Monitoring SARS-CoV-2: Combining clinical and wastewater surveillance

This is Public Health!

13.4.2022

Dr. Jana S. Huisman

The role of mathematical modelling in public health

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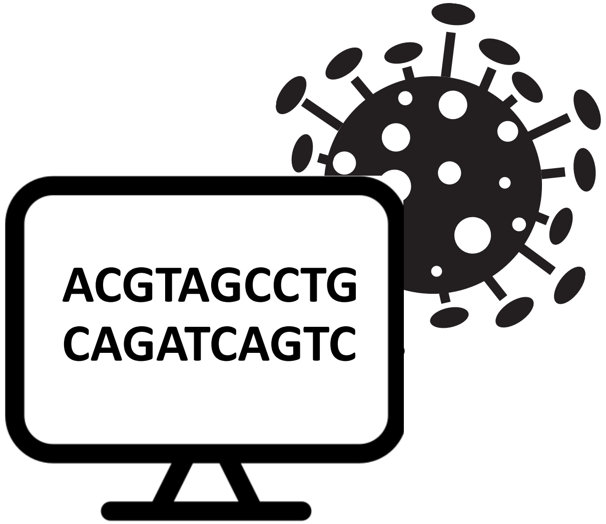
Mathematics in public health

Statistics (planning, analysis, prediction)

Bioinformatics (multi-omics data)

Modelling:

- **Within-host** models
- **Between-host** models (infectious disease dynamics)



Mathematical modelling in public health

A. Question

B. Available data:

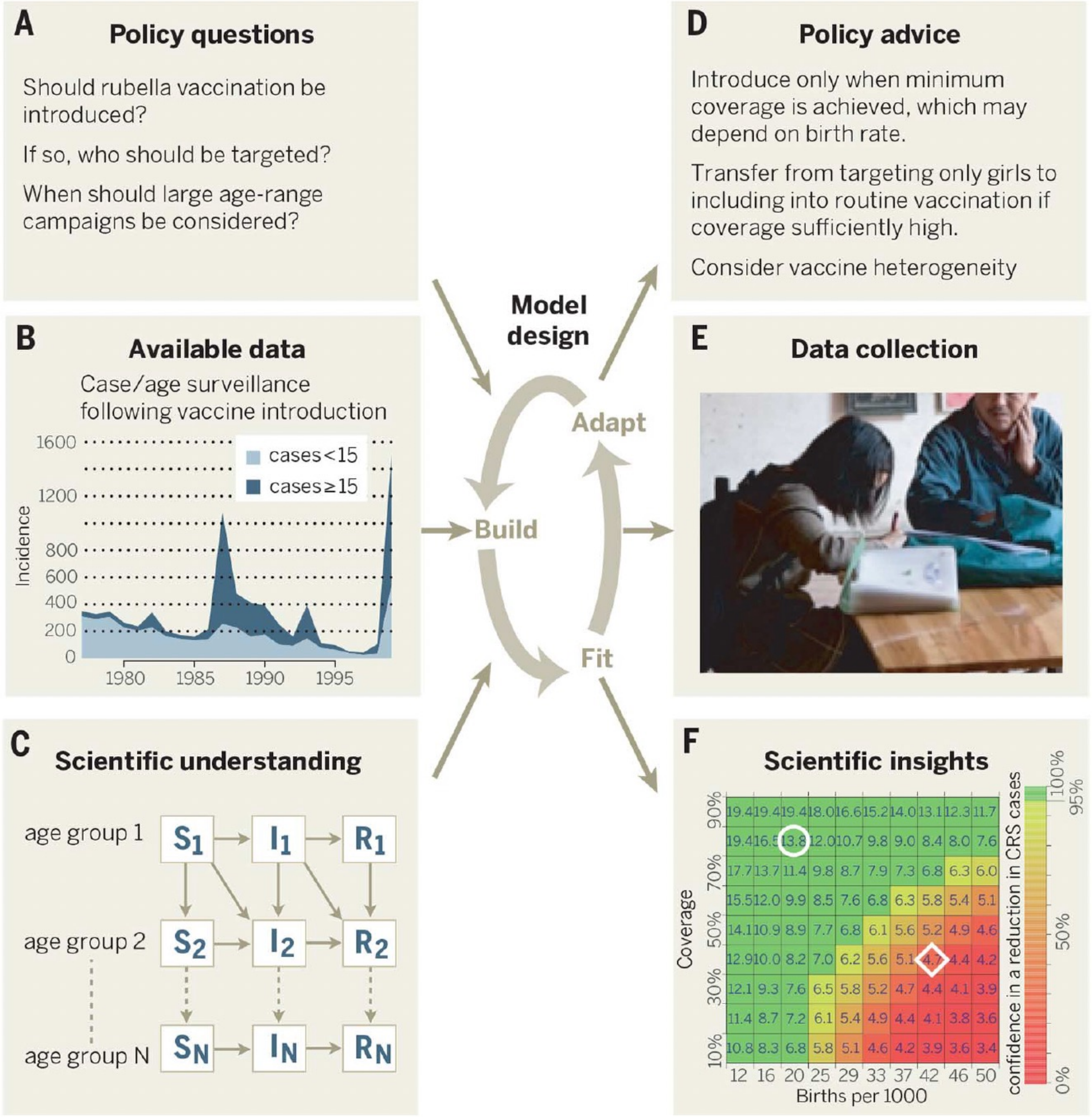
(i) To inform and fit the model

(ii) To quantify / validate outcome

C. Model with mechanistic and phenomenological parts

D. Research

E. Advice / Conclusion



Heesterbeek et al. *Science* (2015)

Why modelling?

Test what cannot be tested otherwise:

- Experiments would be unfeasible
- Counterfactual scenarios: what if?

"all models are wrong, but some are useful"

– George Box

Test mechanistic understanding:

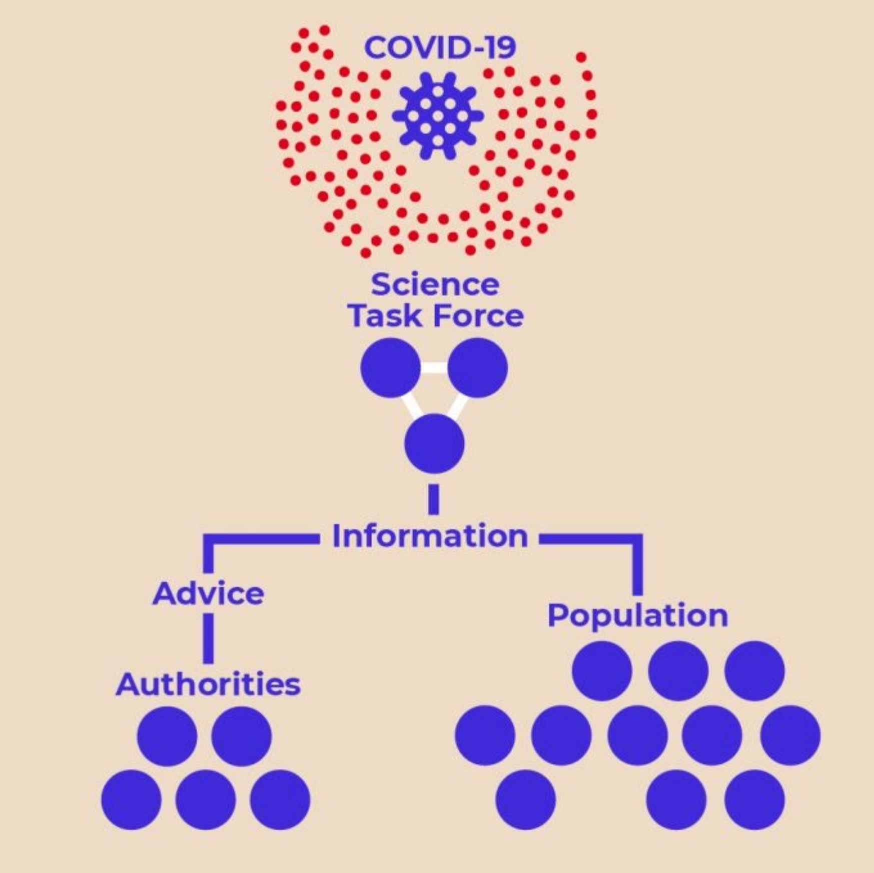
- All relevant parameters and no more?

Generate quantitative insight and comparison

Mathematical modelling during COVID-19

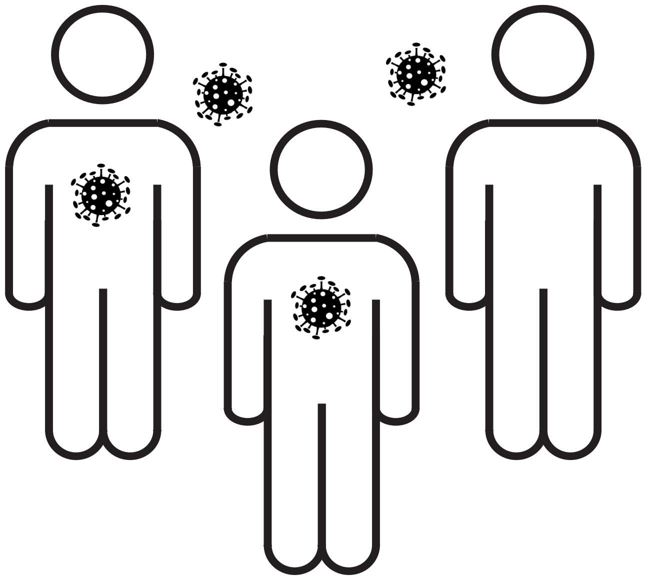
Policy questions:

- Predict when and where people will be **infected**
- Predict **ICU bed** occupancy
- Assess the impact of **interventions** on disease dynamics
- Optimal **vaccination strategy** to prevent death / infection
- Optimal **quarantine duration**
- Impact of **variants** with different transmission dynamics
- Assess **underreporting** and true cases ("Dunkelziffer")



SWISS NATIONAL
COVID-19
SCIENCE TASK FORCE

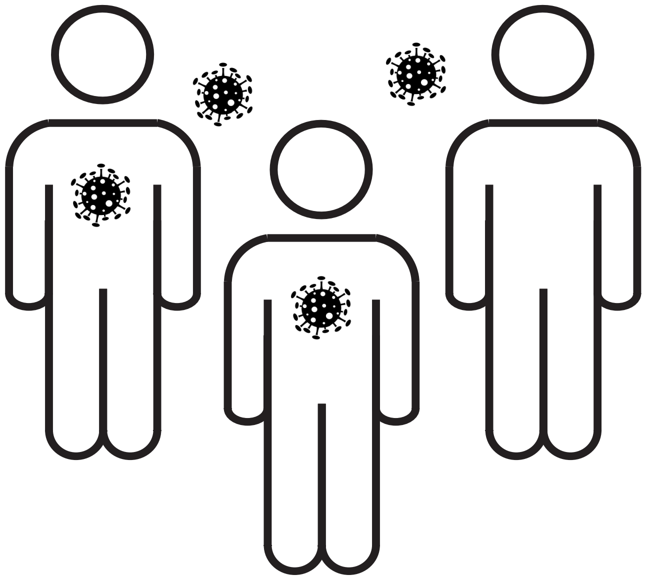
I. R_e



II. Wastewater

III. Variants

I. R_e

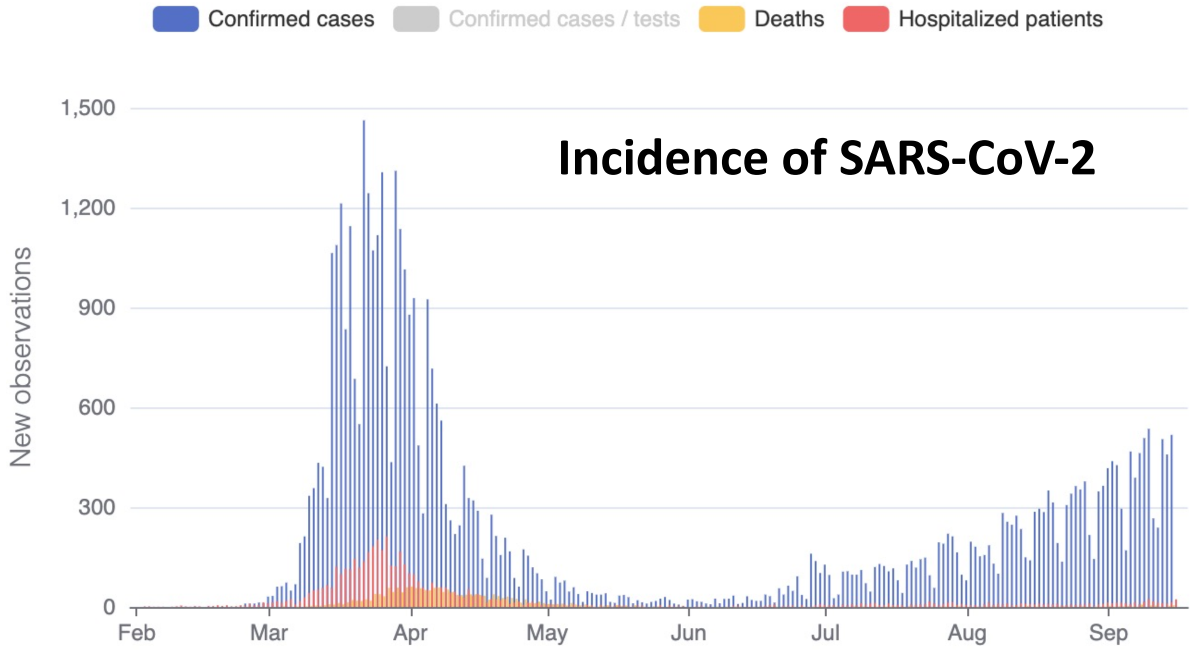


II. Wastewater

III. Variants

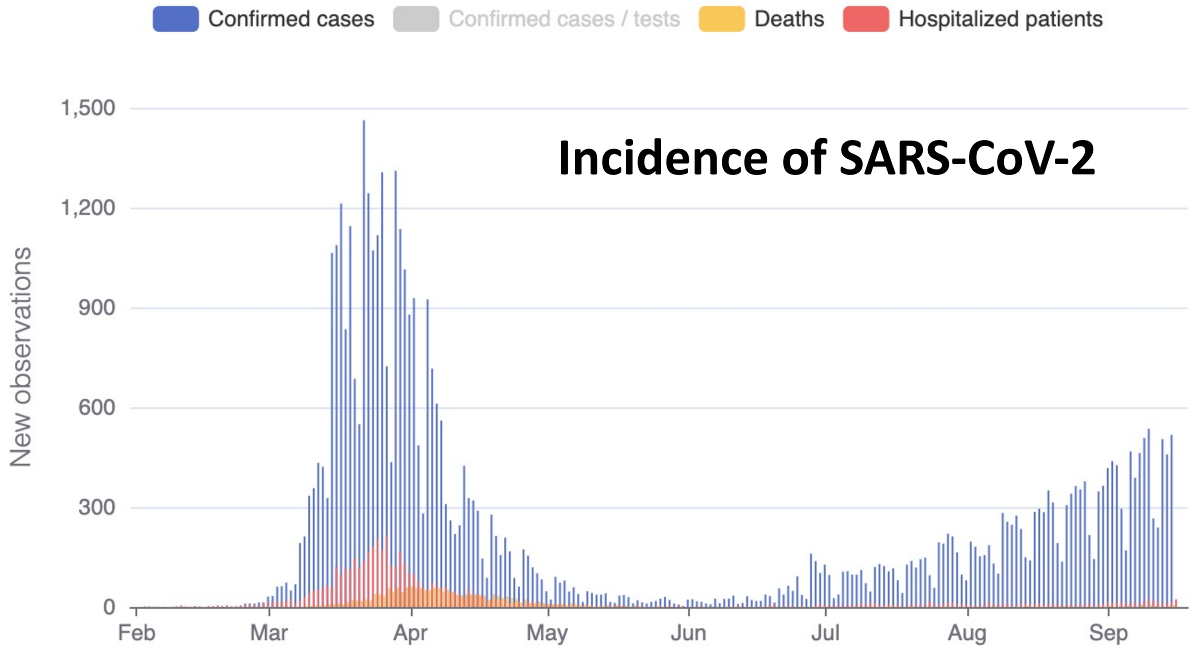
Monitoring an infectious disease epidemic

