Modelling and policy: a retrospective look at the SARS-CoV-2 pandemic in Belgium

Prof. Dr. Niel Hens
on behalf of the SIMID group

EpiPose project

Universiteit Antwerpen

SIMID
Simulation Models of Infectious Diseases

UHASSELT
KNOWLEDGE IN ACTION

ASCID evening symposium on
COVID-19 PANDEMIC: 2 YEARS LATER
14 June 2022

Overview

A brief recap of last year's ASCID presentation

An eco-system of models

A first qualitative evaluation of the reference model

Further evaluation of the pandemic response

A recap …

Daniel Bernoulli (1700 – 1782)

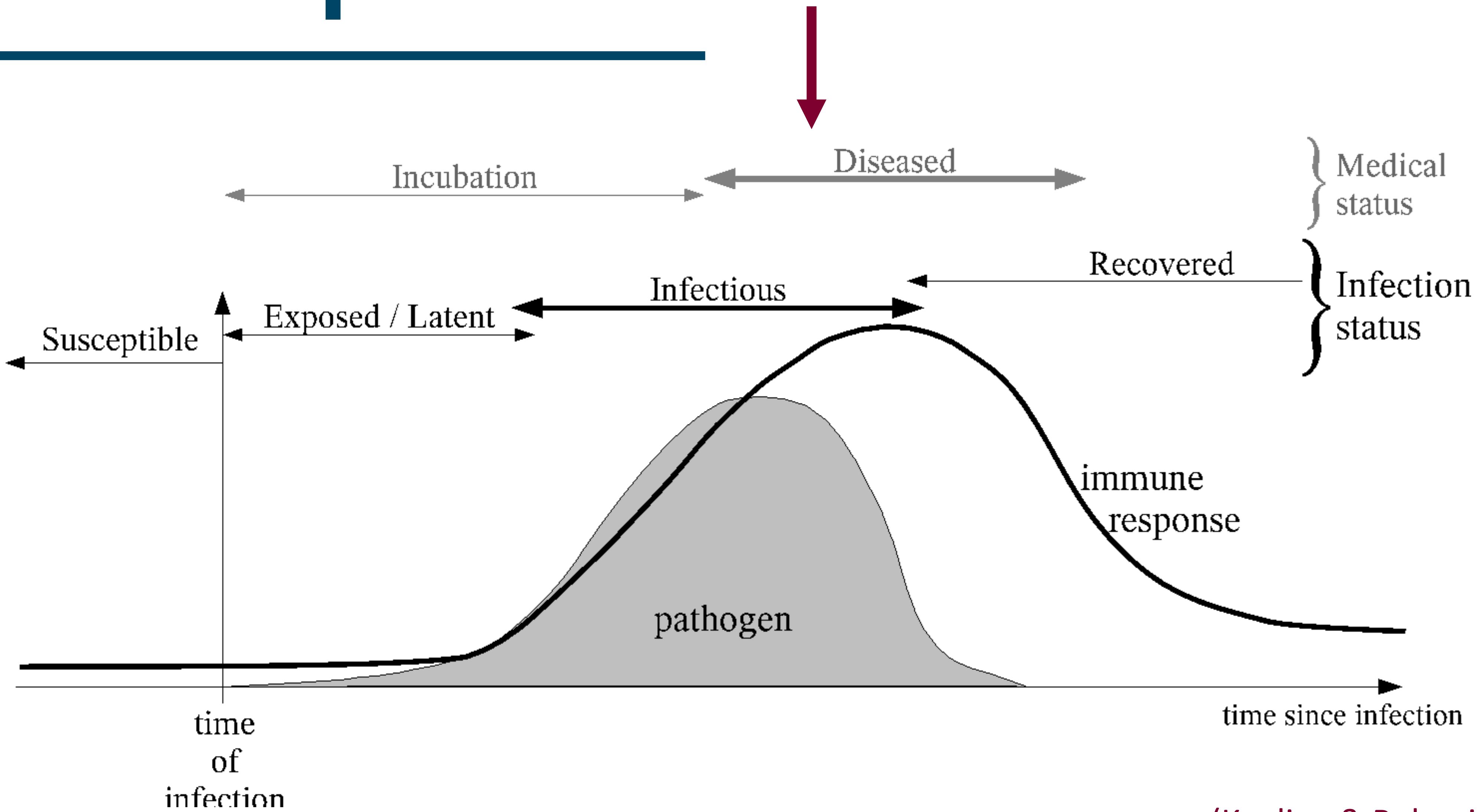
mathematical model of smallpox (1760-1766)

Mathematical models

understanding of transmission dynamics

forecasting – ‘prognosis’ – what-if scenarios

A recap …



(Keeling & Rohani, 2008)

