keep warm, get fresh air and sunshine.
Don't use common drinking cups, towels, etc.
Cover your mouth when you cough and sneeze.
Avoid Worry, Fear and Fatigue.
Stay at home if you have a cold.
Walk to your work or office.
In sick rooms wear a gauze mask like in illustration.



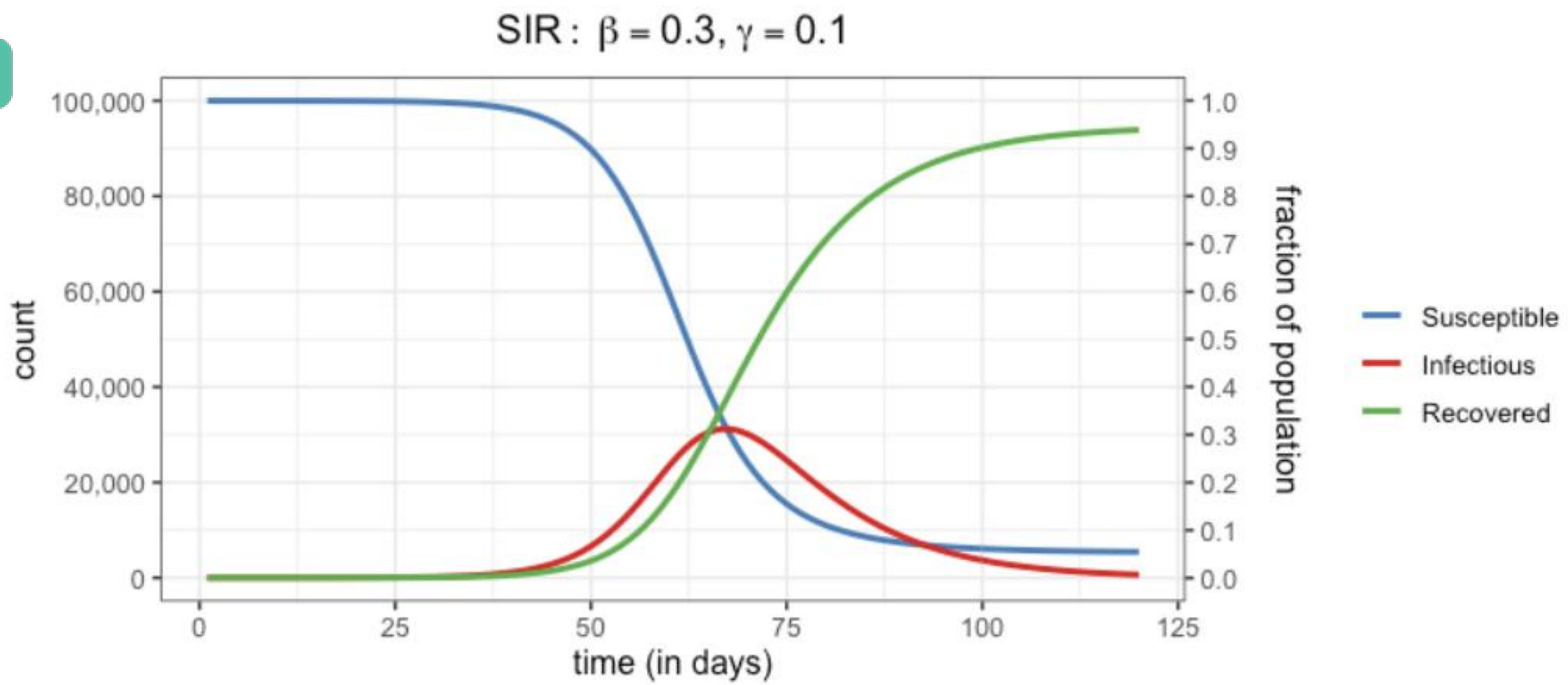
- Bell shape (Farr's Law)
- Public health measures:
- Don't visit poorly ventilated places
- Stay at home if you have a cold
- In sick rooms wear a mask

SIR and Reed Frost model

$$\frac{dS}{dt} = -\frac{\beta IS}{N},$$

$$\frac{dI}{dt} = \frac{\beta IS}{N} - \gamma I,$$

$$\frac{dR}{dt} = \gamma I,$$



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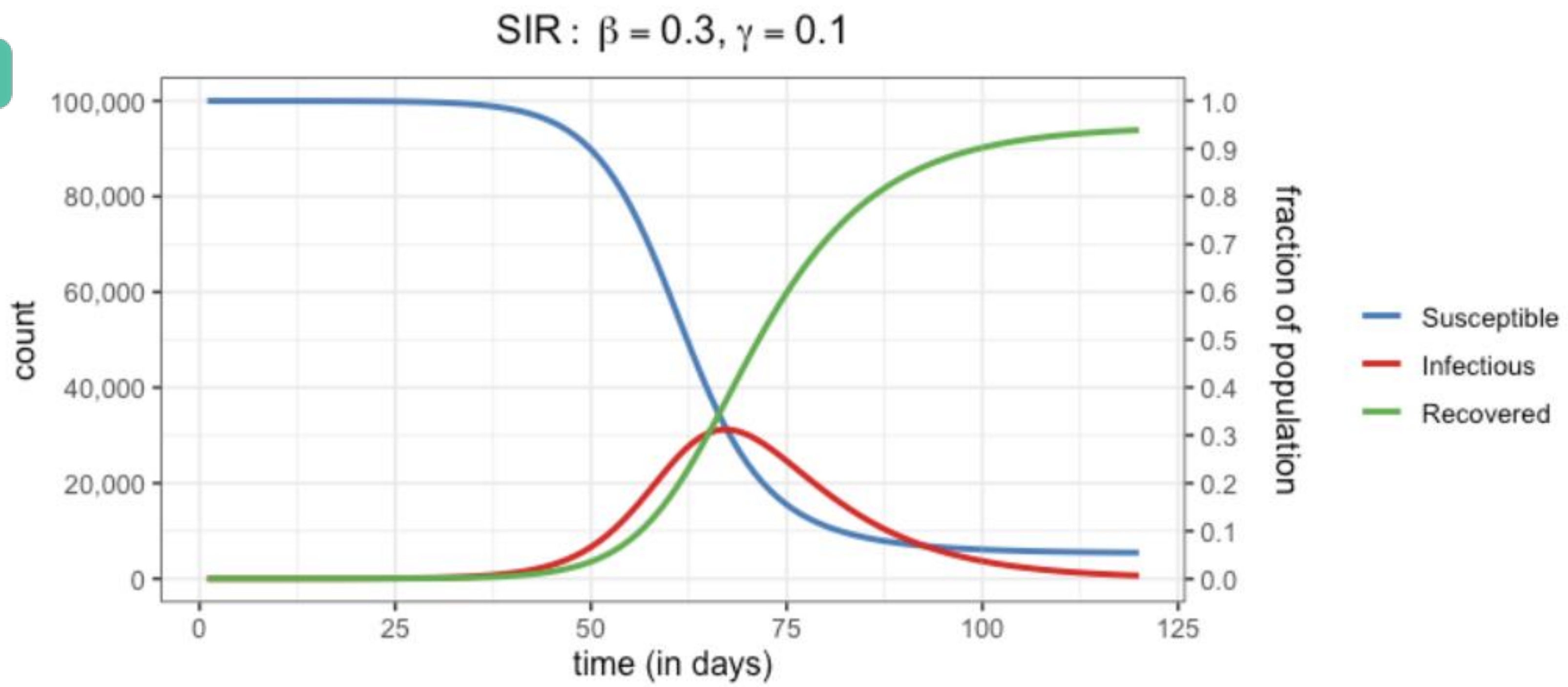
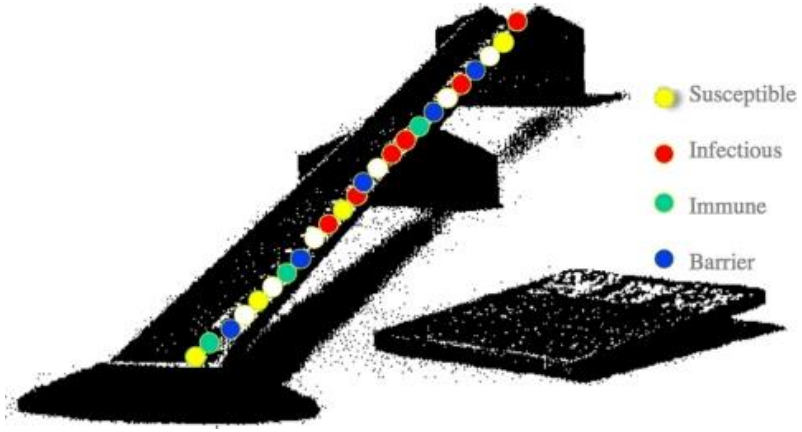