Essential to monitor disease **prevalence, incidence**, and **changes to the incidence**



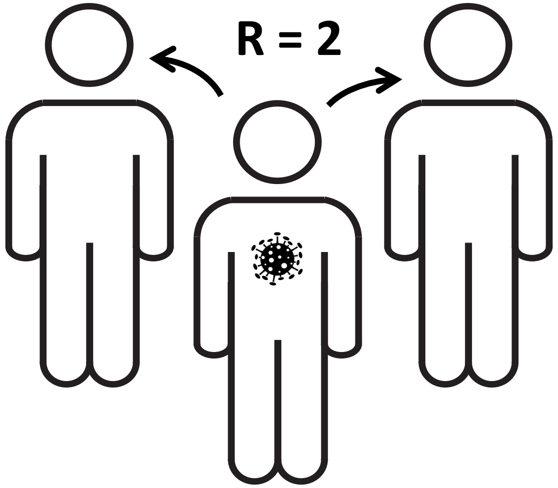
COVID-19 Re Shiny App (15.9);
Huisman *et al.* (in review, 2020);
Scire *et al.* (Swiss Med. Wkly, 2020)

Monitoring an infectious disease epidemic



Essential to monitor disease **prevalence, incidence**, and **changes to the incidence**

The **effective reproductive number** R_e :
average number of secondary infections caused by an infected individual



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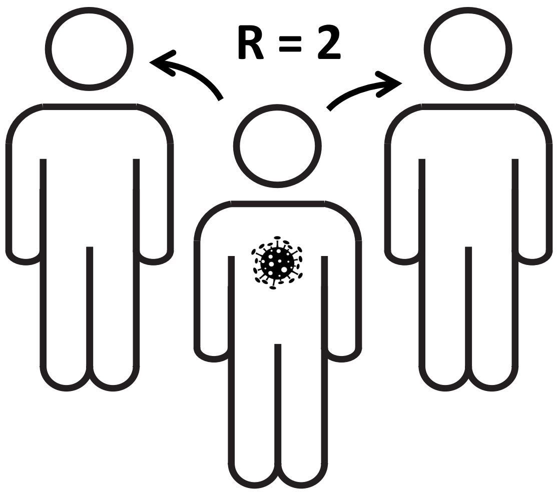
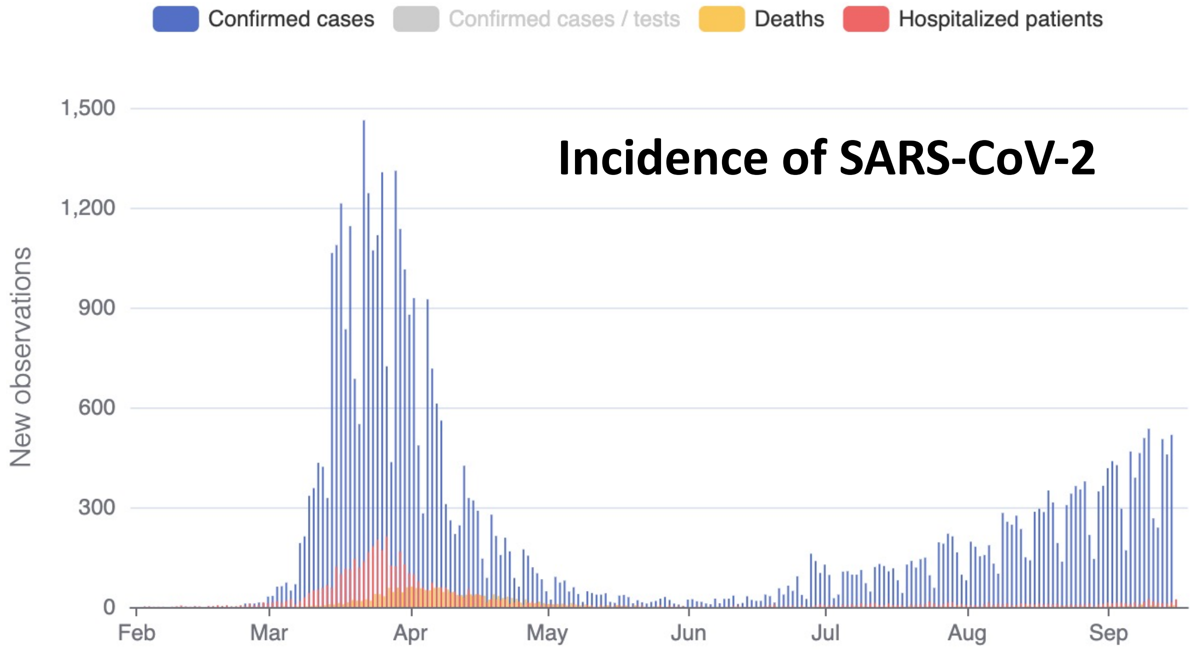
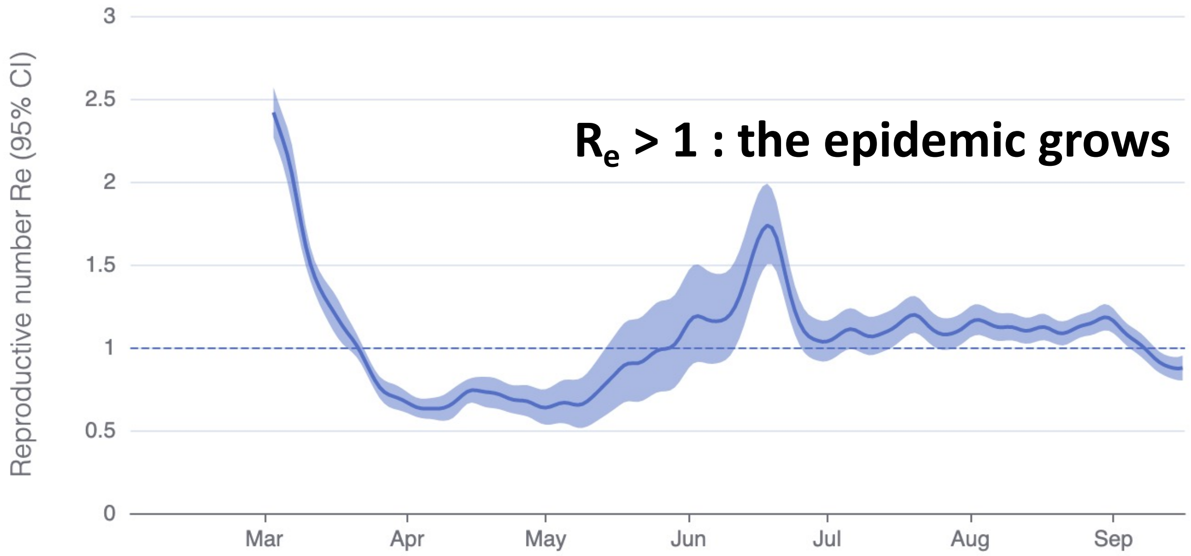
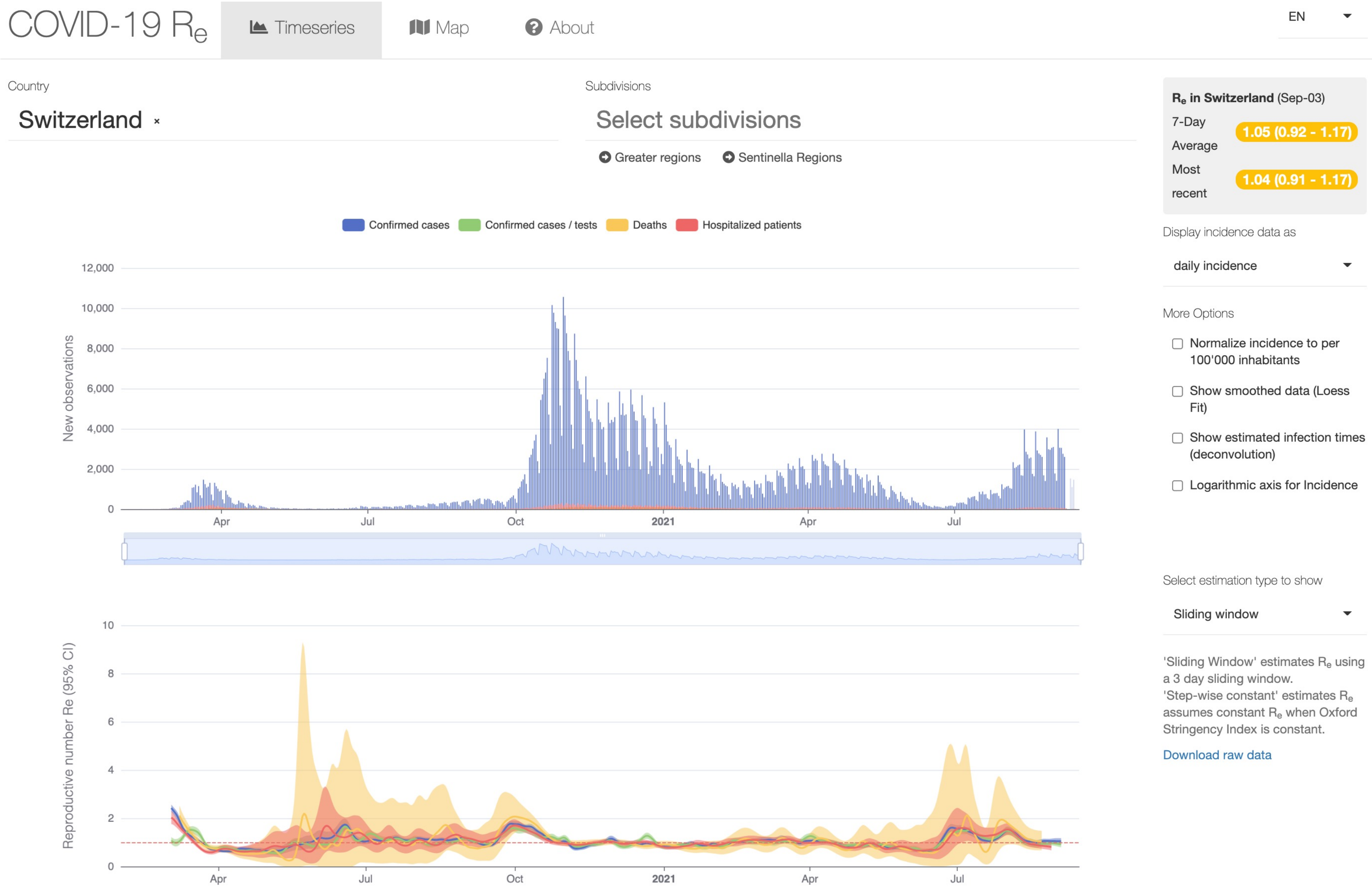






Monitoring SARS-CoV-2



Since March 2020 we **estimate R_e** for SARS-CoV-2 in Switzerland and abroad

COVID-19 Re Shiny App (15.9);
Huisman *et al.* (in review, 2020);
Scire *et al.* (Swiss Med. Wkly, 2020)

Monitoring SARS-CoV-2

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

AS 2020
www.bundesrecht.admin.ch
Massgebend ist die signierte
elektronische Fassung

Verordnung
über Massnahmen in der besonderen Lage
zur Bekämpfung der Covid-19-Epidemie

Art. 7 Abs. 2–5

Tagen liegt unter 1; massgebend sind die von der *Theoretical Biology Group* des Instituts für Integrative Biologie der Eidgenössischen Technischen Hochschule Zürich veröffentlichten Daten[2].