A recap …

Factors that make an infectious disease outbreak controllable

Christophe Fraser*†, Steven Riley*, Roy M. Anderson, and Neil M. Ferguson

Department of Infectious Disease Epidemiology, Imperial College, St. Mary's, London W2 1PG, United Kingdom

6146–6151 | PNAS | April 20, 2004 | vol. 101 | no. 16 www.pnas.org/cgi/doi/10.1073/pnas.0307506101

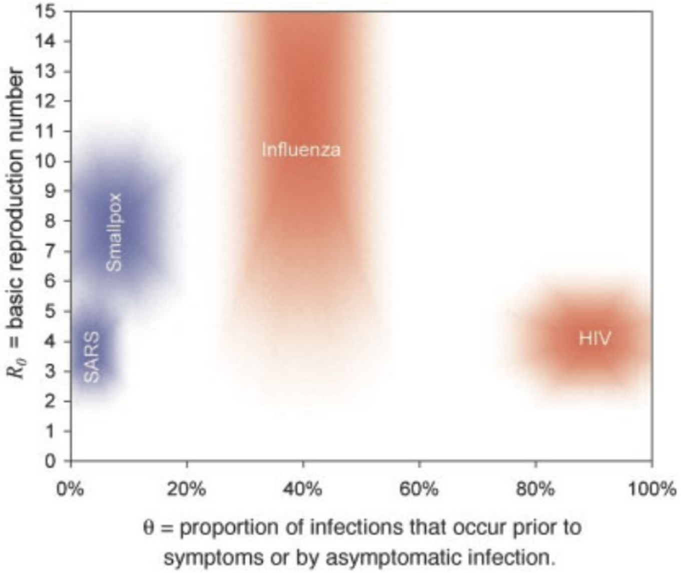


Fig. 2. Parameter estimates. Plausible ranges for the key parameters R_0 and θ (see main text for sources) for four viral infections of public concern are shown as shaded regions. The size of the shaded area reflects the uncertainties in the parameter estimates. The areas are color-coded to match the assumed variance values for $\beta(\tau)$ and $S(\tau)$ of Fig. 1 appropriate for each disease, for reasons that are apparent in Fig. 3.

Rapid communication

Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020

Jantien A Backer[1], Don Klinkenberg[1], Jacco Wallinga[1,2]

1. Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands
2. Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, Netherlands

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Citation style for this article:
Backer Jantien A , Klinkenberg Don , Wallinga Jacco . Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. Euro Surveill. 2020;25(5):pii=2000062. https://doi.org/10.2807/1560-7917.ES.2020.25.5.2000062

Article submitted on 27 Jan 2020 / accepted on 06 Feb 2020 / published on 06 Feb 2020

Research

Estimating the generation interval for coronavirus disease (COVID-19) based on symptom onset data, March 2020

Tapiwa Ganyani[1] , Cécile Kremer[1] , Dongxuan Chen[2,3] , Andrea Torneri[1,4] , Christel Faes[1] , Jacco Wallinga[2,3] , Niel Hens[1,4]

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2. Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands
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4. Centre for Health Economics Research and Modelling Infectious Diseases (CHERMID), Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium

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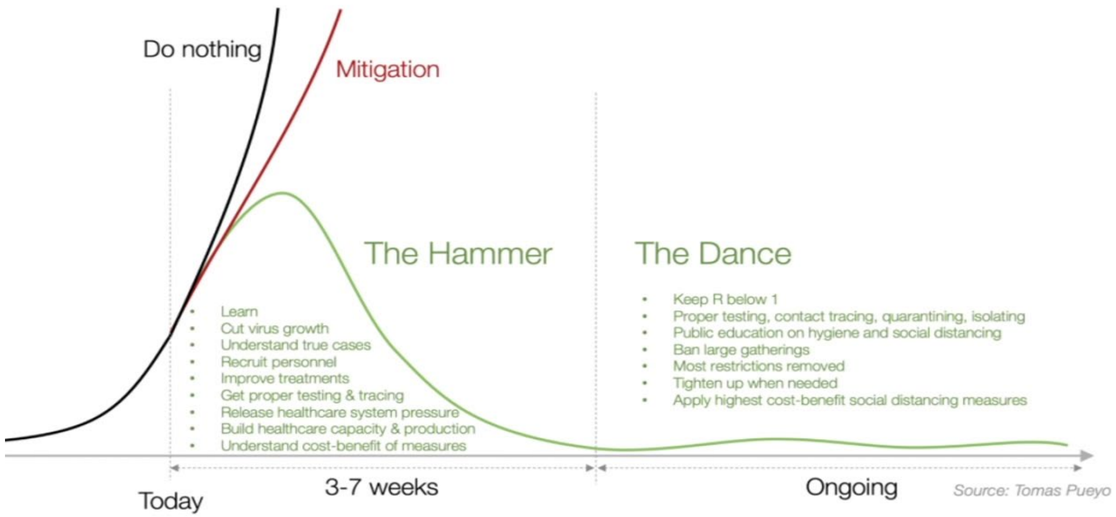
Ganyani Tapiwa , Kremer Cécile , Chen Dongxuan , Torneri Andrea , Faes Christel , Wallinga Jacco , Hens Niel . Estimating the generation interval for coronavirus disease (COVID-19) based on symptom onset data, March 2020. Euro Surveill. 2020;25(17):pii=2000257. https://doi.org/10.2807/1560-7917.ES.2020.25.17.2000257