$$I_{t+1} = S_t \left(1 - (1-p)^{I_t}\right),$$

$$S_{t+1} = S_t \left(1-p\right)^{I_t}$$

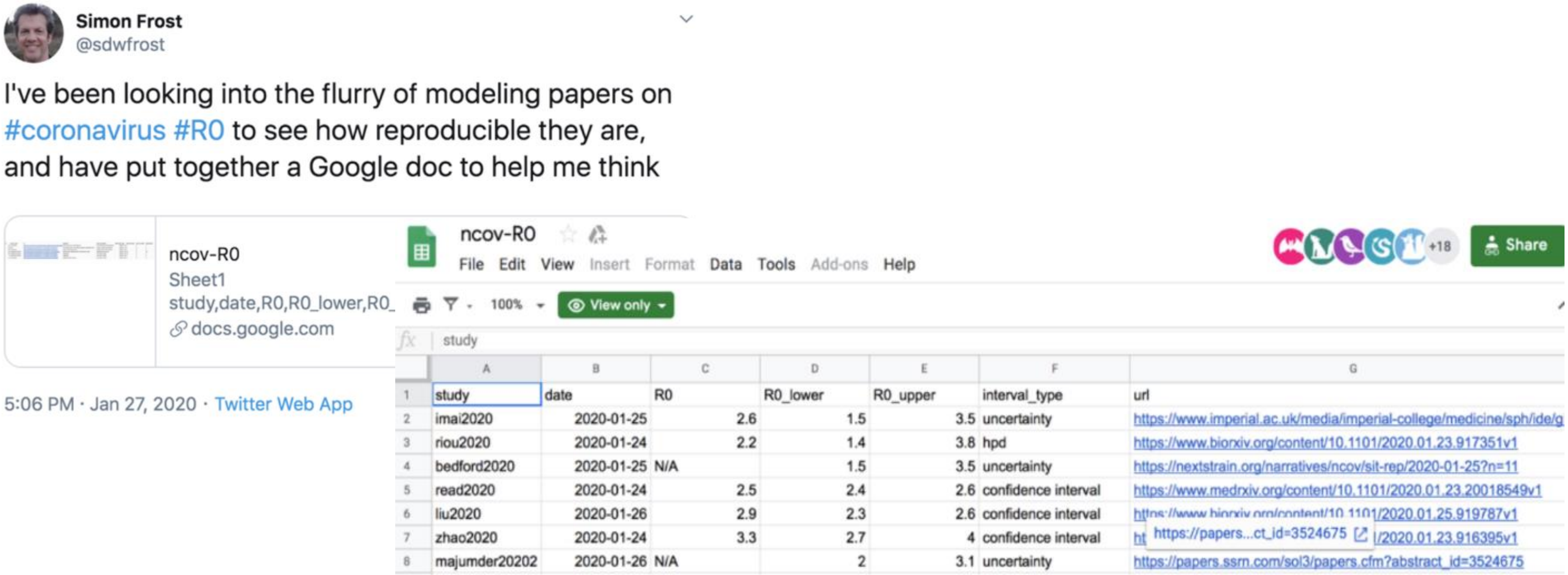
Reproductive number

- Most well-known epidemiological parameter
- R_0, R_t
- Average new case per case
- Useful for disease control

Values of R_0 and herd immunity thresholds (HITs) of infectious diseases prior to intervention

Disease	Transmission	R_0	HIT[a]
Measles	Aerosol	12–18[40][7]	92–94%
Chickenpox (varicella)	Aerosol	10–12[41]	90–92%
Mumps	Respiratory droplets	10–12[42]	90–92%
Rubella	Respiratory droplets	6–7[b]	83–86%
Polio	Fecal–oral route	5–7[b]	80–86%
Pertussis	Respiratory droplets	5.5[47]	82%
Smallpox	Respiratory droplets	3.5–6.0[48]	71–83%
HIV/AIDS	Body fluids	2–5[49]	50–80%
COVID-19 (ancestral strain)	Respiratory droplets and aerosol[50]	2.9 (2.4–3.4)[51]	65% (58–71%)
SARS	Respiratory droplets	2–4[52]	50–75%
Diphtheria	Saliva	2.6 (1.7–4.3)[53]	62% (41–77%)
Common cold (e.g., rhinovirus)	Respiratory droplets	2–3[54][medical citation needed]	50–67%
Mpox	Physical contact, body fluids, respiratory droplets	2.1 (1.5–2.7)[55]	53% (31–63%)
Ebola (2014 outbreak)	Body fluids	1.8 (1.4–1.8)[56]	44% (31–44%)
Influenza (seasonal strains)	Respiratory droplets	1.3 (1.2–1.4)[57]	23% (17–29%)
Andes hantavirus	Respiratory droplets and body fluids	1.2 (0.8–1.6)[58]	16% (0–36%)[c]
Nipah virus	Body fluids	0.5[59]	0%[c]
MERS	Respiratory droplets	0.5 (0.3–0.8)[60]	0%[c]

Present



Simon Frost
@sdwfrost

I've been looking into the flurry of modeling papers on #coronavirus #R0 to see how reproducible they are, and have put together a Google doc to help me think

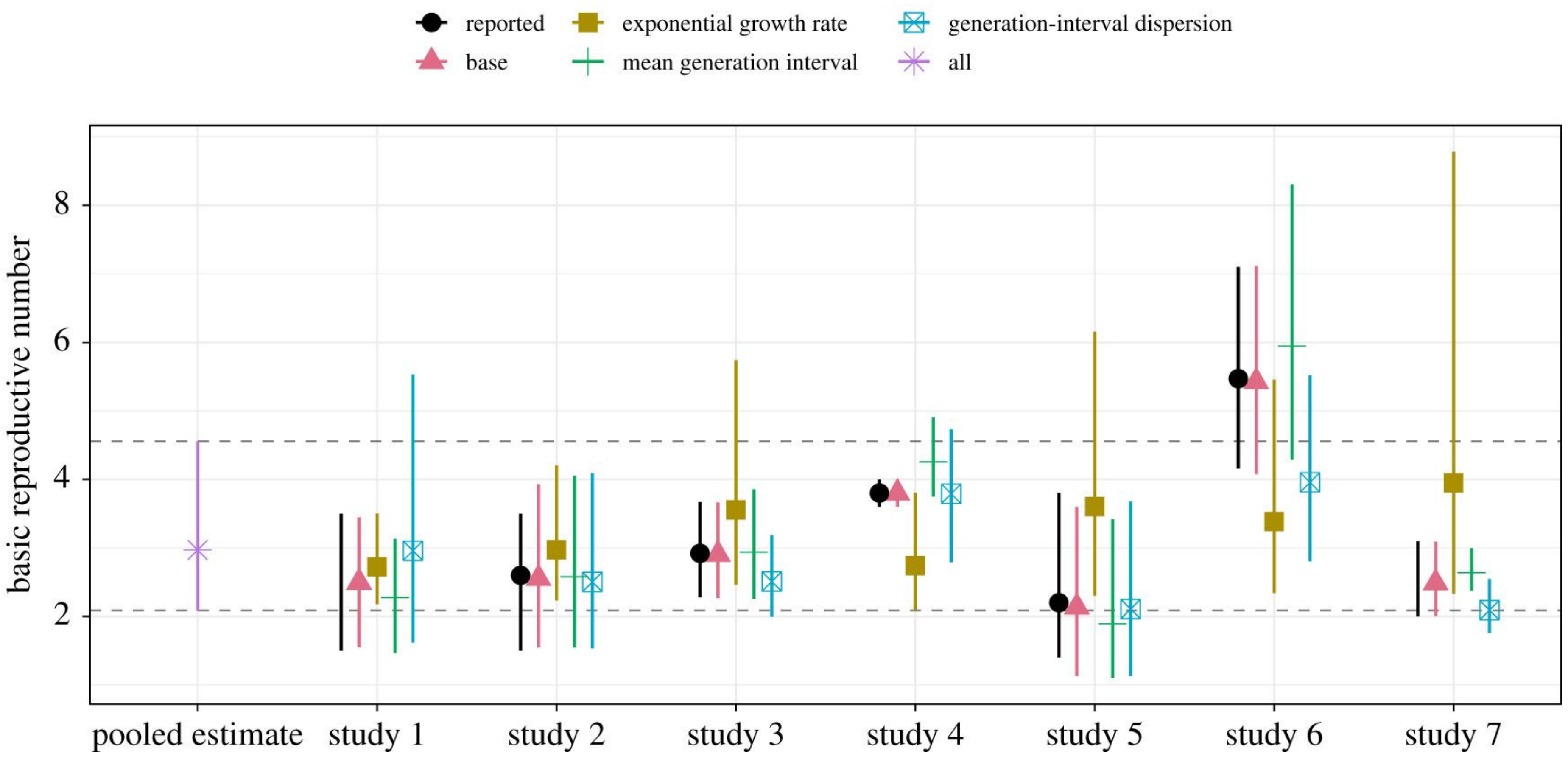
ncov-R0
Sheet1
study,date,R0,R0_lower,R0_
docs.google.com

5:06 PM · Jan 27, 2020 · Twitter Web App

ncov-R0
File Edit View Insert Format Data Tools Add-ons Help
100% View only
Share