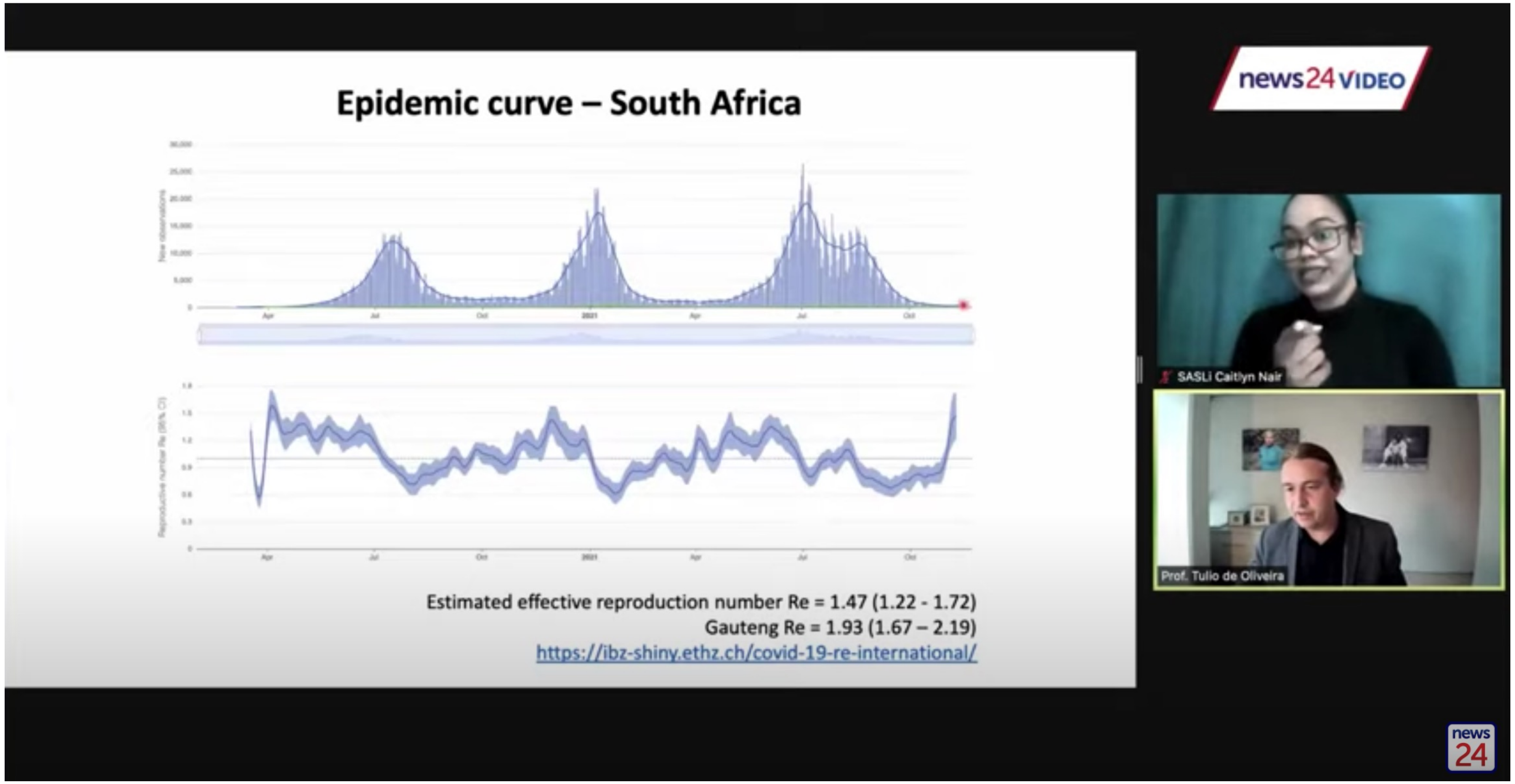
"The data published by the Theoretical Biology Group […] are authoritative"

Since March 2020 we **estimate R_e** for SARS-CoV-2 in Switzerland and abroad

These estimates directly **inform public health policy** in Switzerland

COVID-19 Re Shiny App (15.9);
Huisman *et al.* (in review, 2020);
Scire *et al.* (Swiss Med. Wkly, 2020)
AS 2020 5377 (https://www.admin.ch/opc/de/official-compilation/2020/index_157.html)

Monitoring SARS-CoV-2



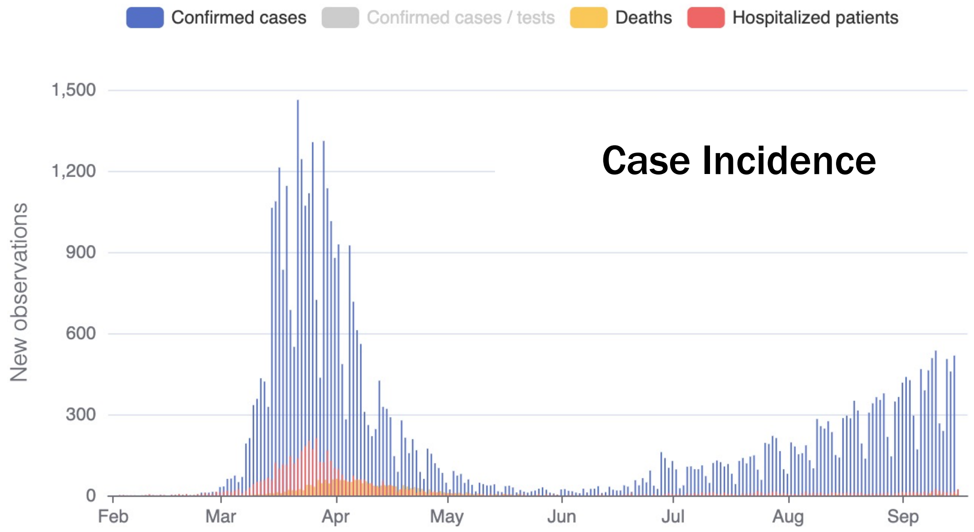
Since March 2020 we **estimate R_e** for SARS-CoV-2 in Switzerland and abroad

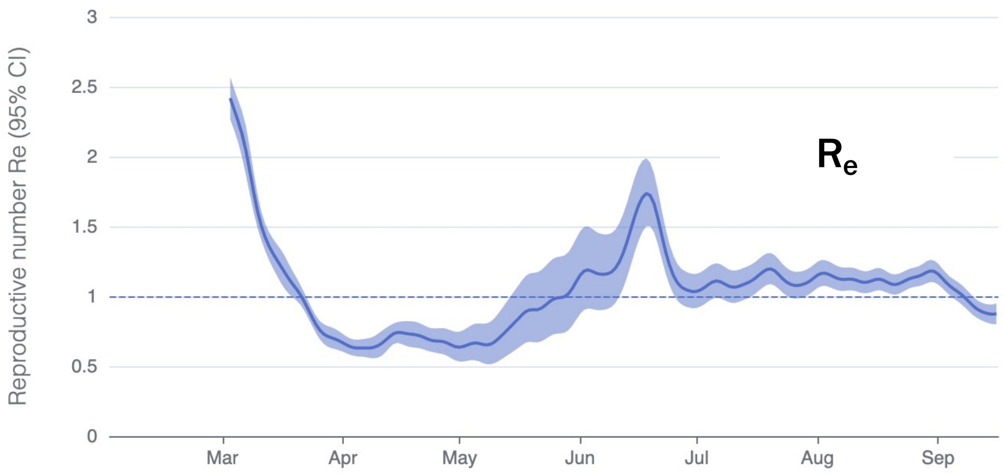
These estimates directly **inform public health policy** in Switzerland **and abroad**

Used in the presentation of omikron to the public; 25.11

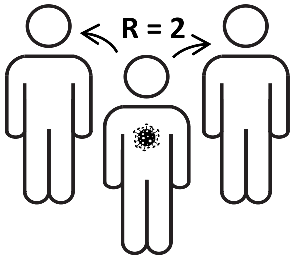
COVID-19 Re Shiny App (15.9);
Huisman *et al.* (in review, 2020);
Scire *et al.* (Swiss Med. Wkly, 2020)
Tulio de Oliveira (https://www.youtube.com/watch?v=Vh4XMueP1zQ&ab_channel=News24)

Our pipeline



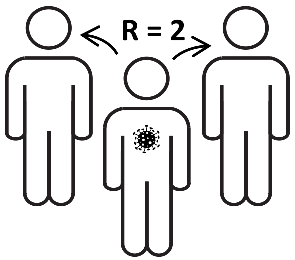


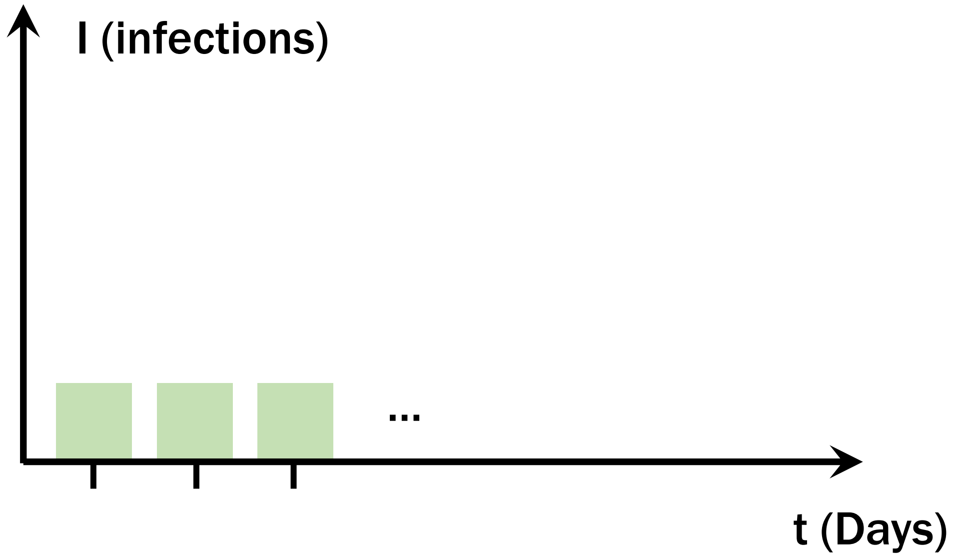
Core idea: infection incidence contains information on R_e

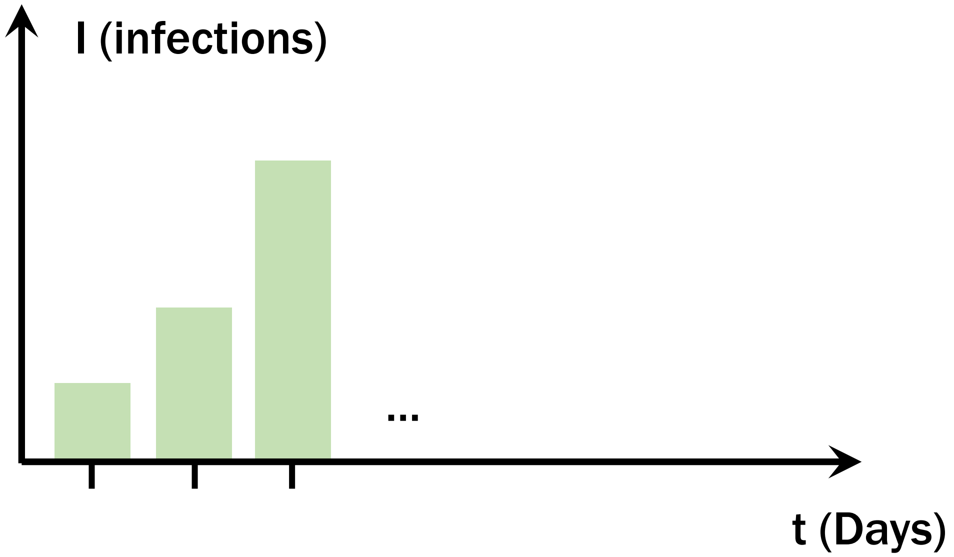


COVID-19 Re Shiny App (16.9)
Huisman *et al.* (in review, 2020)
Scire *et al.* (https://github.com/covid-19-Re/estimateR, 2021)

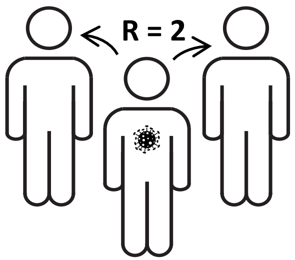
The infection incidence contains information on R_e

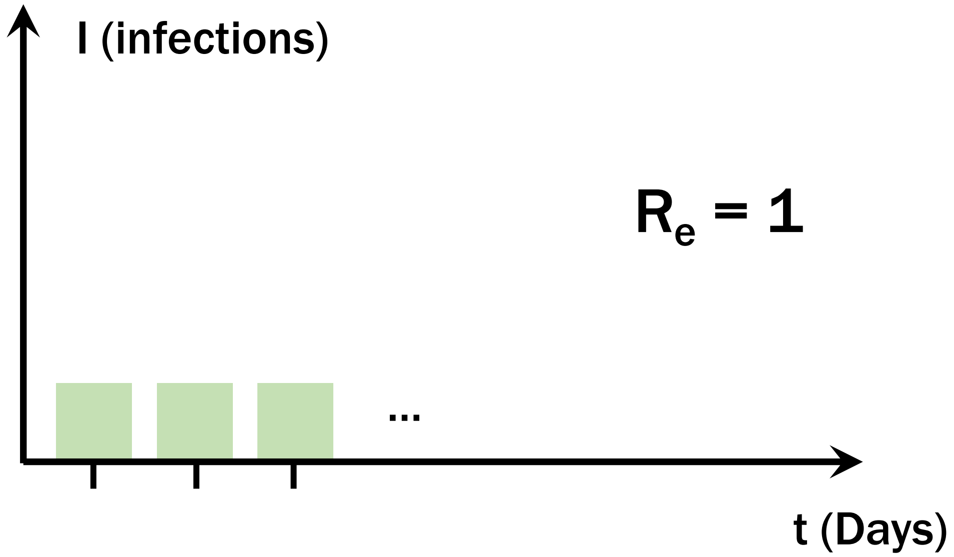


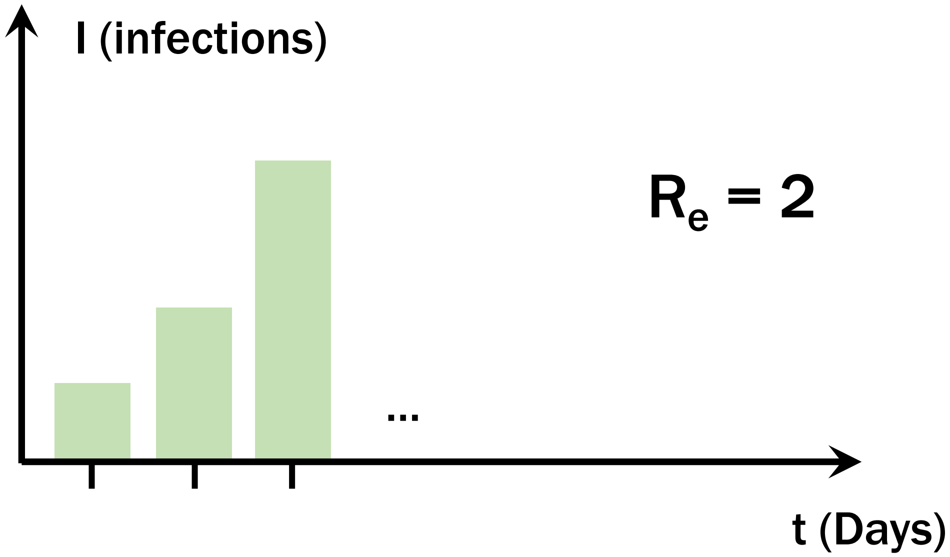




The infection incidence contains information on R_e



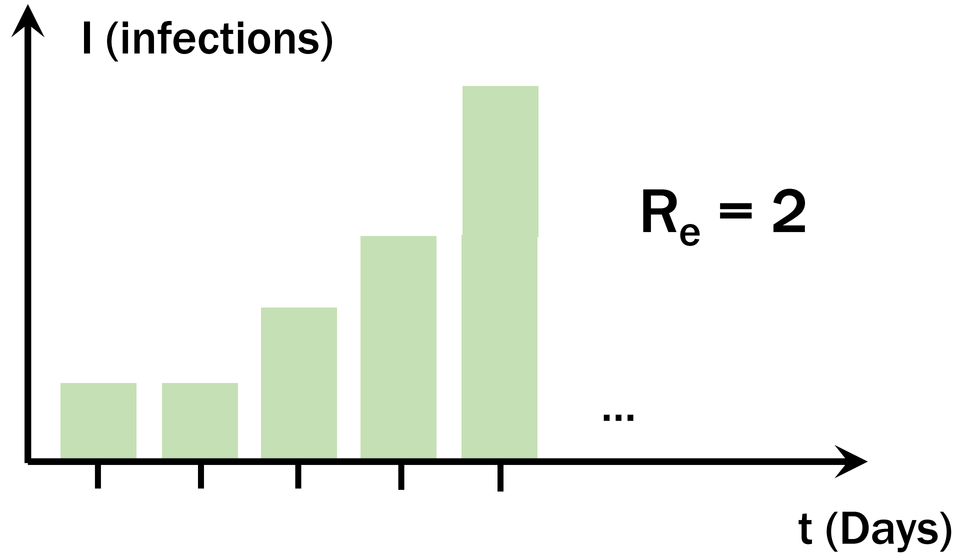




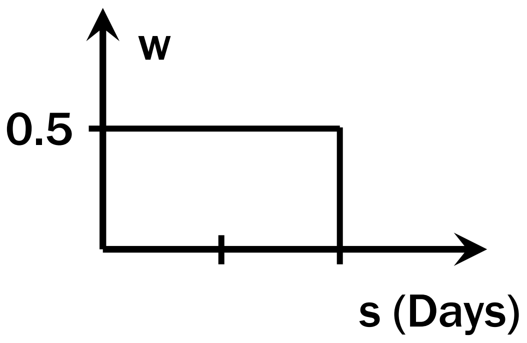
All new infections take place the next day:

$$I_t = R_e(t) \cdot I_{t-1}$$

When infections occur is given by the infectivity profile



Infectivity profile:



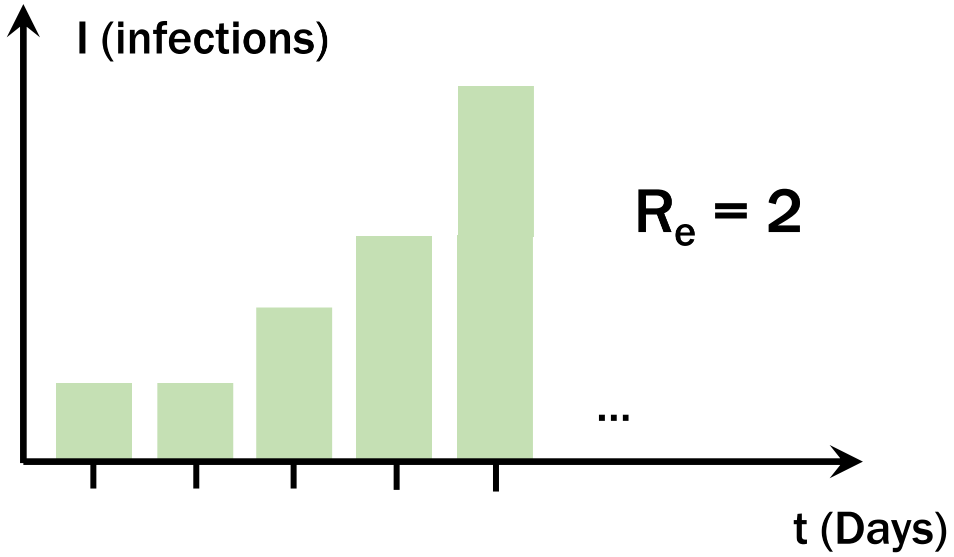
All new infections take place over 2 days:

$$I_t = R_e(t) \cdot (\tfrac{1}{2} I_{t-1} + \tfrac{1}{2} I_{t-2})$$

For a disease,

this can be measured

The EpiEstim method



All new infections take place over 2 days:

$$I_t = R_e(t) \cdot (½\, I_{t-1} + ½\, I_{t-2})$$

Model which describes the incidence I_t by:

(i) Past incidence $I_0 \dots I_{t-1}$,

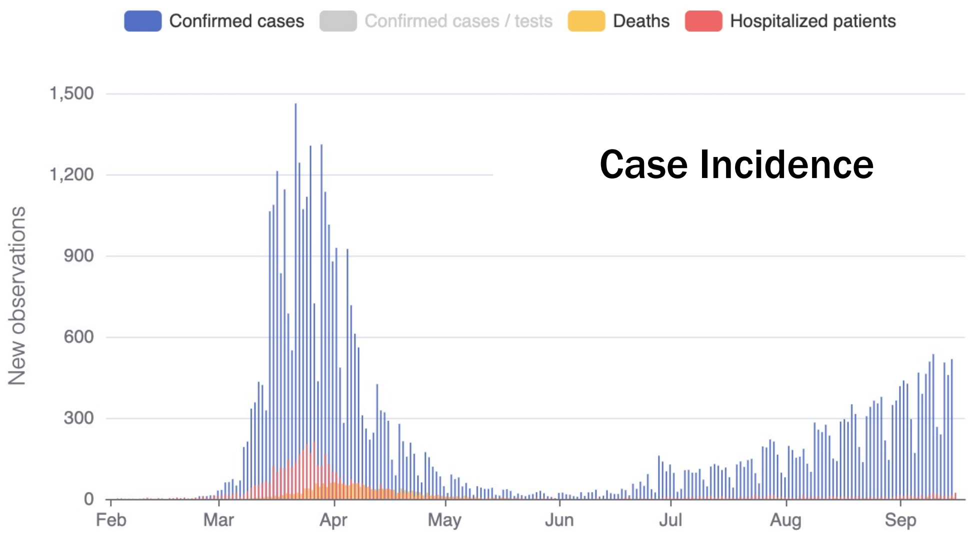
(ii) The infectivity profile

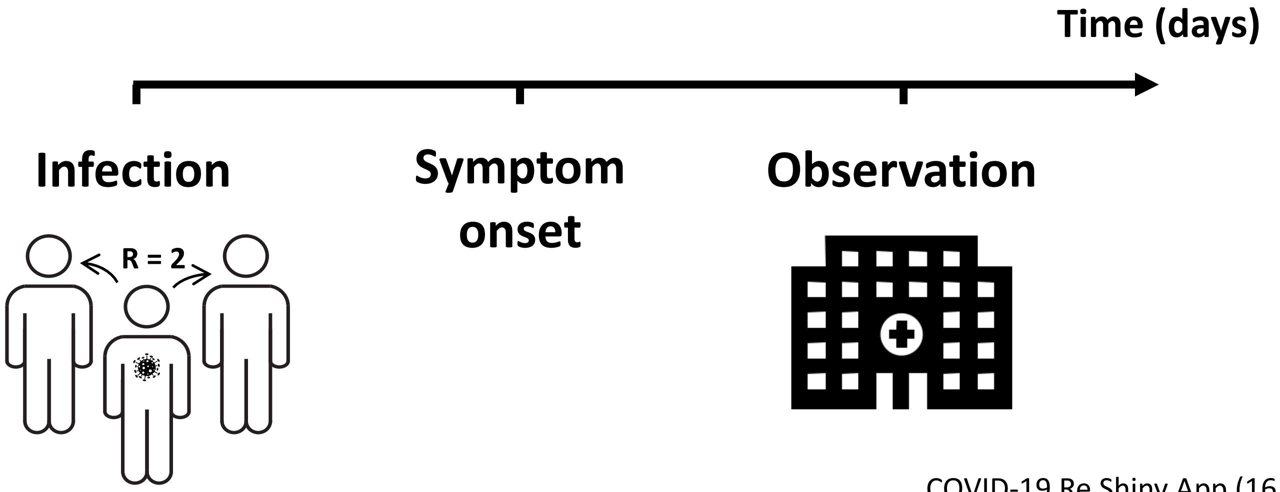
(iii) $R_e(t)$

We estimate the $R_e(t)$ most likely to have led to the observed infection incidence

Cori et al. (2013)

Problem: infections are observed with delay





COVID-19 Re Shiny App (16.9)
Huisman *et al.* (in review, 2020)

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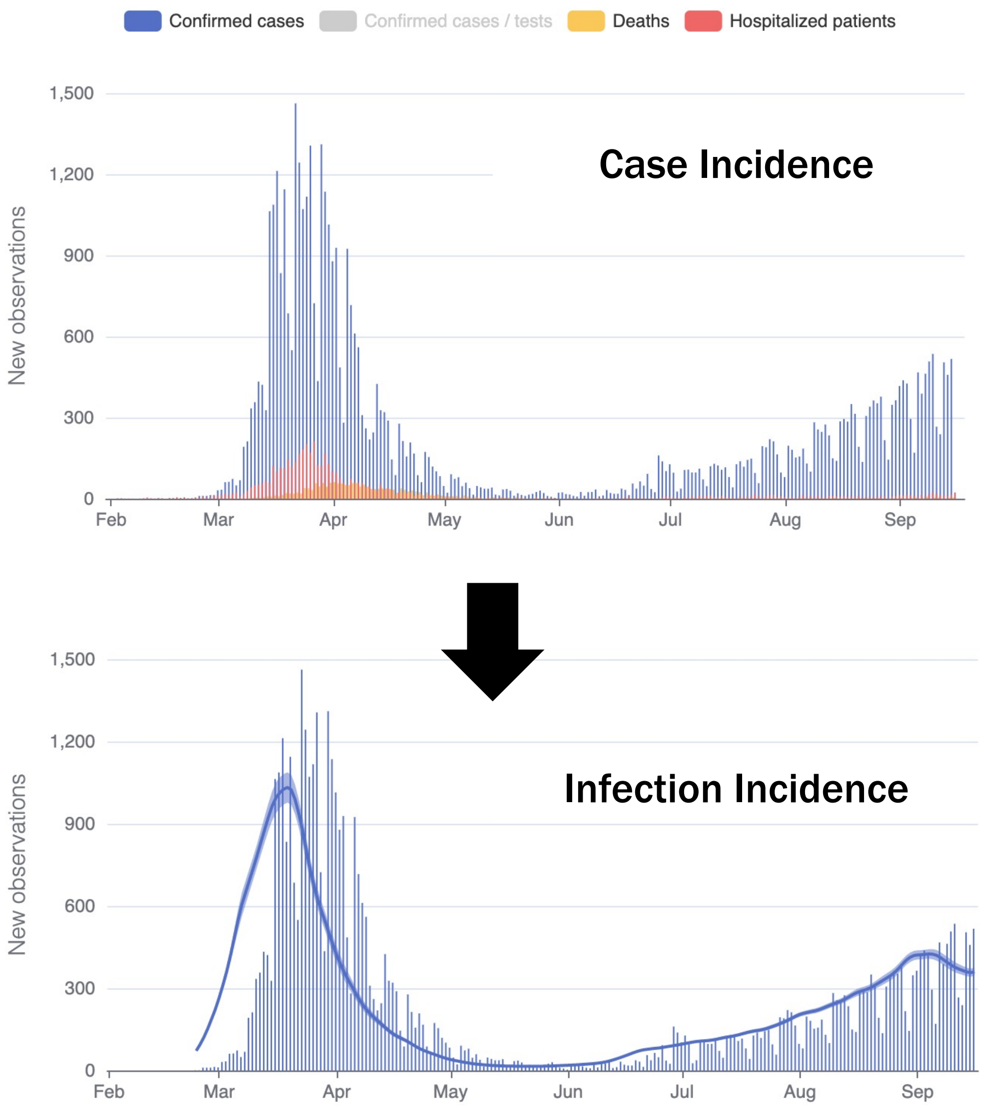
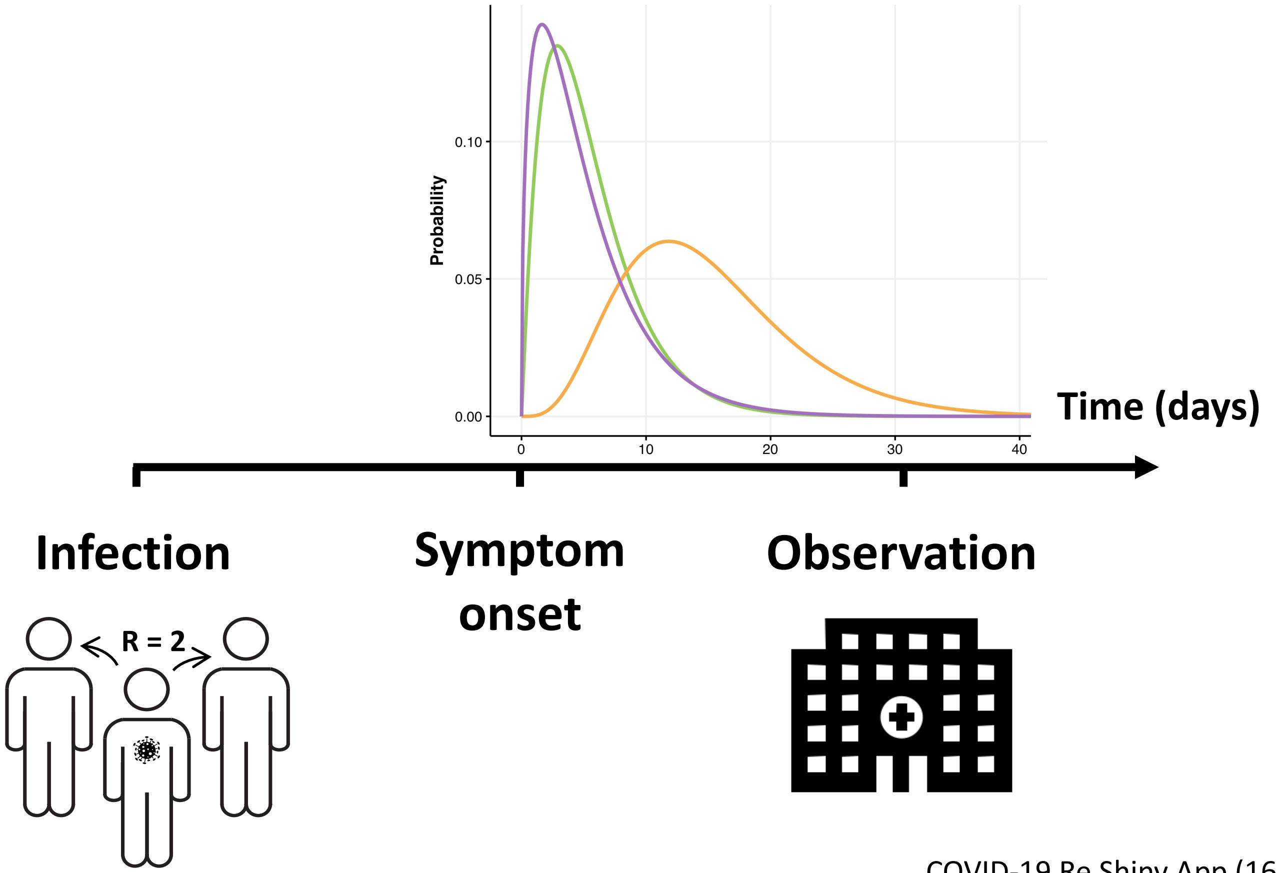


(i) Use a **deconvolution** to infer the time series of infection incidence from the smoothed case observations