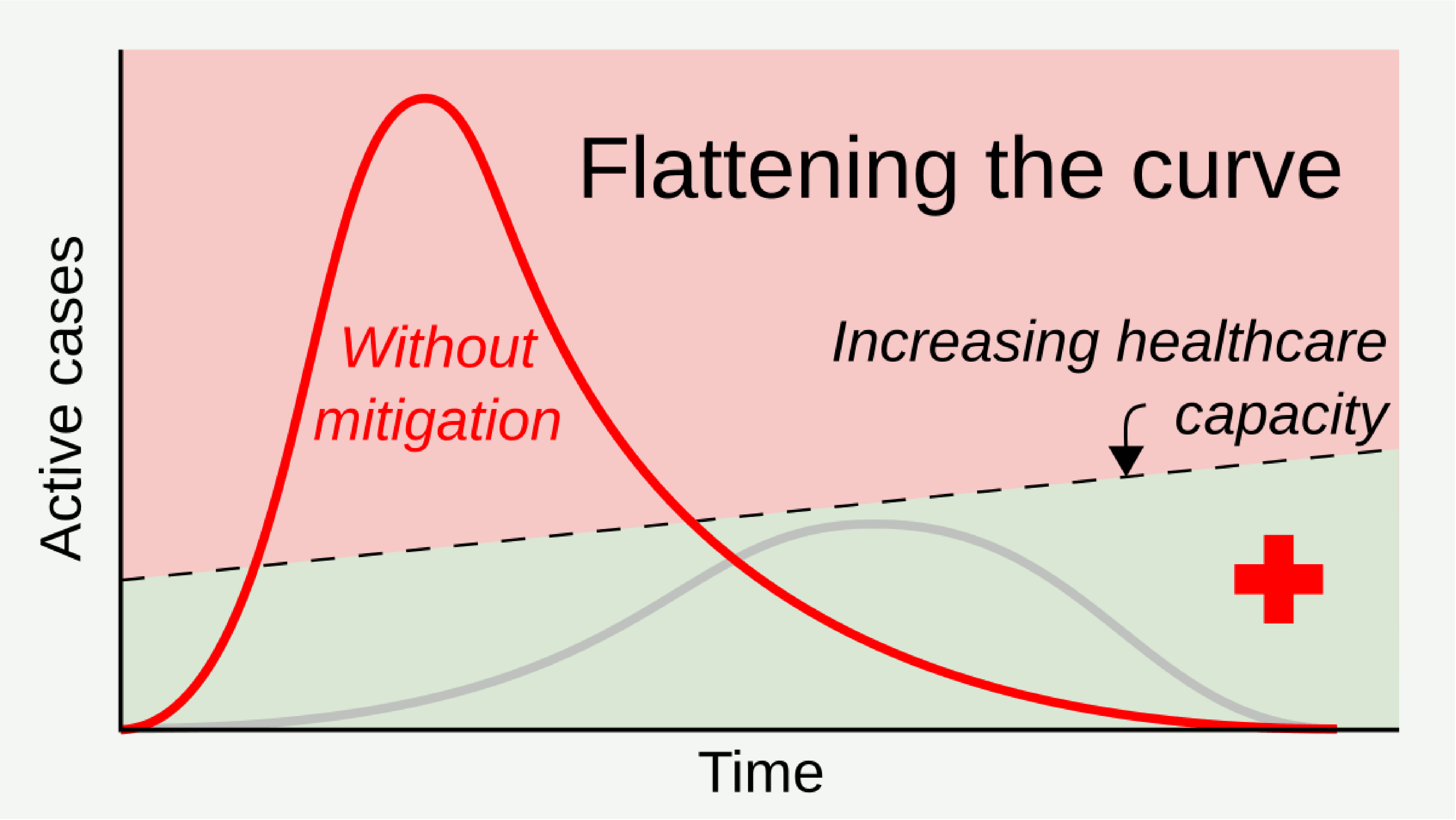
study	date	R0	R0_lower	R0_upper	interval_type	url
imai2020	2020-01-25	2.6	1.5	3.5	uncertainty	https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/g
riou2020	2020-01-24	2.2	1.4	3.8	hpd	https://www.biorxiv.org/content/10.1101/2020.01.23.917351v1
bedford2020	2020-01-25	N/A	1.5	3.5	uncertainty	https://nextstrain.org/narratives/ncov/sit-rep/2020-01-25?n=11
read2020	2020-01-24	2.5	2.4	2.6	confidence interval	https://www.medrxiv.org/content/10.1101/2020.01.23.20018549v1
liu2020	2020-01-26	2.9	2.3	2.6	confidence interval	https://www.biorxiv.org/content/10.1101/2020.01.25.919787v1
zhao2020	2020-01-24	3.3	2.7	4	confidence interval	ht [https://papers...ct_id=3524675] /2020.01.23.916395v1
majumder20202	2020-01-26	N/A	2	3.1	uncertainty	https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3524675

Present



Park et al. (2020)

Present


Flattening the curve
Without mitigation
Increasing healthcare capacity
Active cases
Time

Modelling Challenges

Modelling Challenges

- Making models is challenging
  - Making models that work with the application is hard.

Modelling Challenges

- Making models is challenging
- Making models more realistic is challenging
  - Building realistic features and mechanisms to basic standard models is challenging

Modelling Challenges

- Making models is challenging
- Making models more realistic is challenging
- Making models more realistic without data is challenging
  - Buying assumptions is sometimes necessary but over buying assumptions for models that are too complicated for the application is bad.
  - It is sometimes view as a double-edge sword.

Modelling Challenges

- Making models is challenging
- Making models more realistic is challenging
- Making models more realistic without data is challenging
- Making models more realistic with data is challenging
  - How to incorporate different data streams is hard
  - Fitting to data is also hard!

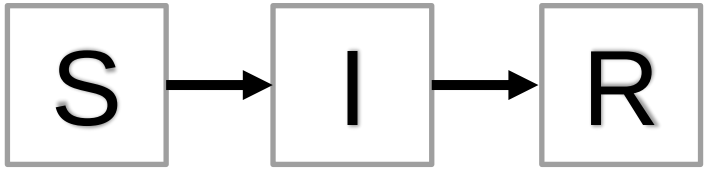
Model Complexities to solve problems

- Product-models
- Time varying parameterizations

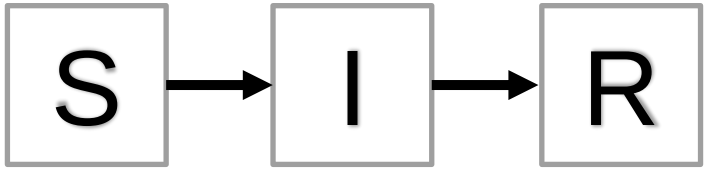
Model Complexities to solve problems

- Product-models
- Time varying parameterizations

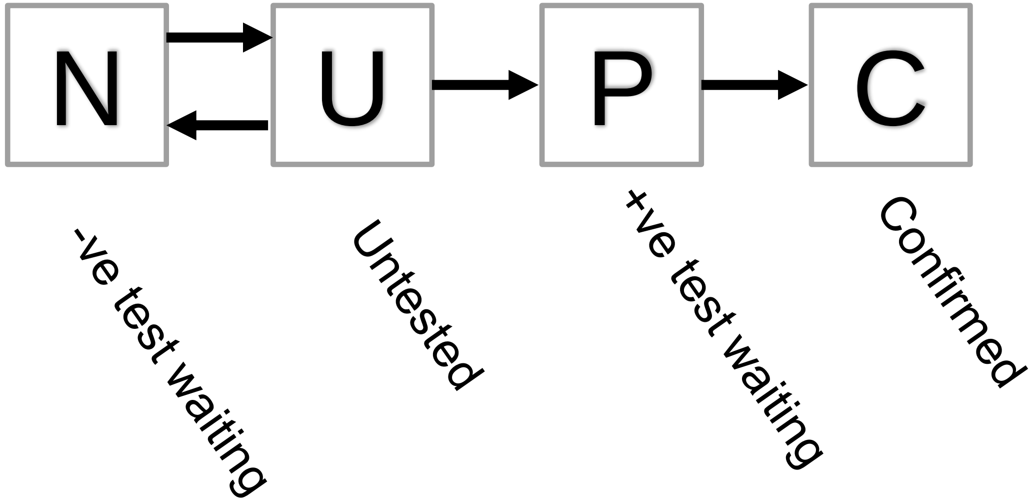
Product-models



Product-models



+ testing mechanism =



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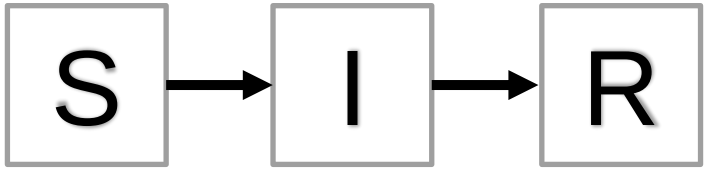

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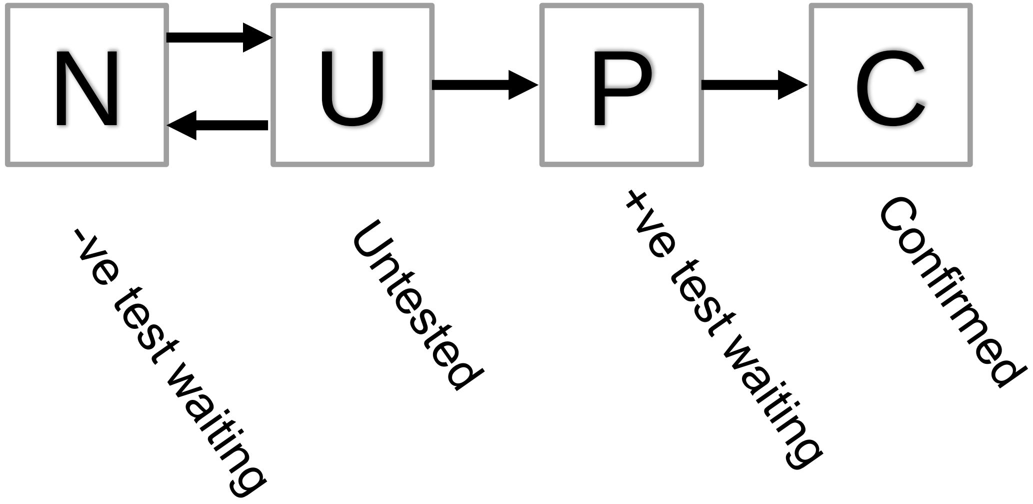
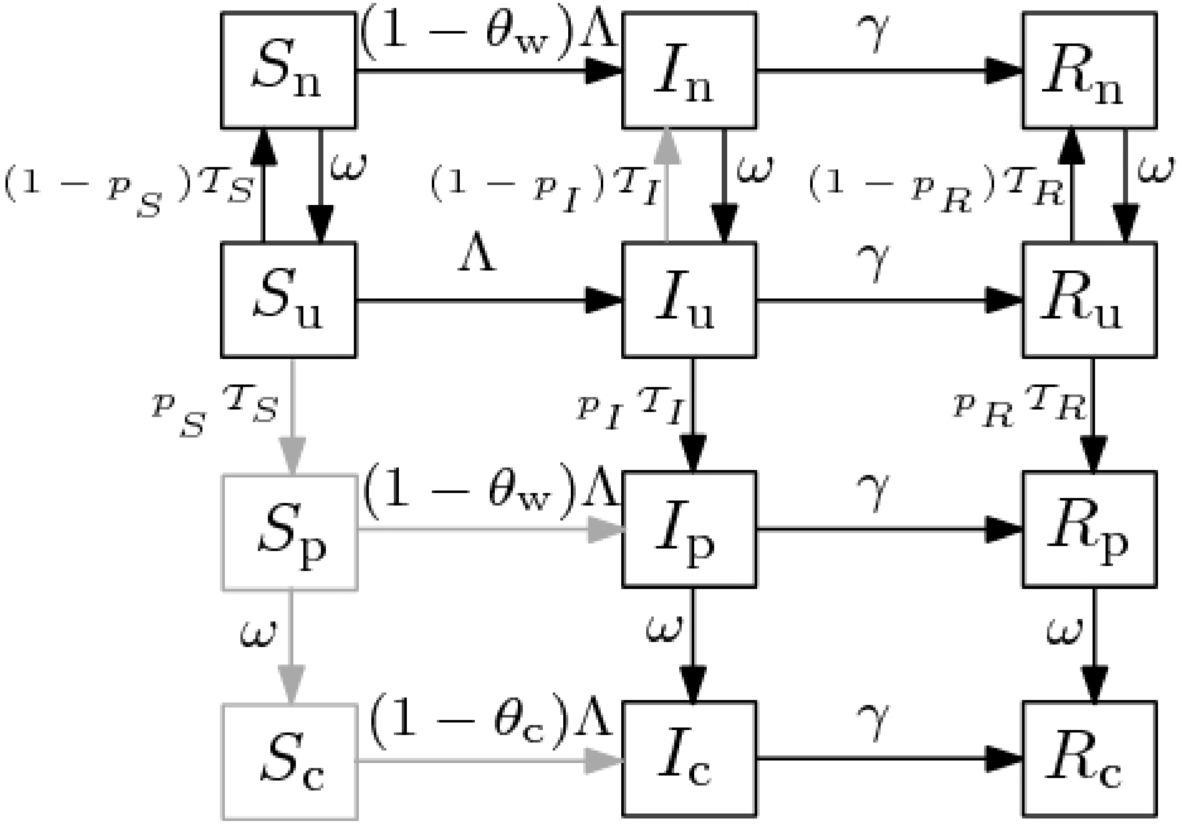
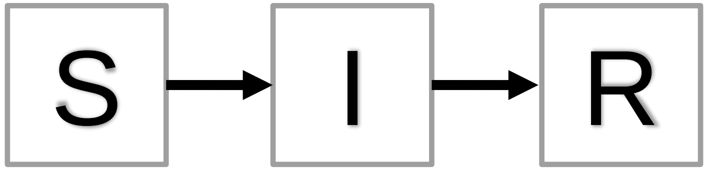




(Gharouni et al. 2022)

Product-models



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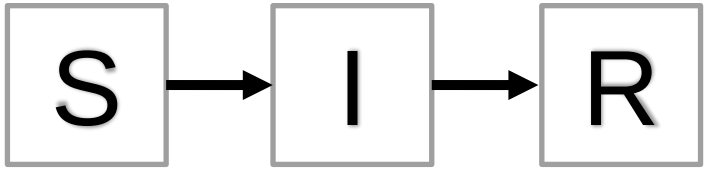
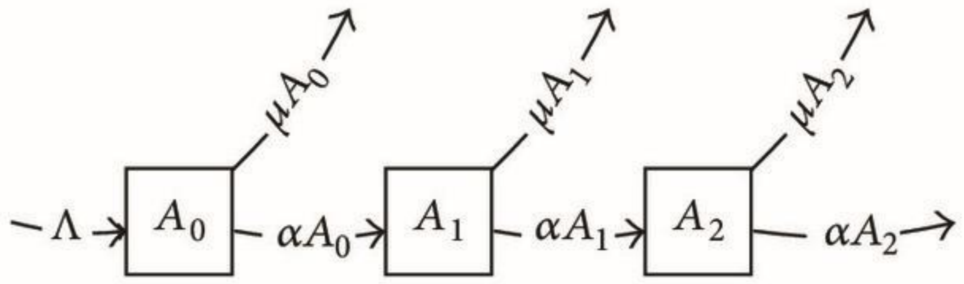
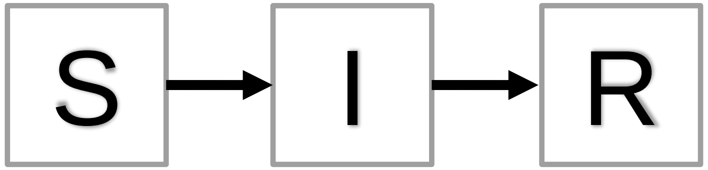


+ age structure =



Product-models



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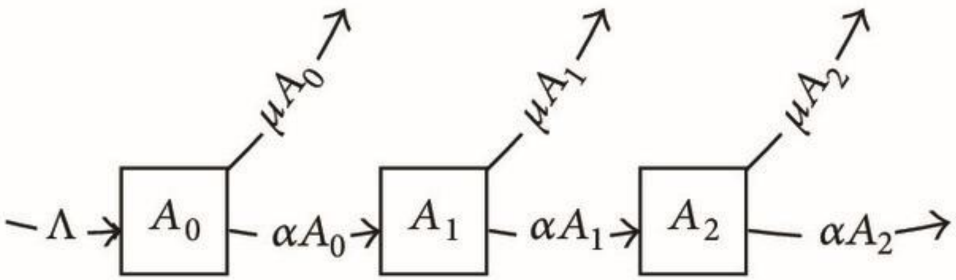
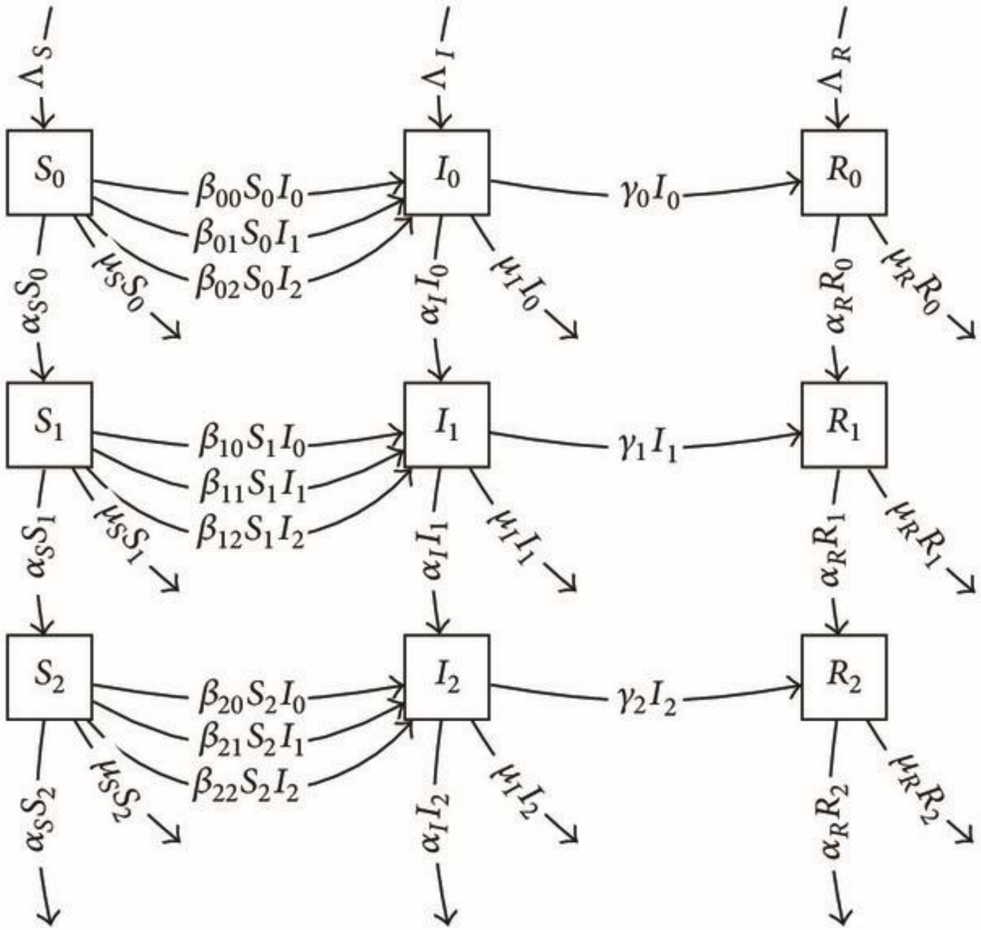
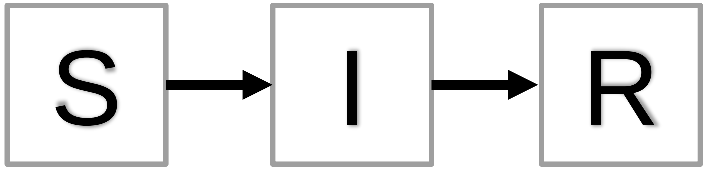




(Worden and Porco, 2017)

Product-models

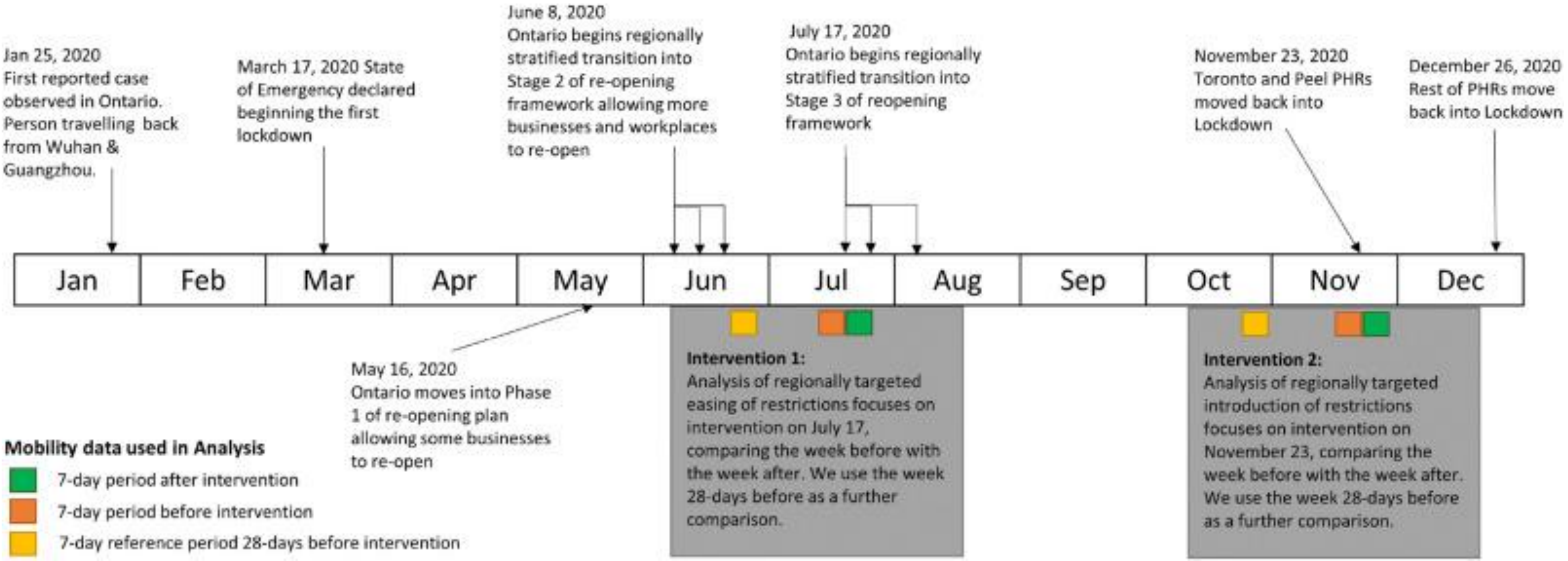


+ Population heterogeneity
+ Vaccination
+ Variants
+ many more ….