COVID-19 Re Shiny App (16.9)
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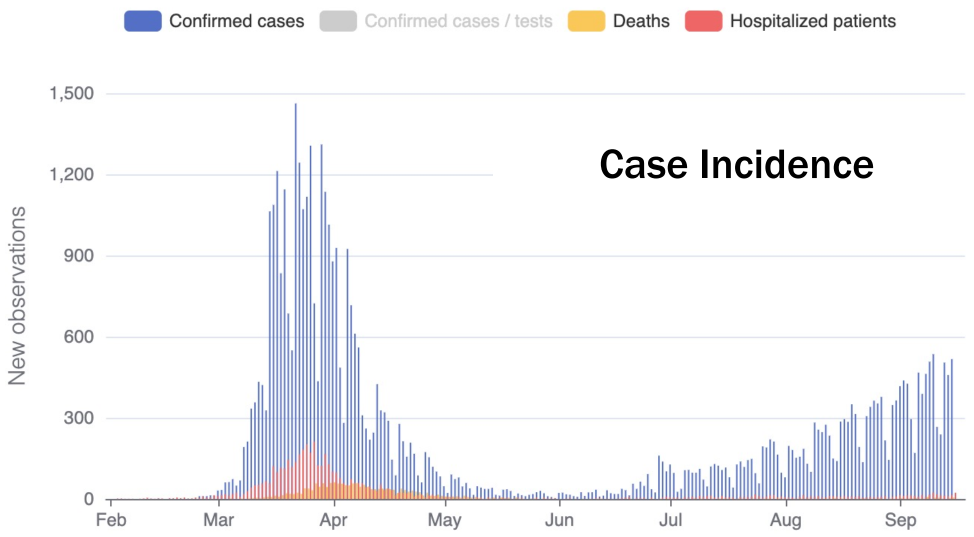
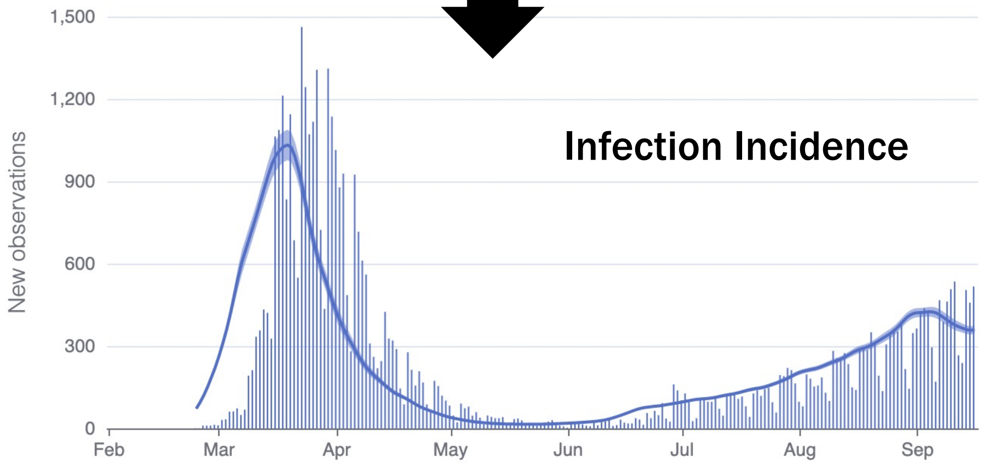
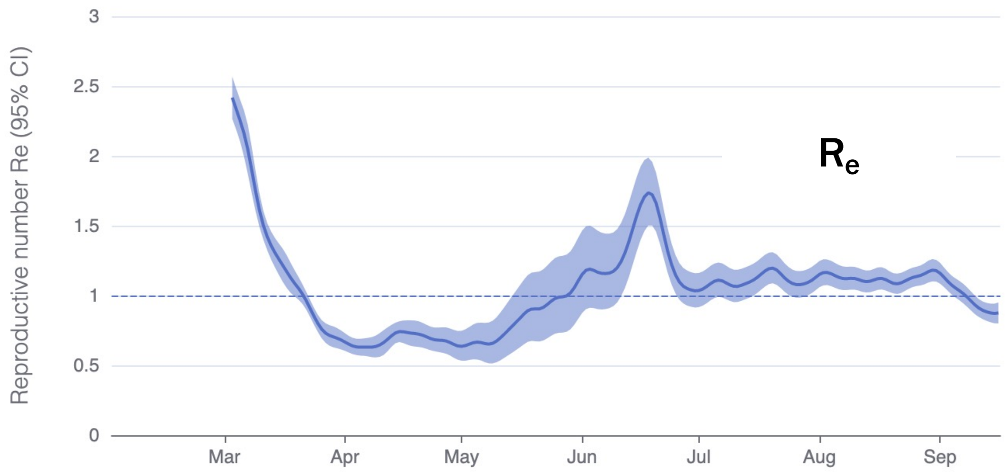
Our pipeline





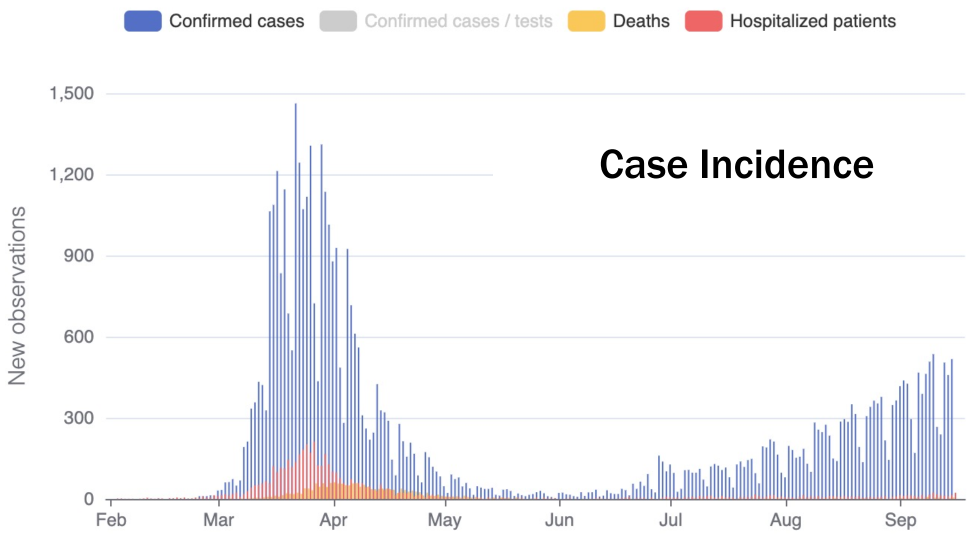
(i) Use a **deconvolution** to infer the time series of infection incidence from the smoothed case observations

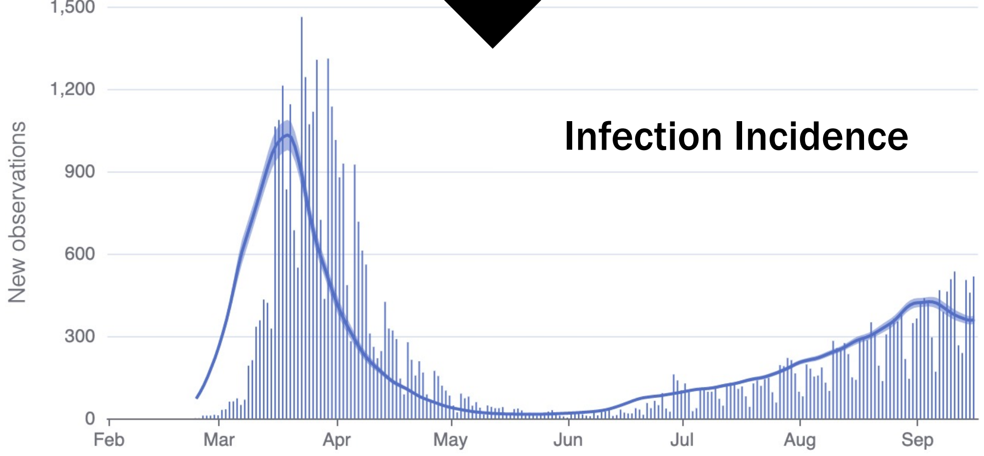
(ii) Use **EpiEstim** to estimate R_e from the infection incidence



Cori et al. (2013)
COVID-19 Re Shiny App (16.9)
Huisman *et al.* (in review, 2020)

Our pipeline

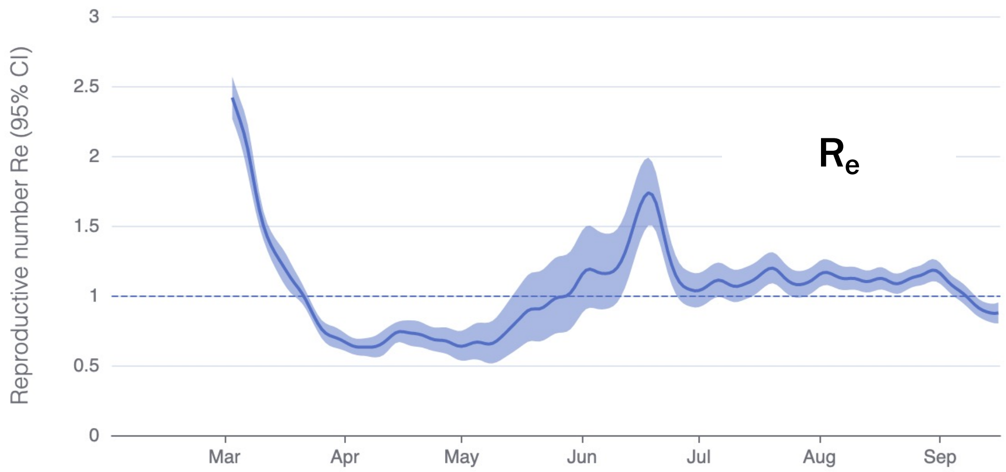




(i) Use a **deconvolution** to infer the time series of infection incidence from the smoothed case observations

(ii) Use **EpiEstim** to estimate R_e from the infection incidence

(iii) **Bootstrap** case incidence and repeat to obtain confidence intervals



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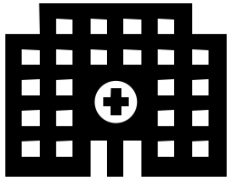
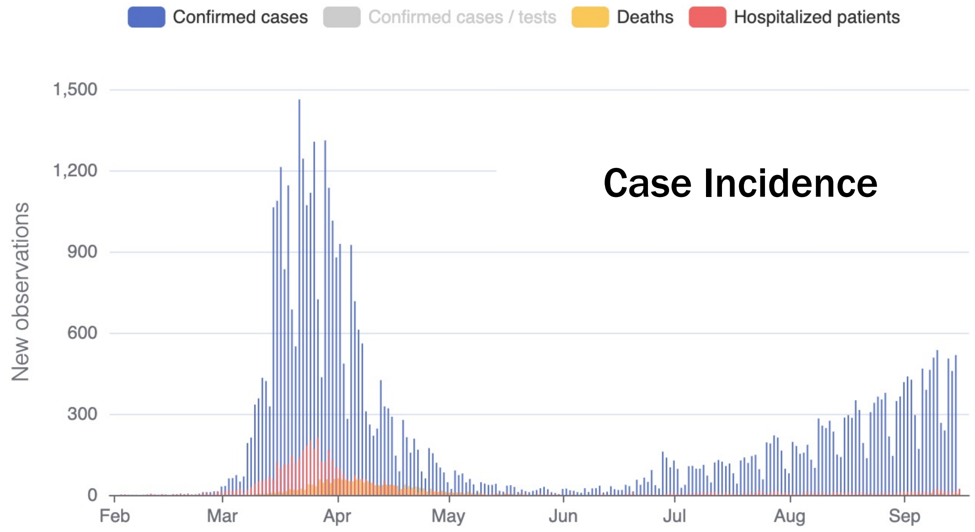
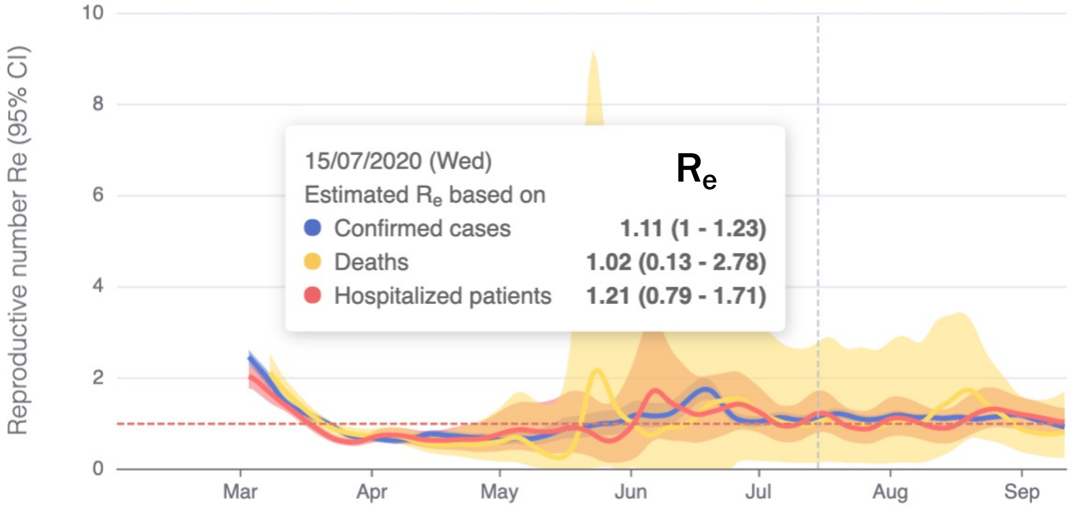






Proxies for infections:

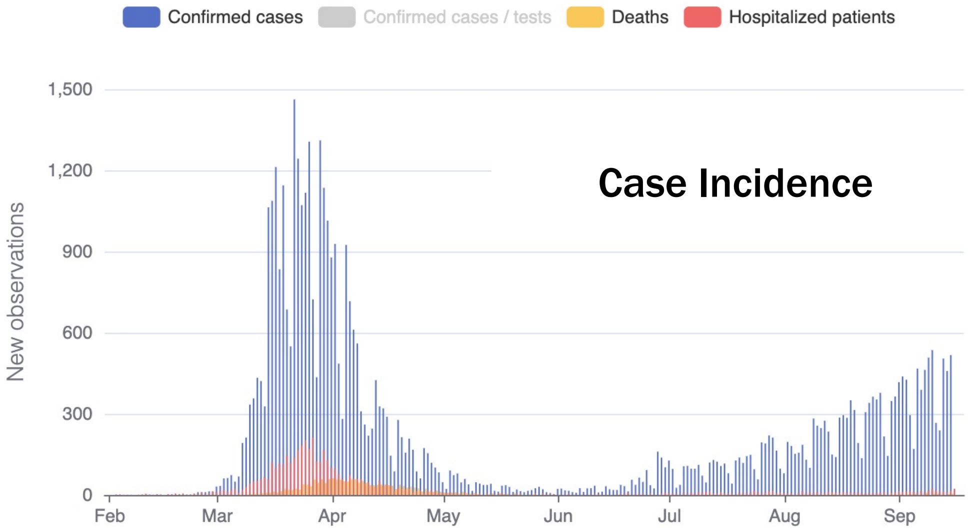
Confirmed cases

Hospitalisations

Deaths

COVID-19 Re Shiny App (16.9)
Huisman *et al.* (in review, 2020)

Goal: independent proxy



Independent, population level proxy?