Model Complexities that makes models more realistic

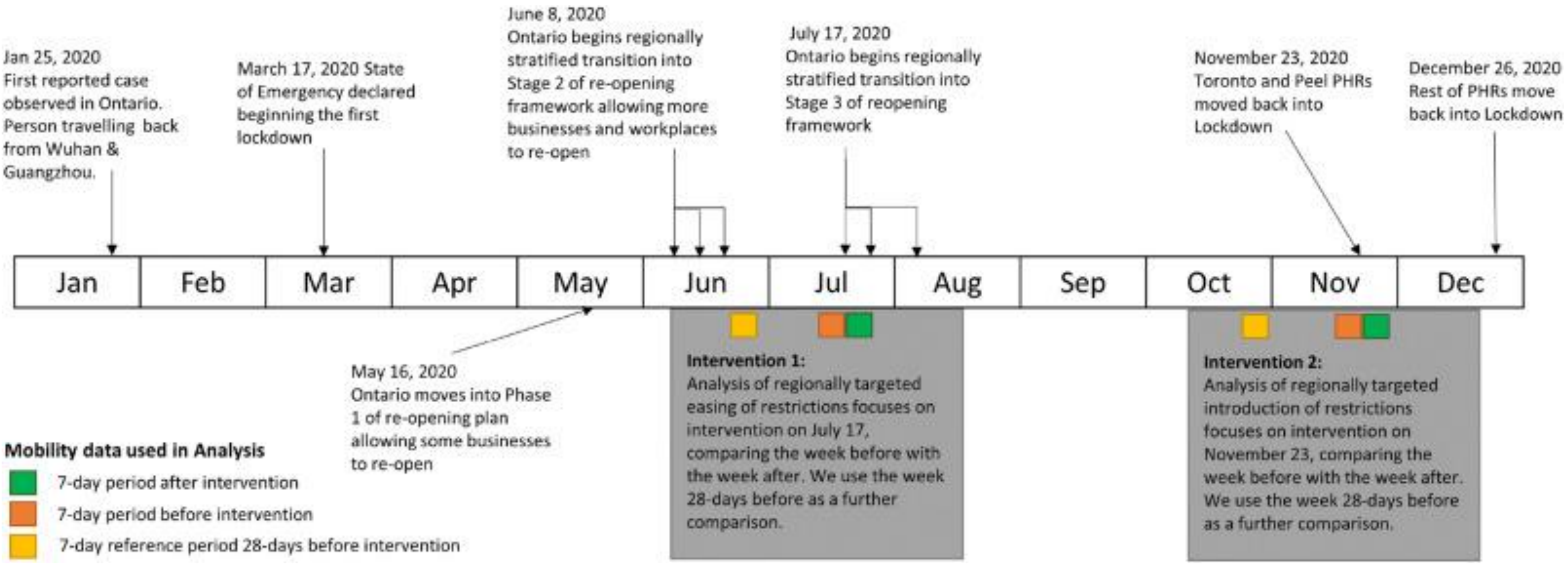
- Product-models
- Time varying parameterizations

Time varying parameterizations



(Long et al, 2021)

Time varying parameterizations



$$\log \beta(t) = \log \beta_0 + \boldsymbol{X}\boldsymbol{c}$$

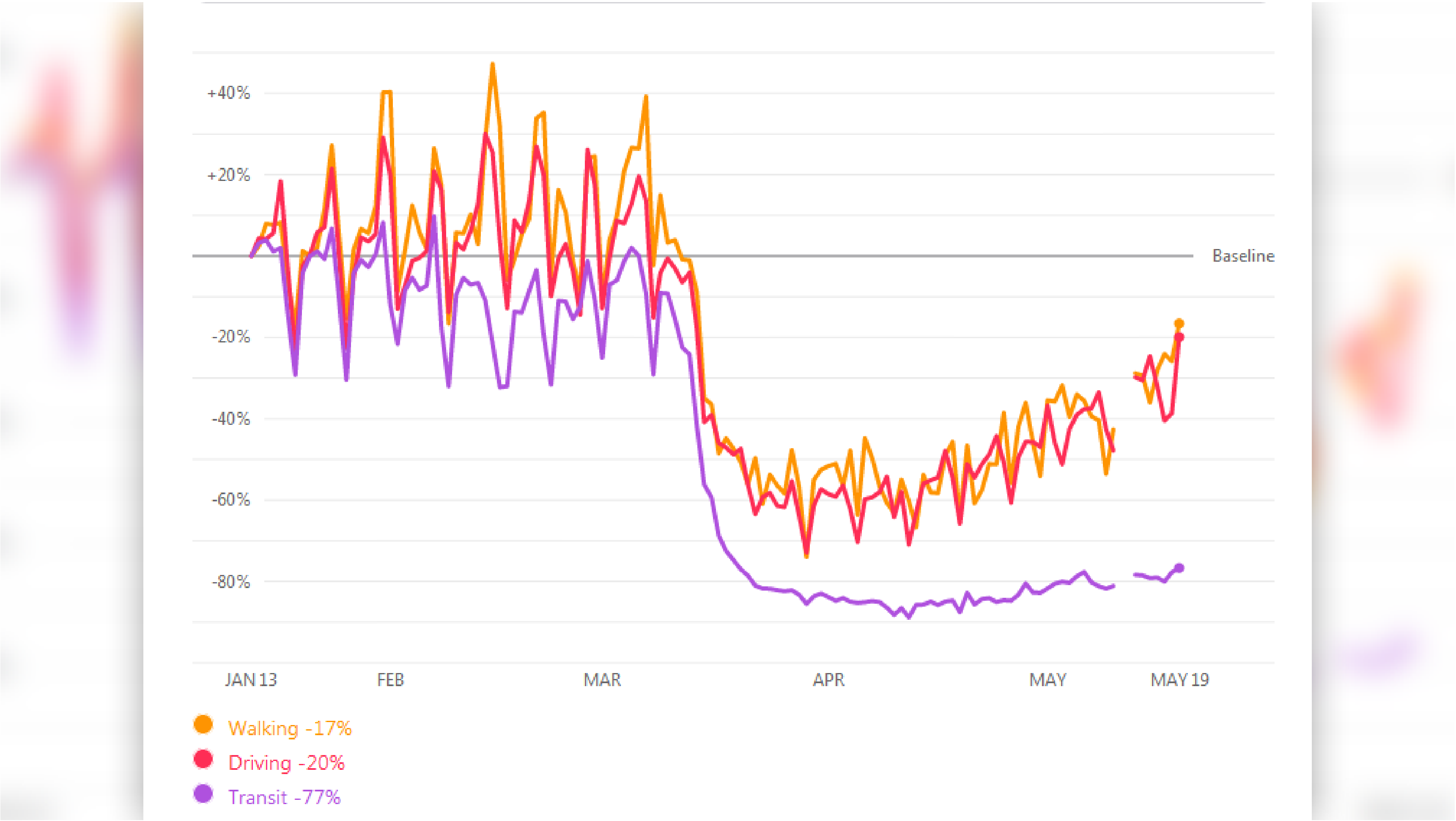
Log-linear function with abrupt (piecewise) changes on specific date when controls are known to have implemented

Time varying parameterizations

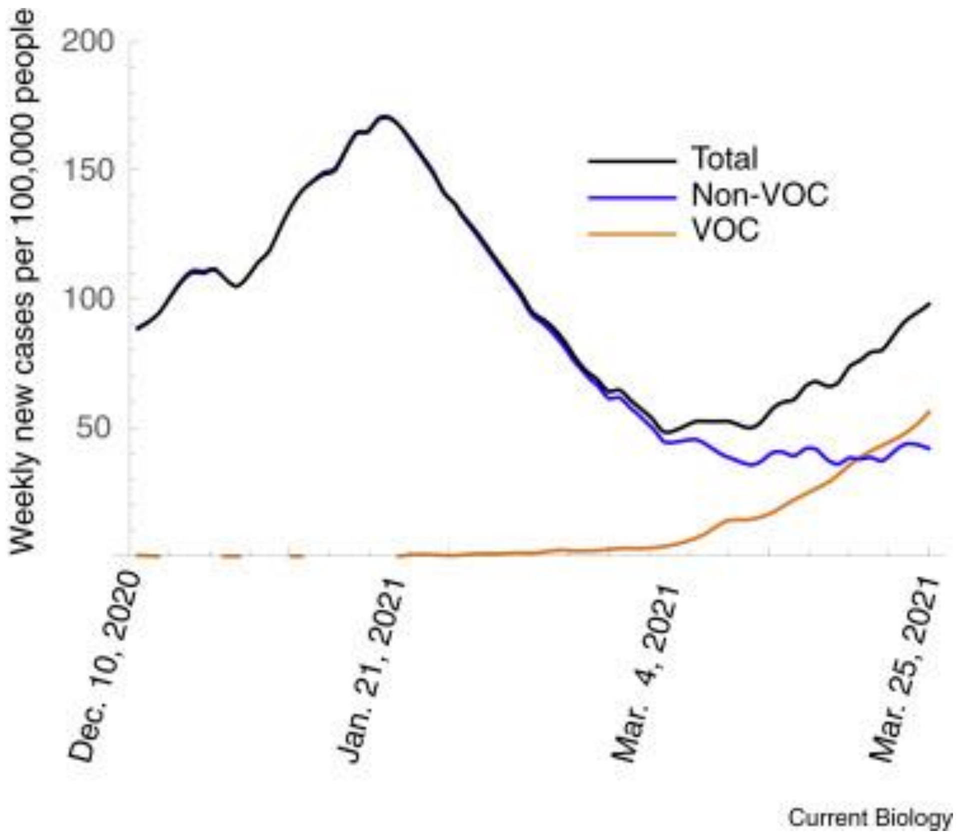
$$\beta_1(t) \propto \log(M(t))^{p_{\text{mob}}}$$