Proxies for infections:

Confirmed cases
Hospitalisations
Deaths

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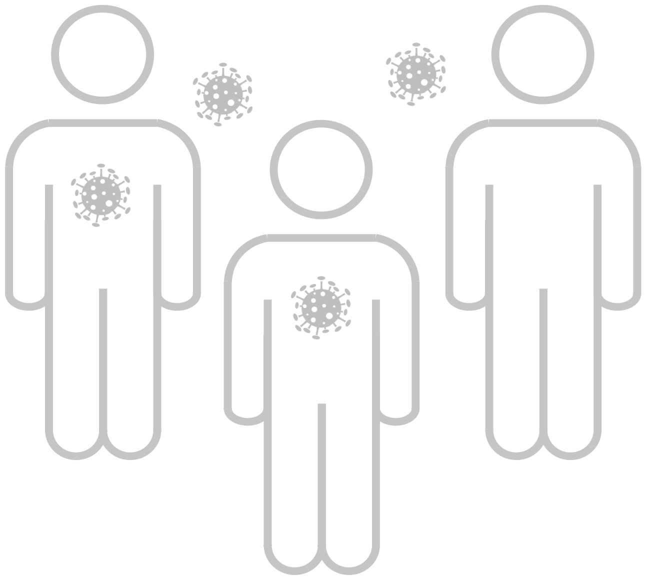
Huisman *et al.* (in review, 2020)

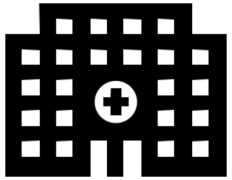
I. R_e

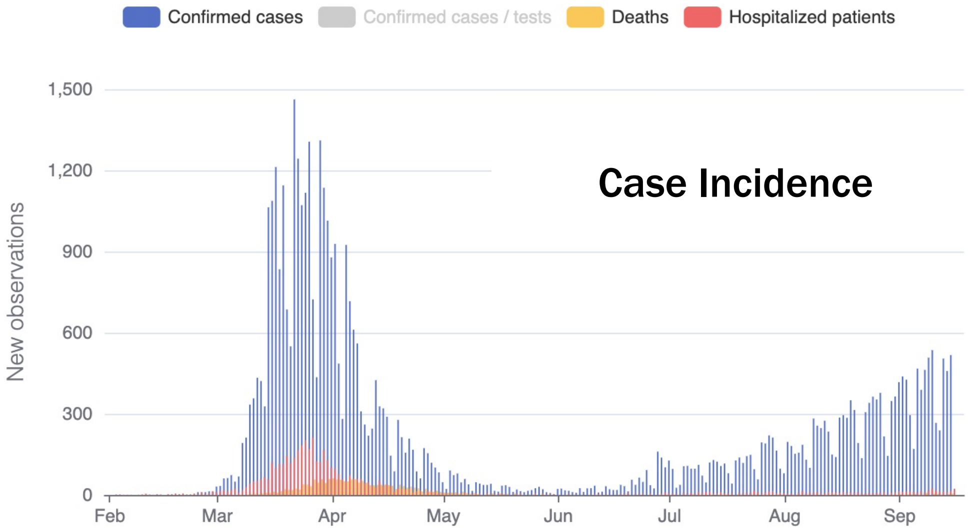


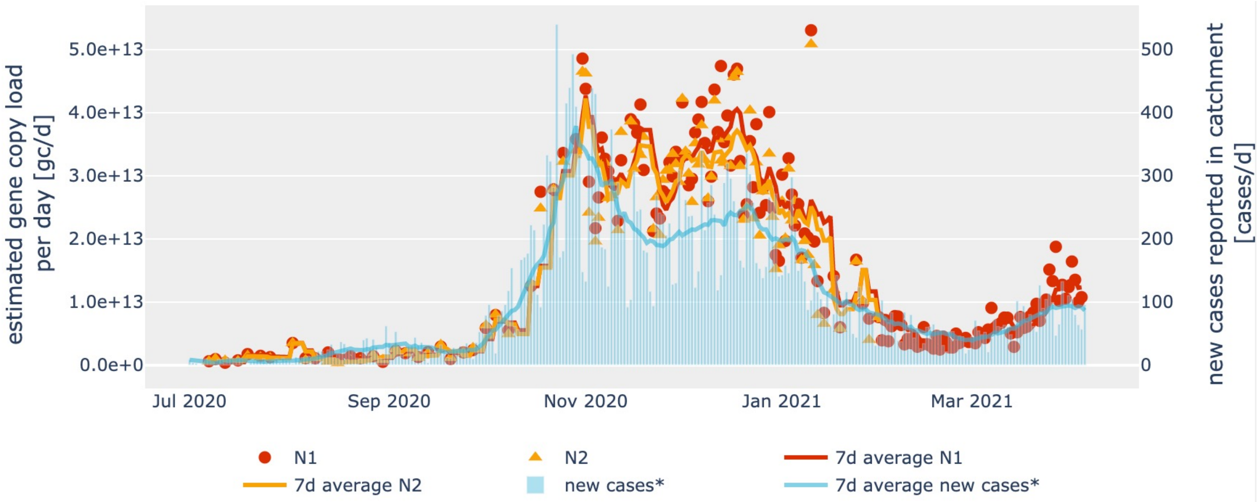
II. Wastewater

III. Variants

Goal: Wastewater-based R_e







Proxies for infections:

- Confirmed cases
- Hospitalisations
- Deaths

Wastewater is an **independent** proxy

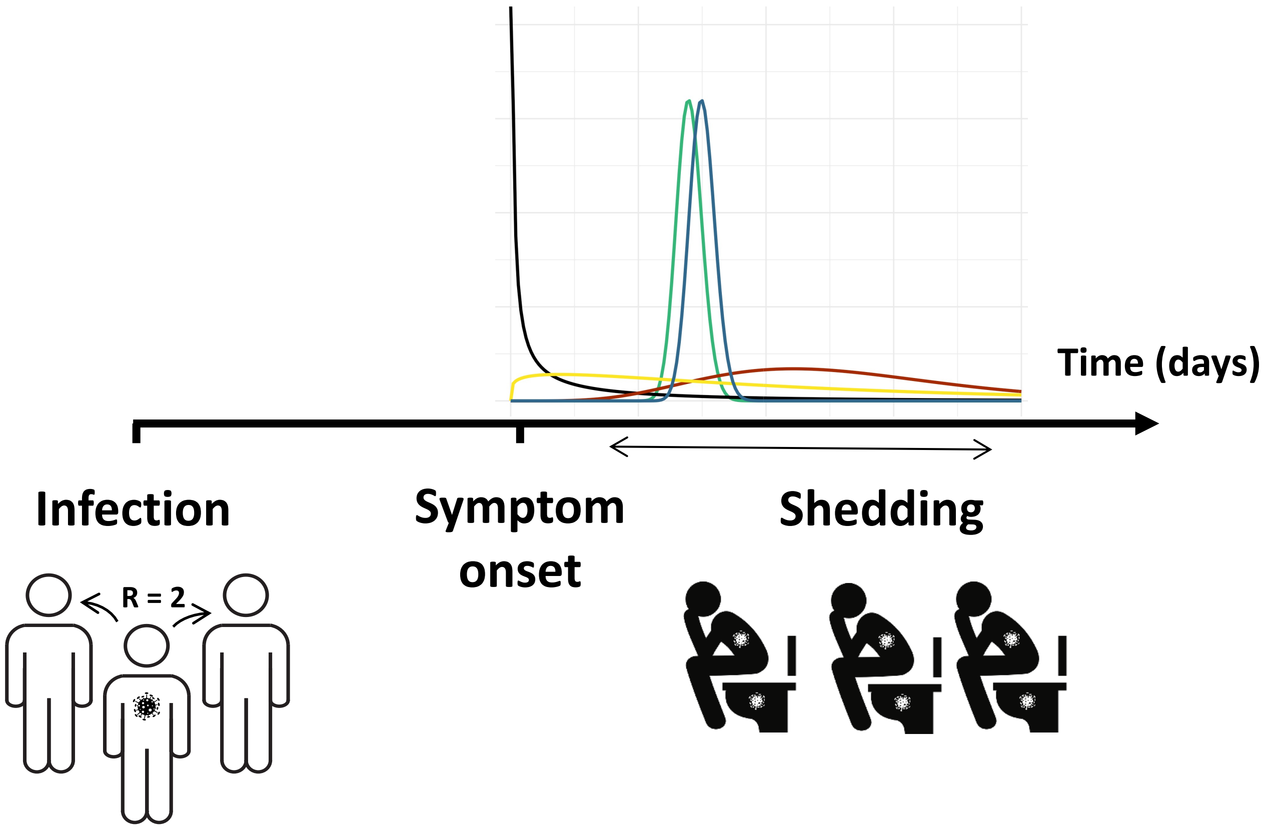
COVID-19 Re Shiny App (16.9)

Huisman *et al.* (in review, 2020)

Status 11.4 (http://parsivel-eawag.ch/sarscov2/ARA_Werdhoelzli_ddPCR.html)

How delayed is wastewater wrt. infection?

(i) Use a **deconvolution** to infer the time series of infection incidence from the smoothed ~~case~~ wastewater observations



Huisman *et al.* (in review, 2021)

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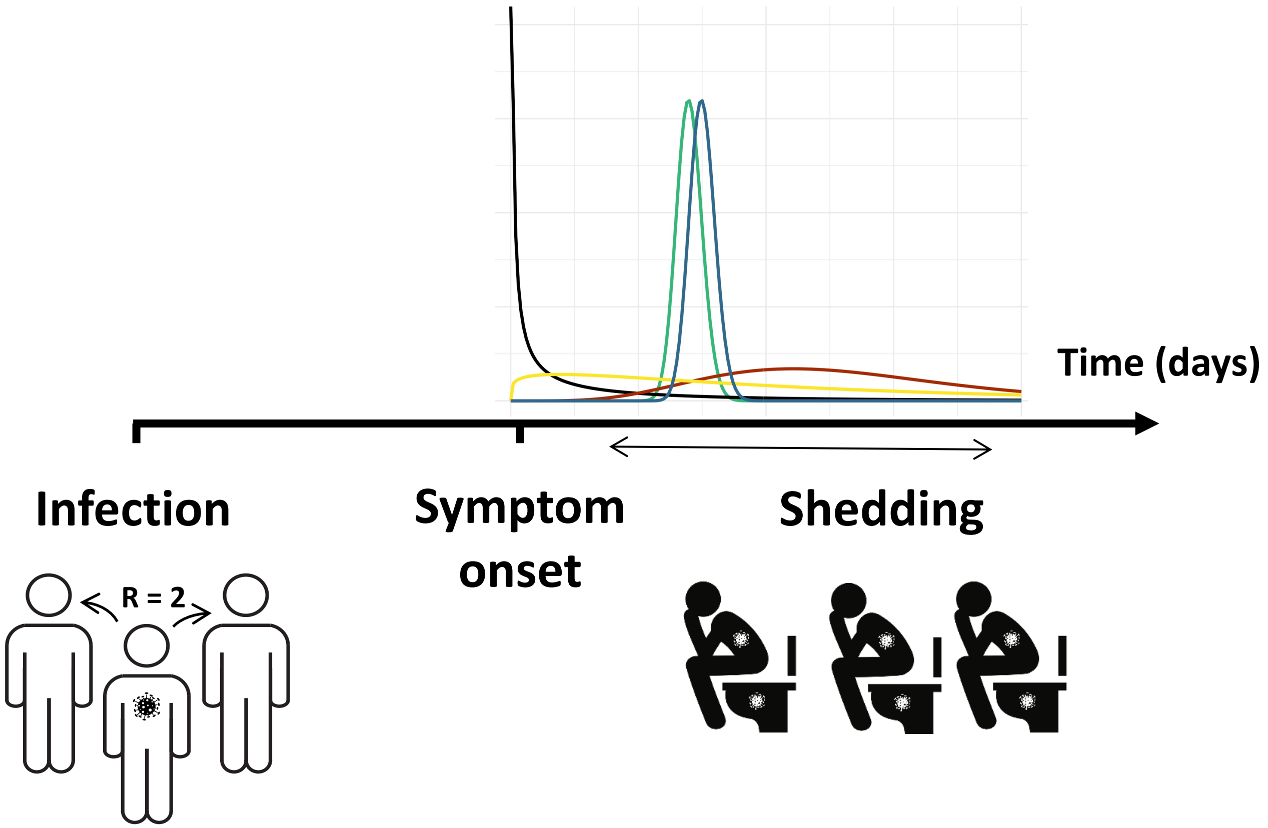
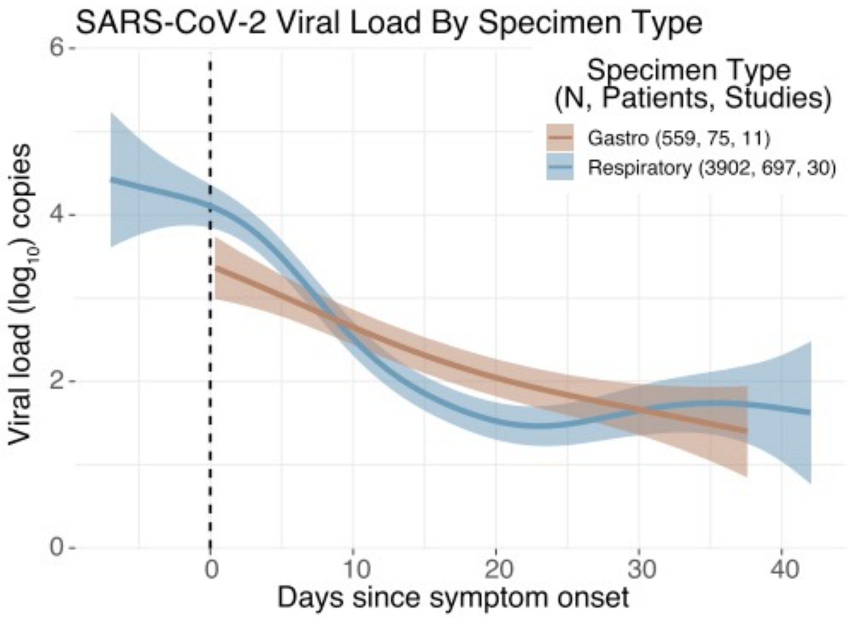
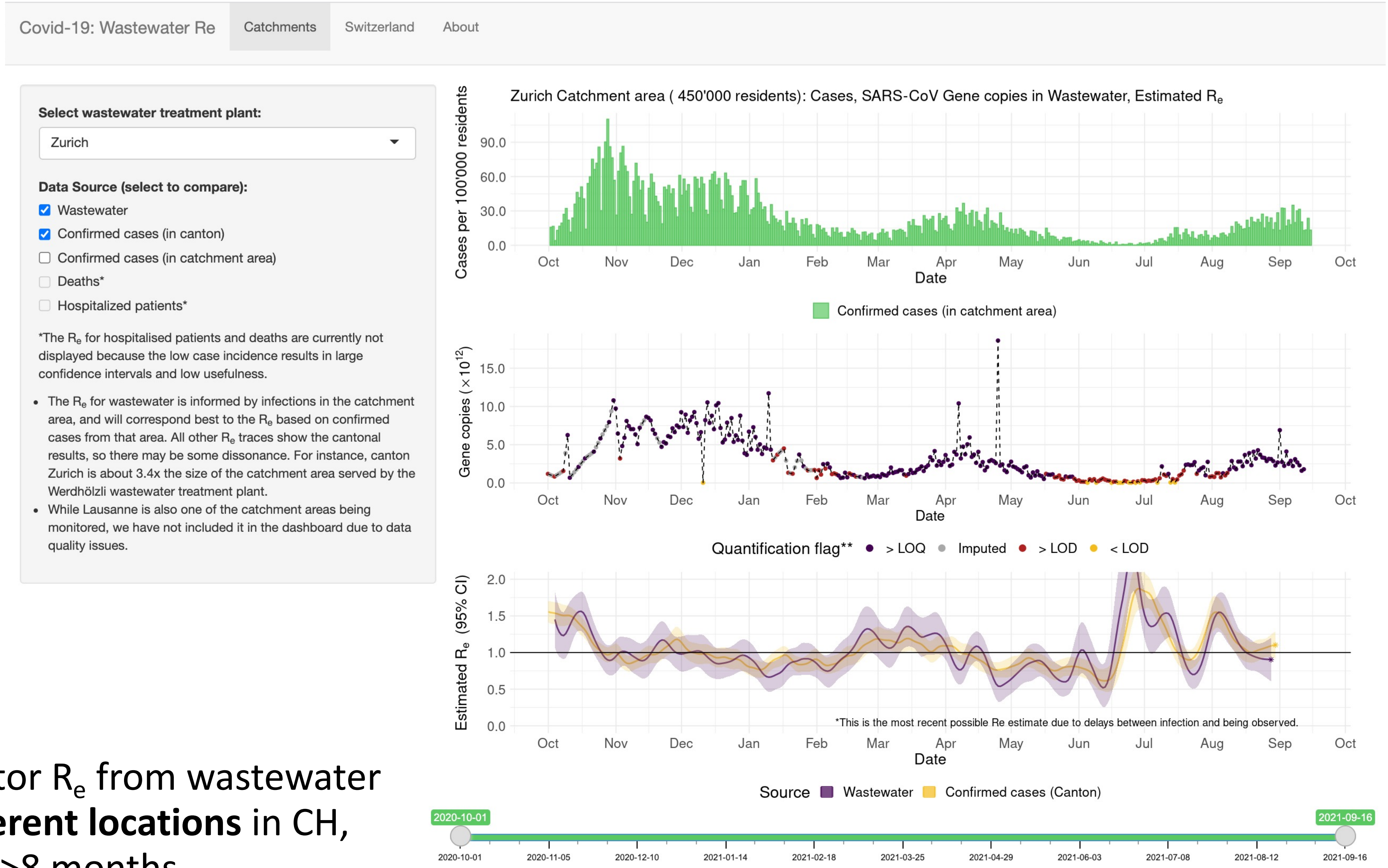