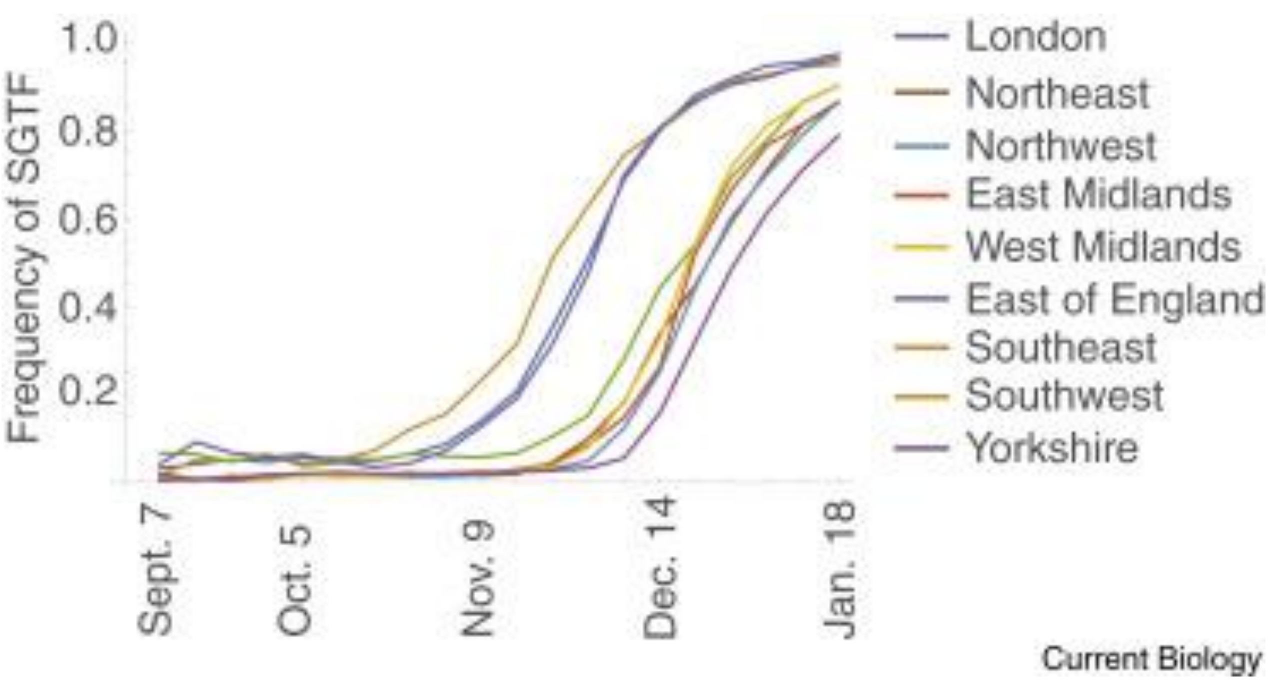
Proportional to a power of observed mobility or some other exogenous proxy for contact behavior

The Apple Mobility Trends data for Ottawa as of May 19



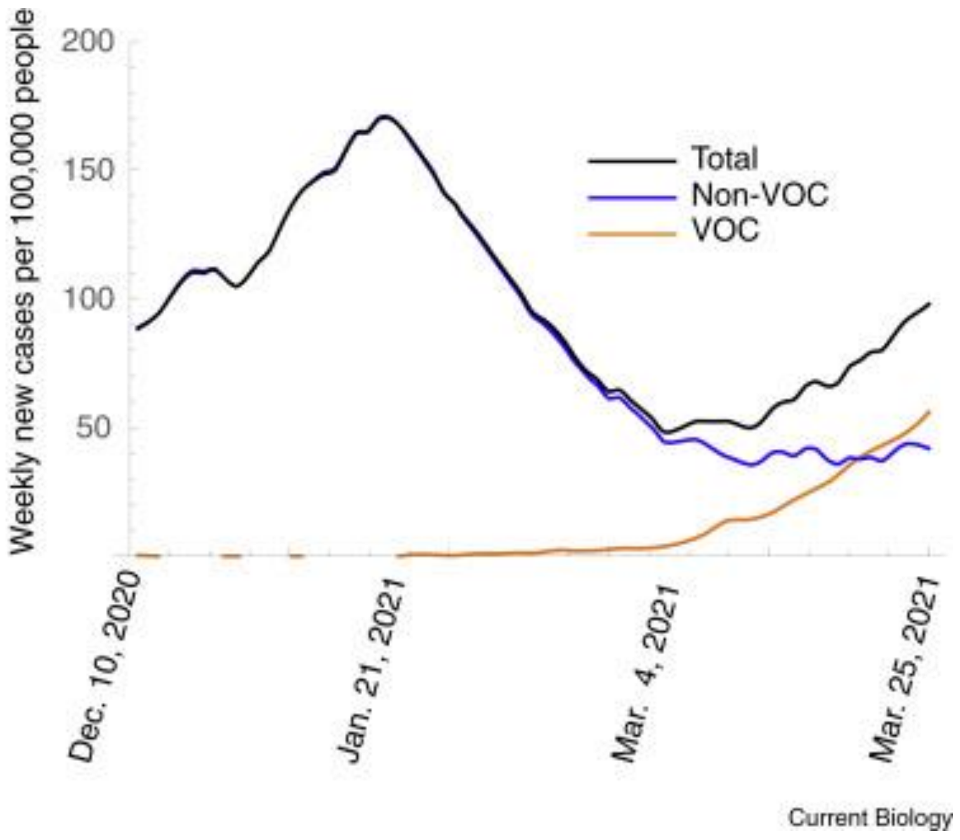
Time varying parameterizations

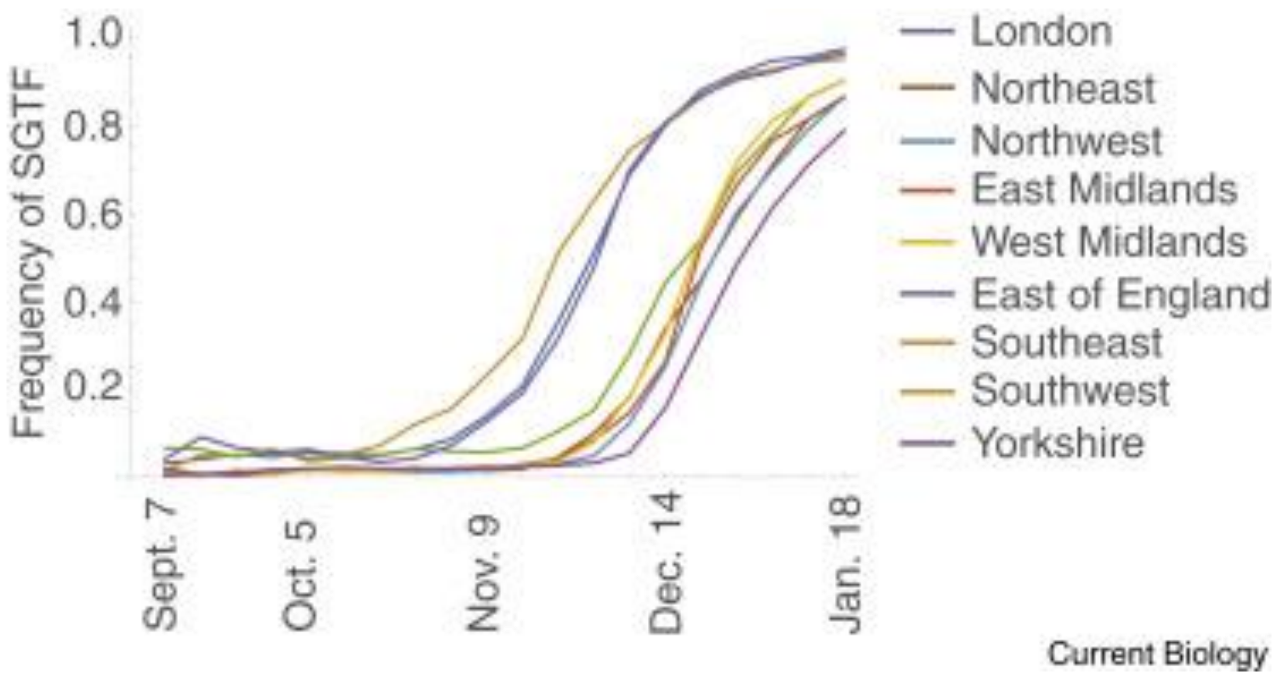




(Otto et al, 2021)