We care about the temporal dynamics of shedding **not** the absolute magnitude

Huisman *et al.* (in review, 2021)
Benefield *et al.* (medRxiv, 2020)

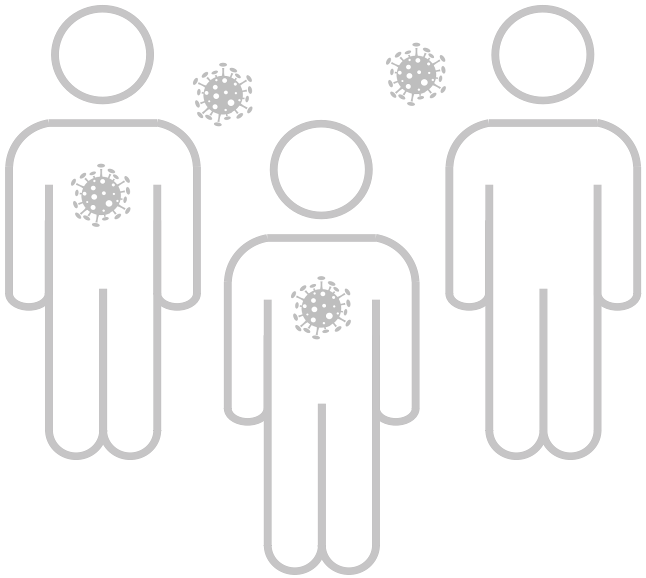
Continuous monitoring of the wastewater-based R_e



We monitor R_e from wastewater for **6 different locations** in CH, some for >8 months

https://ibz-shiny.ethz.ch/wastewaterRe/ (16.9);
Huisman *et al.* (in review, 2021)

I. R_e



II. Wastewater

III. Variants

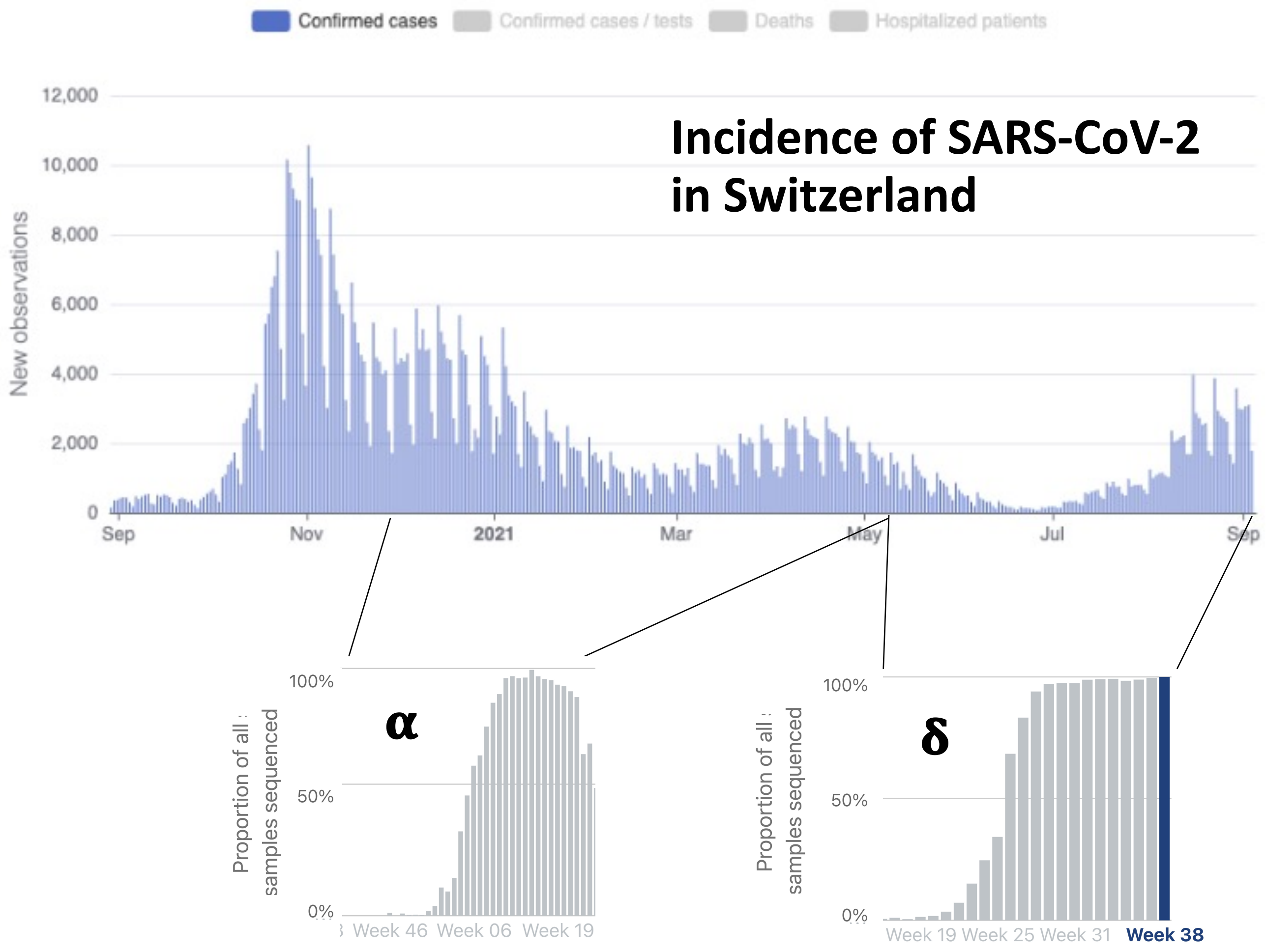
Variants: the hidden danger

Genomics can reveal dynamics that would otherwise remain hidden

- **Source** and frequency of introductions
- Population structure (**variants**)

Variants of concern exhibit one of the following characteristics (WHO):

- Increased transmission
- Increased severity
- Decreased effectiveness diagnostics, therapeutics, vaccines



https://ibz-shiny.ethz.ch/covid-19-re-international/ (15.9.2021)
Huisman*, Scire* *et al.* (in review)
www.cov-spectrum.ethz.ch (28.9.2021)

A busy Christmas

Report 42 - Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: insights from linking epidemiological and genetic data

WHO Collaborating Centre for Infectious Disease Modelling, MRC Centre for Global Infectious Disease Analysis, Abdul Latif Jameel Institute for Disease and Emergency Analytics (J-IDEA), in collaboration with the Department of Mathematics, Imperial College London, University of Edinburgh, Public Health England (PHE), the Wellcome Sanger Institute, University of Birmingham and the COVID-19 Genomics UK (COG-UK) Consortium+.

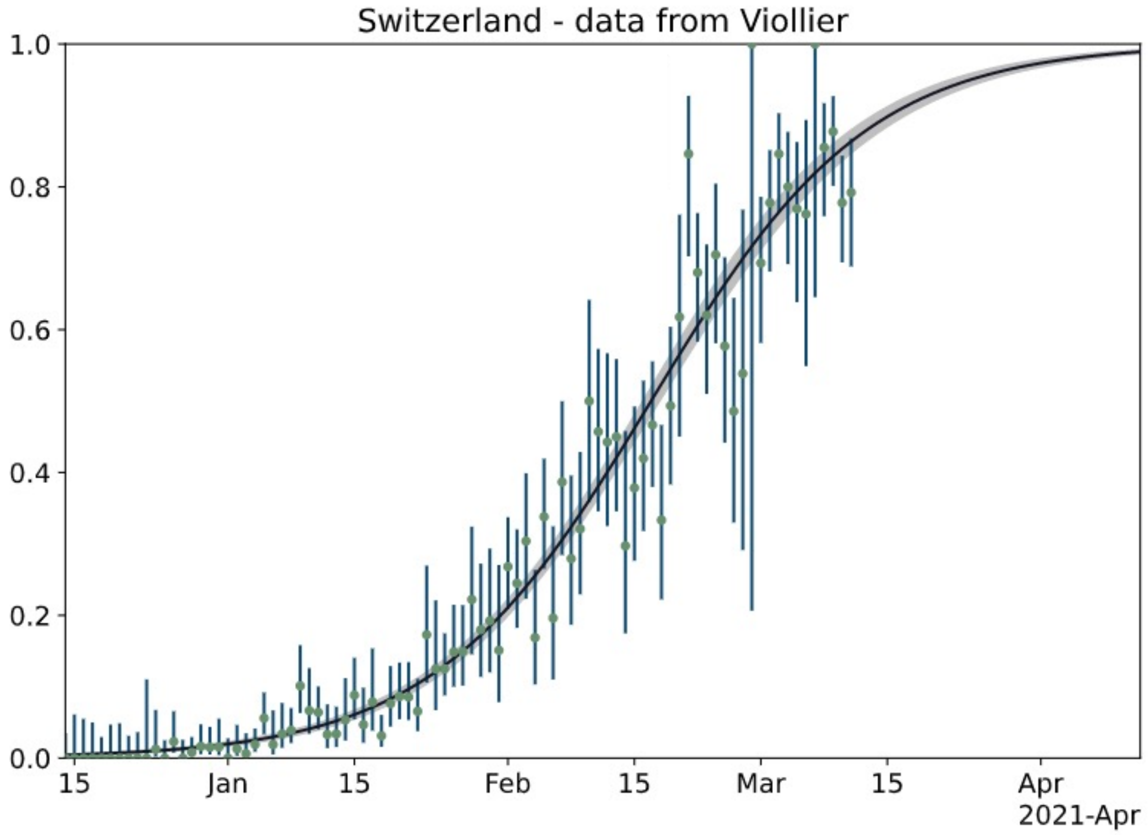
Key info

Date:
31 December 2020

Policy question mid Dec. 2020:
Does B.1.1.7 have a transmission advantage and
how will it impact the Swiss epidemic?