Time varying parameterizations



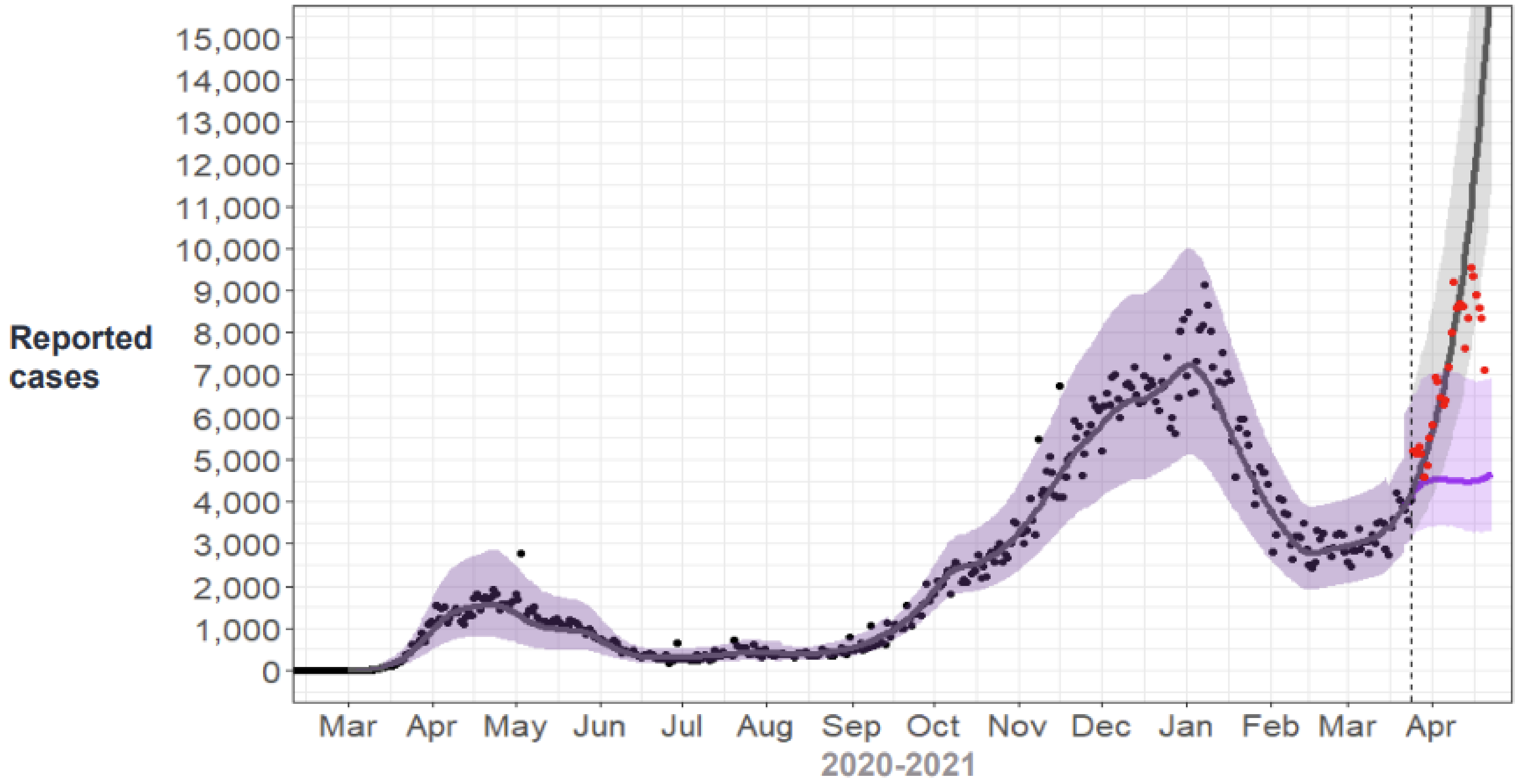


$$s = r_{inv} - r_{res}$$
$$\mathrm{p(t) = Logistic(s, t - t_0)}$$
$$\beta(\mathrm{t}) = \beta_{\mathrm{res}} * (1 - \mathrm{p(t)}) + \beta_{\mathrm{inv}} * \mathrm{p(t)}$$

(Otto et al, 2021)

Alpha variant in Canada

The previous longer-range modelling forecast from March 26th continues to play out in the data we are seeing now

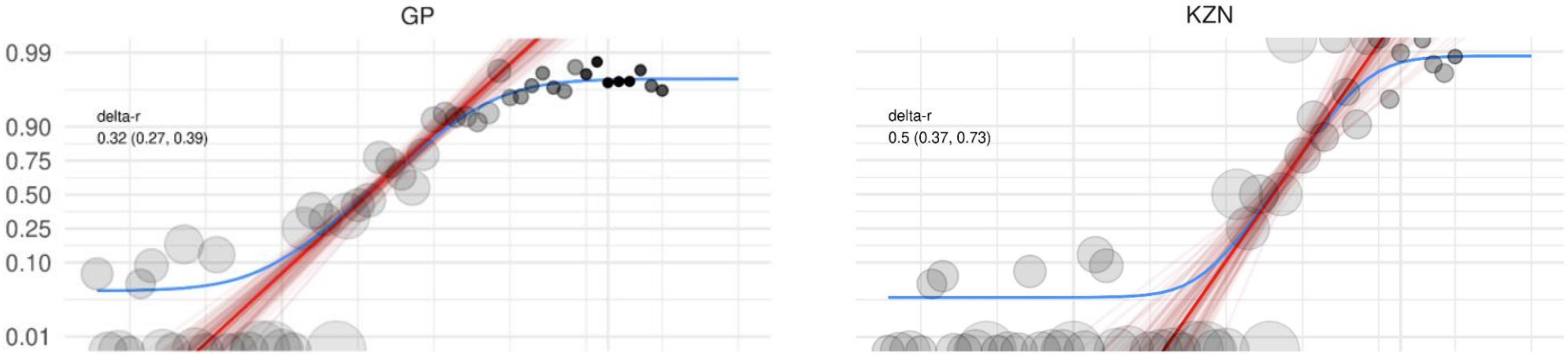


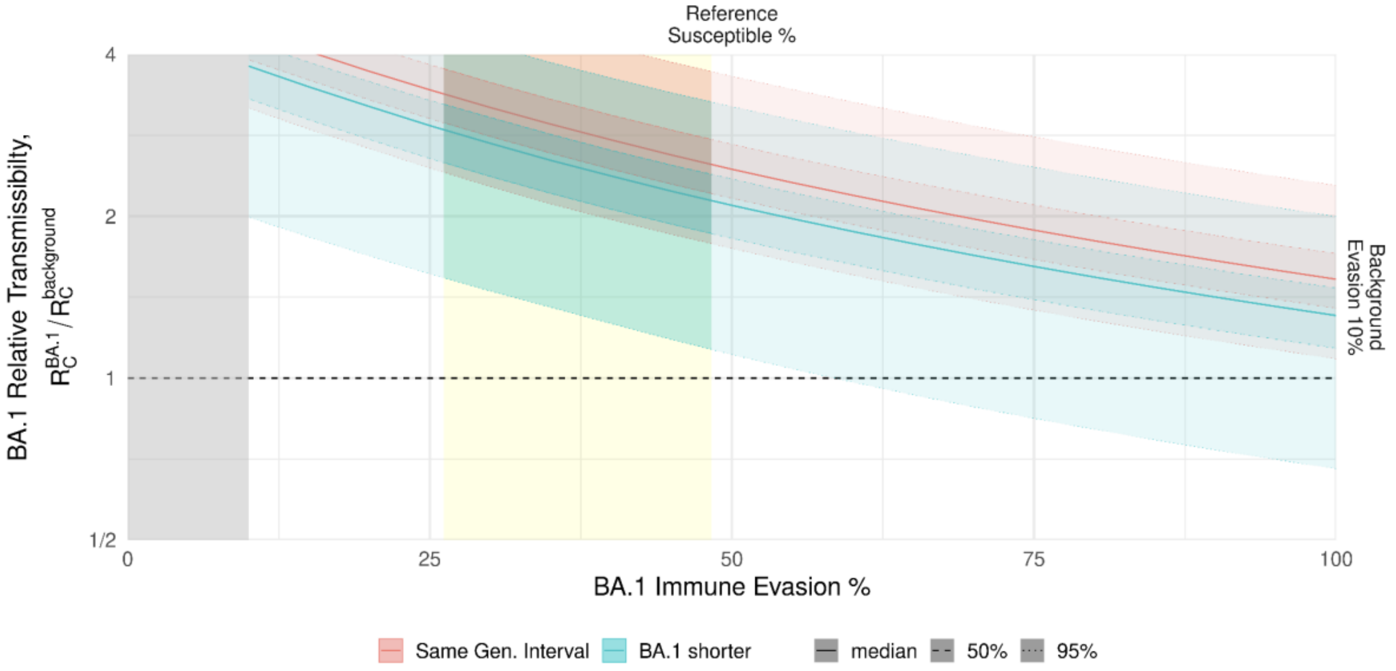
*Grey line - with spread of VOCs and we maintain the current number of people we contact each day

*Purple line - If VOCs are controlled by reducing the current number of people we contact each day by 20-30%