Sequencing reveals the proportion of B.1.1.7 (α)

Date	Region	# Total sequenced	# B.1.1.7
2020-12-21	Nordwestschweiz	9	5
2020-12-21	Grossregion Zurich	3	3
2020-12-22	Central Switzerland	2	1
…	…	…	…



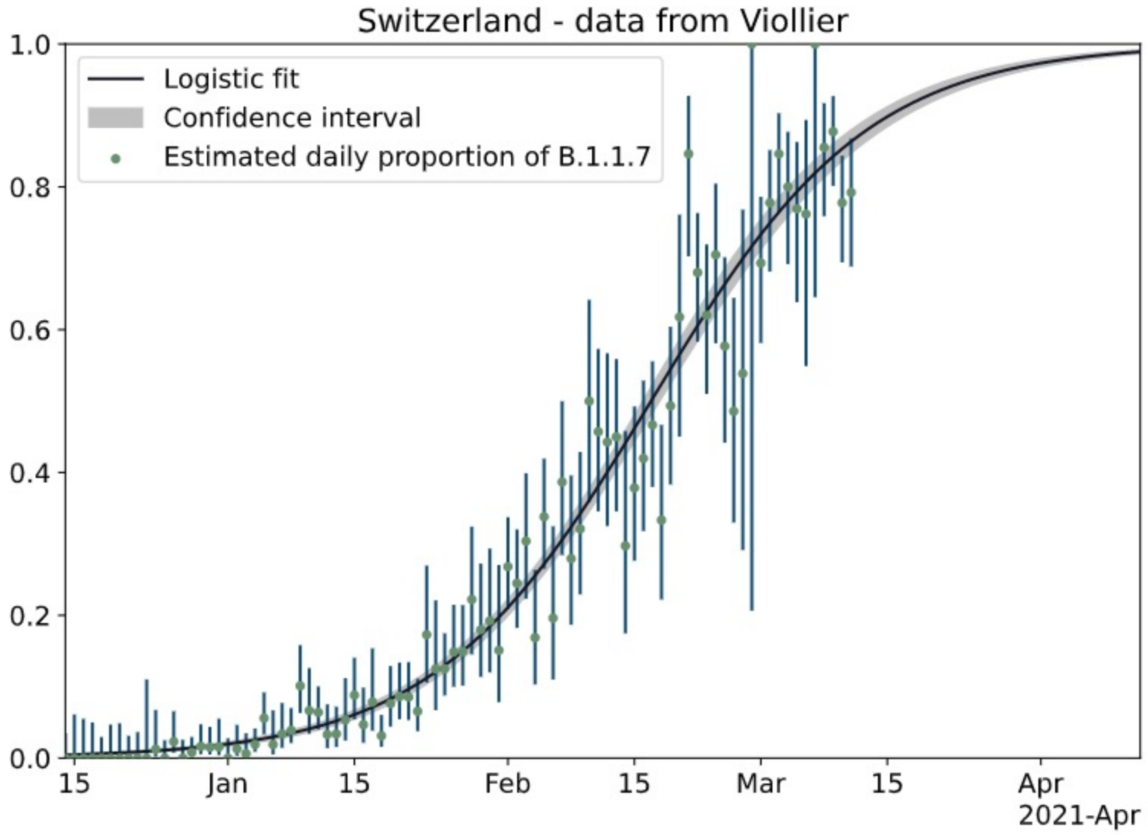
Chen *et al.* (Epidemics, 2021)

Transmission fitness advantage of B.1.1.7 (α)

Fit a logistic curve to variant proportions; estimate growth rate

This allows to estimate the fitness advantage compared to other variants

Transmission **fitness advantage** of 43–52 % compared to other variants



Chen *et al.* (Epidemics, 2021)

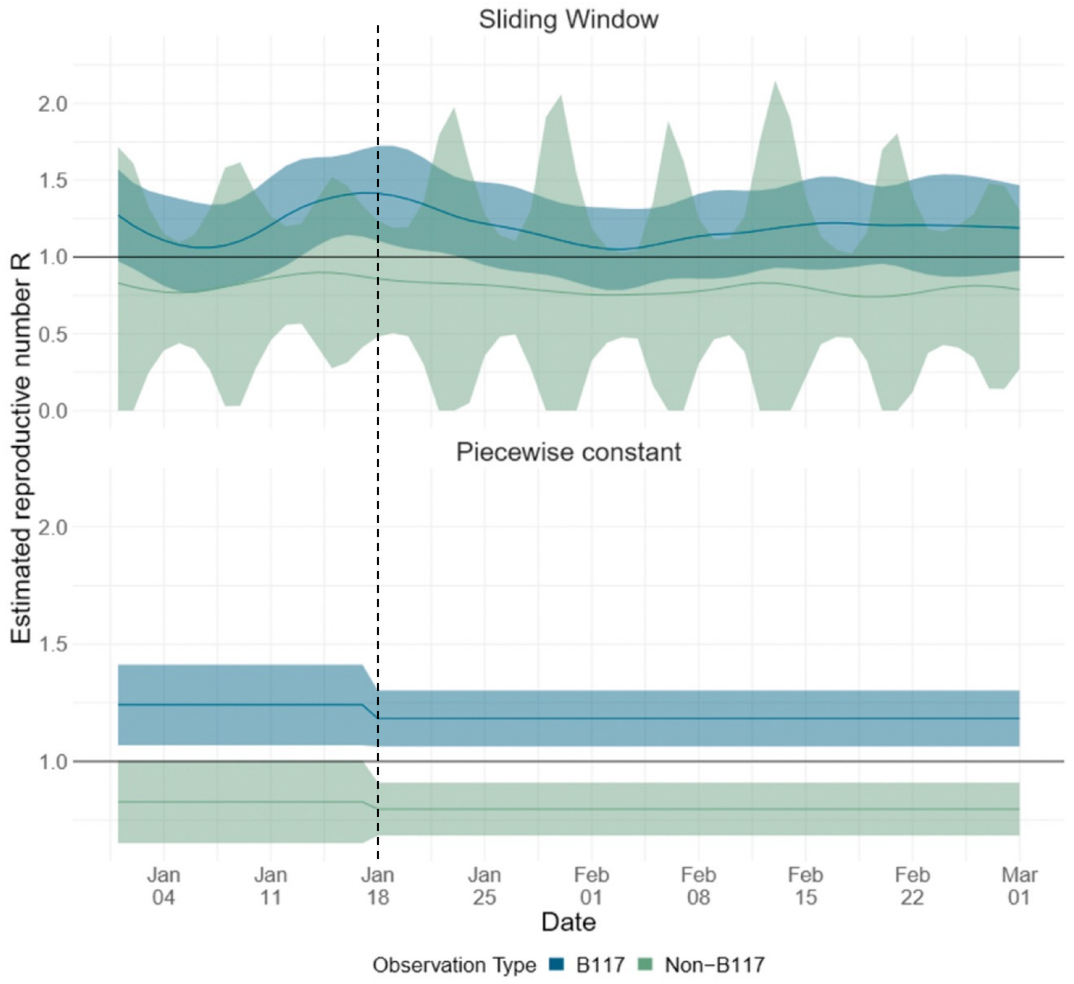
Application: variant-specific R_e

Estimate **variant incidence** from the variant proportions and case incidence

Markedly different R_e estimates (early Jan.)

B1.1.7: 1.24 [1.07–1.41]

Non-B1.1.7: 0.83 [0.65–1.00]

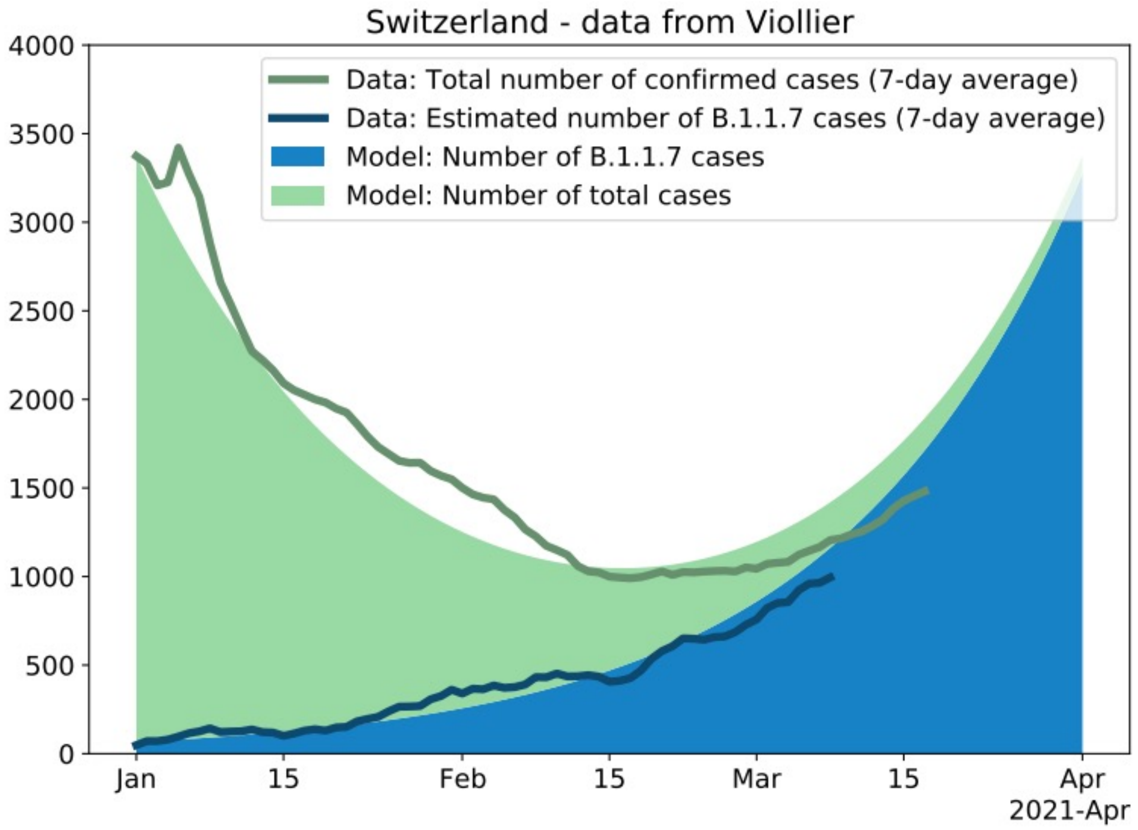


Chen *et al.* (Epidemics, 2021)
Huisman*, Scire* *et al.* (in review)

Predict future development of the epidemic

How will this transmission advantage impact the Swiss epidemic?

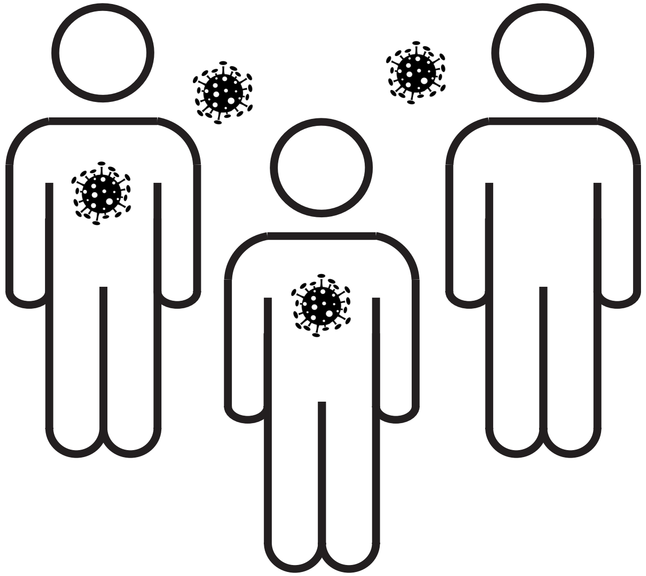
Predict the number of absolute cases assuming a constant R_e



Chen *et al.* (Epidemics, 2021)

Conclusion

Mathematical modelling informed the Swiss public health response to SARS-CoV-2



We developed a pipeline to estimate R_e from noisy observational data, including wastewater

R_e can be used to study the effect of interventions and variants

Further Sources

Course at ETH Zurich:

701-1708-00L Infectious Disease Dynamics

Book:

Keeling & Rohani, *Modeling Infectious Diseases in Humans and Animals*, Princeton Univ. Press 2008

REVIEW

EPIDEMIOLOGY

Modeling infectious disease dynamics in the complex landscape of global health

Hans Heesterbeek,[1*†] Roy M. Anderson,[2] Viggo Andreasen,[3] Shweta Bansal,[4] Daniela De Angelis,[5] Chris Dye,[6] Ken T. D. Eames,[7] W. John Edmunds,[7] Simon D. W. Frost,[8] Sebastian Funk,[4] T. Deirdre Hollingsworth,[9,10] Thomas House,[11] Valerie Isham,[12] Petra Klepac,[8] Justin Lessler,[13] James O. Lloyd-Smith,[14] C. Jessica E. Metcalf,[15] Denis Mollison,[16] Lorenzo Pellis,[11] Juliet R. C. Pulliam,[17,18] Mick G. Roberts,[19] Cecile Viboud,[18] Isaac Newton Institute IDD Collaboration‡§

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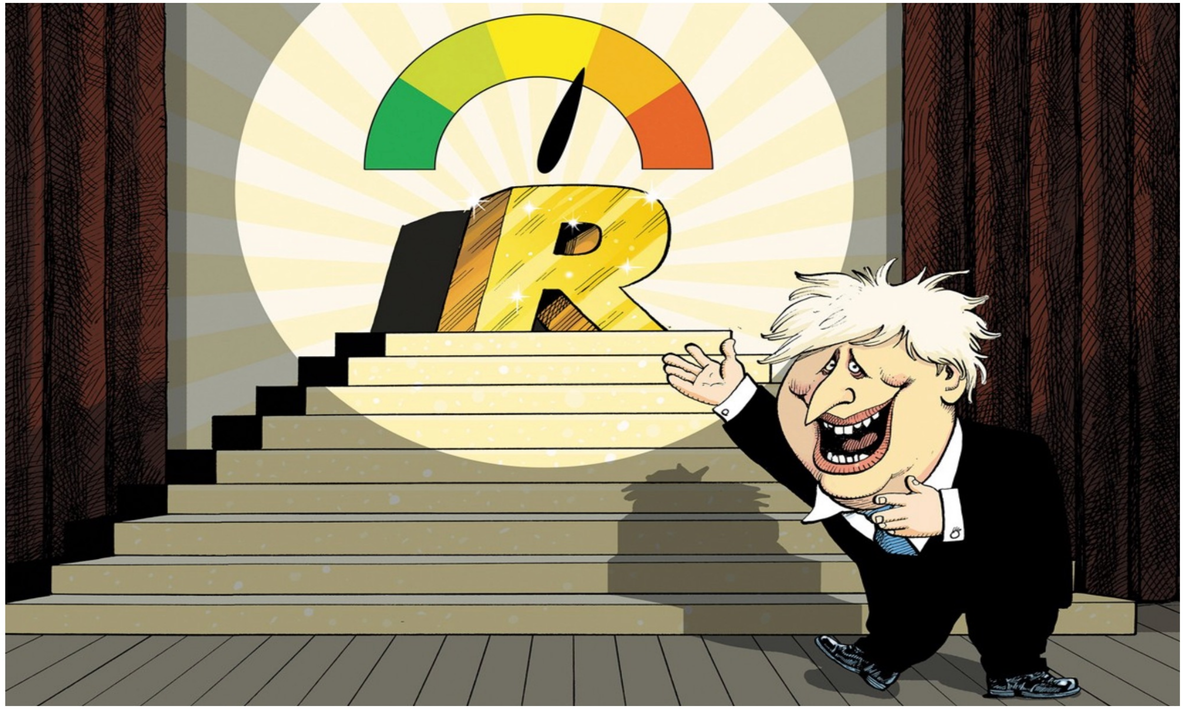

Illustration by David Parkins   Nature, 3.7.2020

Jinzhou Li

Richard Neher

Marloes Maathuis

Christoph Ort

Tamar Kohn

Tim Julian

et al.

Check out the websites:

https://ibz-shiny.ethz.ch/covid-19-re-international/

https://ibz-shiny.ethz.ch/wastewaterRe/

Questions?

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Siouxsie Wiles & Toby Morris