Red points - surveillance data after the forecast from March 25th to April 20th

Omicron in RSA

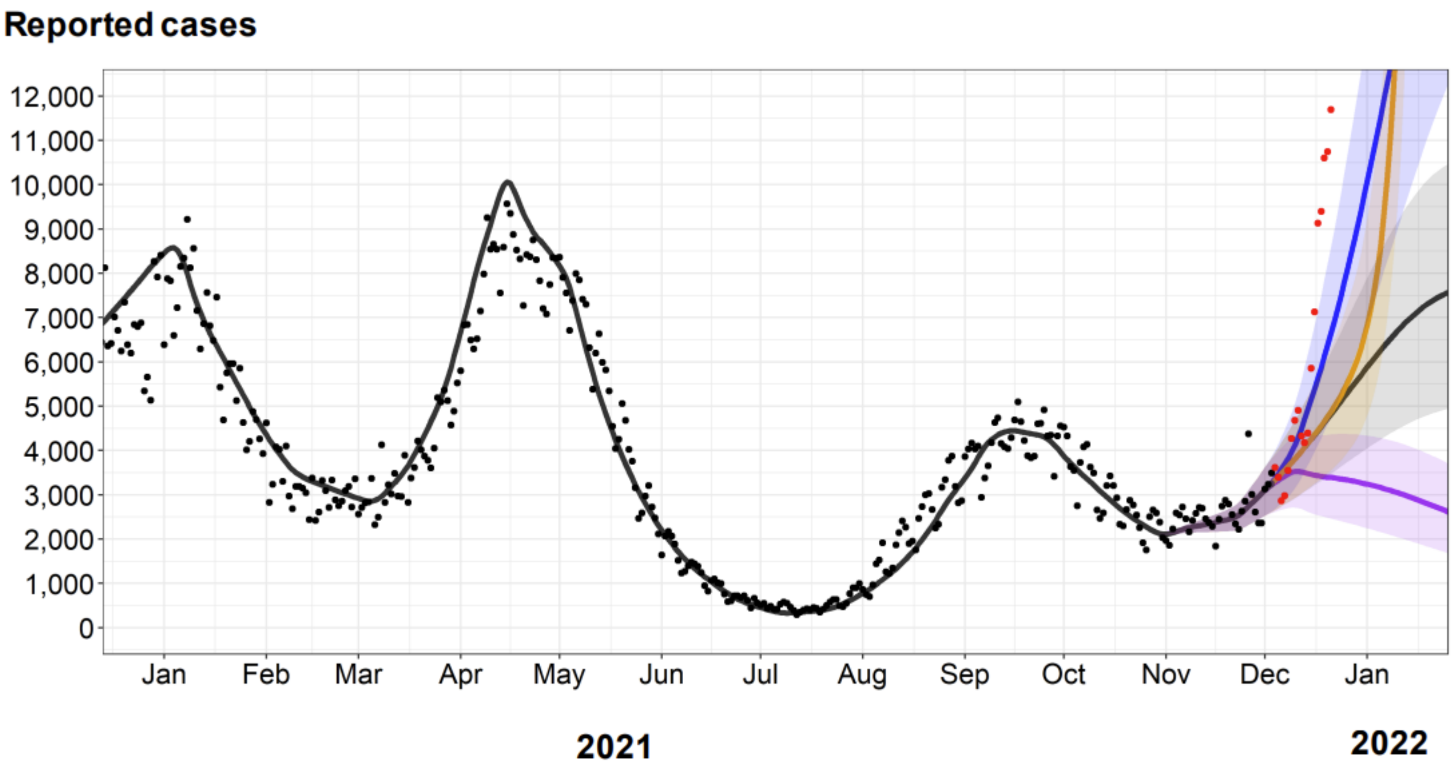




(Pearson et al, 2021)

Omicron BA.1 in Canada

Since December 10th forecast, cases have exceeded the increased transmission trajectory (blue)



DELTA Predominant

If transmission **increases** by 15%

If we **maintain** the current levels of transmission

If public health measures **reduce** transmission by 15% today

OMICRON Replacement

If we maintain the current levels of transmission and Omicron successfully establishes*

*Underestimate - accounts for only increased transmissibility but not immune evasion

Red points – *Surveillance data after the forecast*

Data as of December 20, 2021; fit as of December 3, 2021

Note: *Output from PHAC-McMaster model. Model considers impact of vaccination and increased transmissibility of VOCs (including Omicron), refer to annex for detailed assumptions on modelling. At the time, the speed and introduction of Omicron were uncertain.*

Summary

- Making models is challenging
- Making models more realistic is challenging
- Making models more realistic without data is challenging
- Making models more realistic with data is challenging

Present

Summary

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- Traditional modelers are forced to wear too many hats

Present

Modeler

Present

Designer

Modeler

Present

Expert
Math, Biology and etc

Designer

Modeler

Present

Public / Stakeholders

Expert
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Public Health Official

Designer

Modeler

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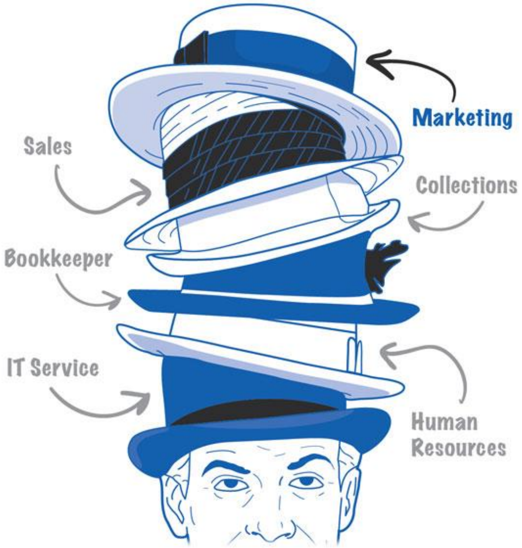

Public Health Official

Designer

Modeler

Software developer

Present

Division of Labour

Modelers

- **Focus on the biology, math, understand the needs/motivations from clients**

Present

Division of Labour

Modelers

- Focus on the biology, math, understand the needs/motivations from clients

Software Developers and Product Managers

- **Finding out what *slows* down modelers**
- **Building tools that *speeds* them up**

Footnote: Speed has two meanings in this context: Implementation speed and computational speed.

Flexibility and Speed

Flexibility (Implementation speed)

- Straight-forward to implement from model design -> software
- Add-ons for complexities
- Modular
- Compatible with widely use software and techniques

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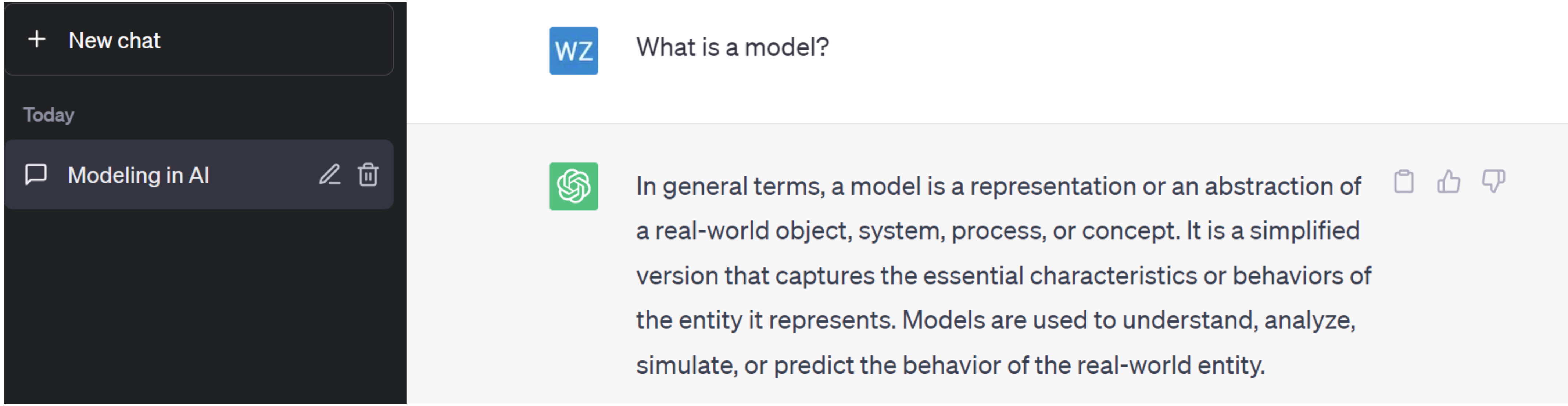
Computational Speed

- Model fitting
- Forecast confidence intervals
- Scenario exploration
- Sensitivity analysis

Future



Present

To face the challenges we encounter

Knowledge
Experience
Lesson

Past

Future

Improve
Support

What is the "end" of "endemic"?

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The end of:

- **E**mergency

What is the "end" of "endemic"?

The end of:

- **E**mergency
- **M**onitoring
- **I**nitiatives
- **C**ollaborations

War time vs Peace time

	War time	Peace time
Emergency	increase	decrease
Monitoring	increase	decrease
Initiatives	increase	decrease
Collaboration	increase	decrease
Duration	short	long

Success is challenging, and long-term success is even more challenging. Peace time is the real battle after the short war time. The goal is to prolong peace time as long as possible and to do so, it is important to be proactive.

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Proactive Monitoring

Develop better surveillance systems

- **Genomics**
- Serology
- Sentinel
- Citizen science
- Wastewater

Develop ways to routinely analyze, and ways to connect the individual pieces. Models can help!

Proactive Initiatives

Research and Development

Research

- Much more to be learned
- Only scratched the tip

Development

- Develop capacities

Proactive Collaborations

There are still tons of questions out there and opportunities to collaborate.

WHO collaboratory pandemic and epidemic intelligence
- EpiParameter Community

https://worldhealthorganization.github.io/collaboratory-epiparameter-community/#/

Future

By involving public health experts, policymakers, scientists, and communities in the modeling process, models can be co-developed to address public health challenges.

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Thanks!

Acknowledgements

Public Health Agency of Canada

PHRS
Nick Ogden
Aamir Fazil
Patricia Turgeon

Wastewater
David Champerdon
Shokoofeh Nourbakhsh
Warsame Yusuf

RISK
Irena Papst
Victoria Ng
Ainsley Otten
Ben Smith

Knowledge Synthesis
Lisa Waddell
Austyn Baumeister
Tricia Corrin
Melanie Katz
Kusala Pussegoda

PED
Emily Acheson
Philippe Berthiaume
Vanessa Gabriele-Rivet
Valerie Hongoh
Rachael Milwid
Erin Rees

Genomics Surveillance
Gordon Jolly
Carmen Lia Murall

Bioinformatics
Gary Van Domselaar
Katherine Eaton

NACI
Ashleigh Tuite
Raphael Ximenes

CDSB
Lindsay Whitmore

Other Government/ Organizations

Health Canada
Alan Diener
Mark Latendresse
Olesya Levina
Victoria Spofford

Public Health Ontario
Ali Gharouni

INSPQ
Éric Litvak

WHO

US-CDC

Acknowledgements

Academic Collaborators

McMaster University
Ben Bolker
Jonathan Dushoff
David Earn
Darren Flynn-Primrose
Steve Walker

University of British Columbia
Sally Otto

Simon Fraser University
Caroline Colijn
Jessica Stockdale
Elisha Are
Vitbhuti Gandhi

Queen’s University
Troy Day

University of Toronto
Kumar Murty
Beate Sander

York University
Jianhong Wu

Université Laval
Marc Brisson

Dalhousie University
Finlay Maguire
Nathan Smith

Princeton University
Sang Woo Park

LSHTM
Carl Pearson

SACEMA
Juliet Pulliam
Jeremy Bingham
Reshma Kassanjee
Cari van Schalkwyk
Alex Welte