Article submitted on 06 Mar 2020 / accepted on 07 Apr 2020 / published on 30 Apr 2020

A recap …

Implementing Non-Pharmaceutical Interventions was needed:

- relatively high IFR
- pre & a-symptomatic transmission
- basic reproduction number (Wuhan): R_0=3-3.4
- Feb-March 2020: large seeding due to international travel (spring break)
- lockdown March 2020: advice against closing schools



An ecosystem of models

Statistical models

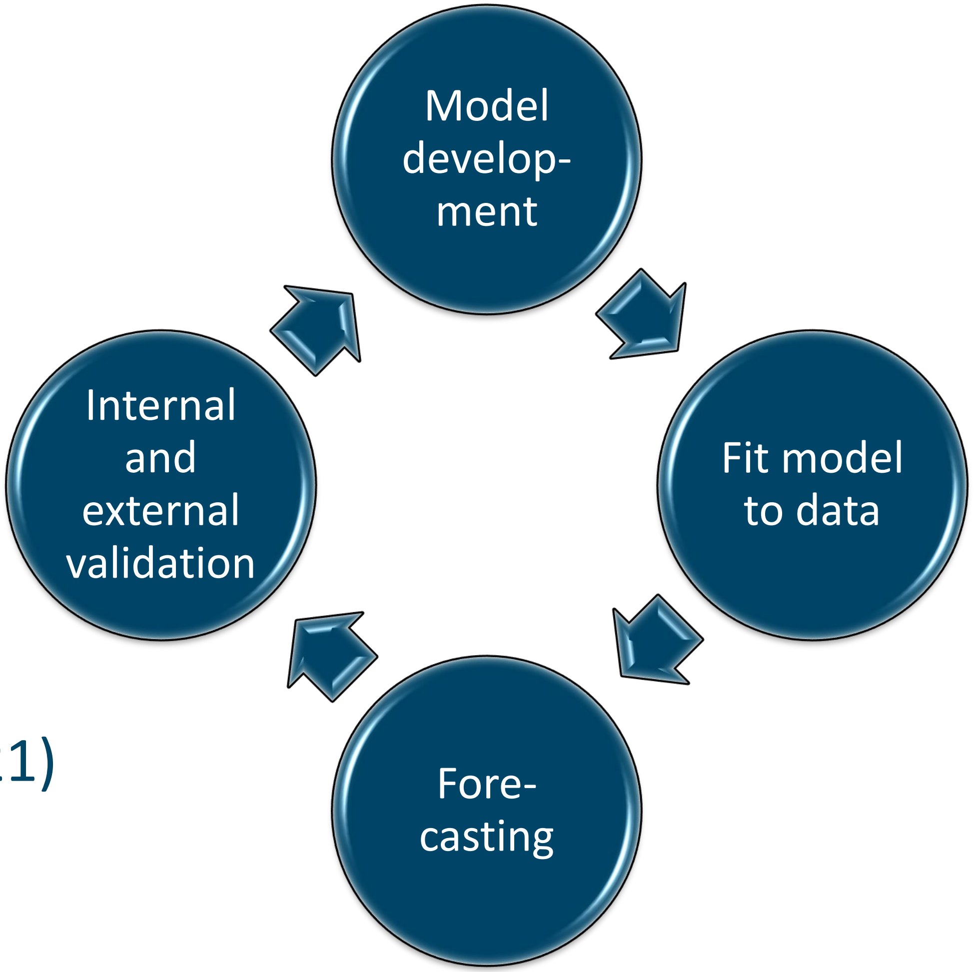
- see e.g. Faes et al. (2021)

Mathematical models

- Meta-population model (Coletti et al. 2021)
- Individual-based model (Willem et al. 2021)
- Stochastic model (Abrams et al. 2021)

  = Belgian reference model
- Next generation approach (Franco et al. 2021)
- Contact process models:

  schools (Torneri et al. 2021)



Key player: 'age'

Age-specific features
- burden
- transmission

Burden - mortality:
- IFR - Molenberghs et al., 2022
- excess mortality

Transmission – mixing patterns:
- POLYMOD & sequel (2006, 2011)
- CoMIX

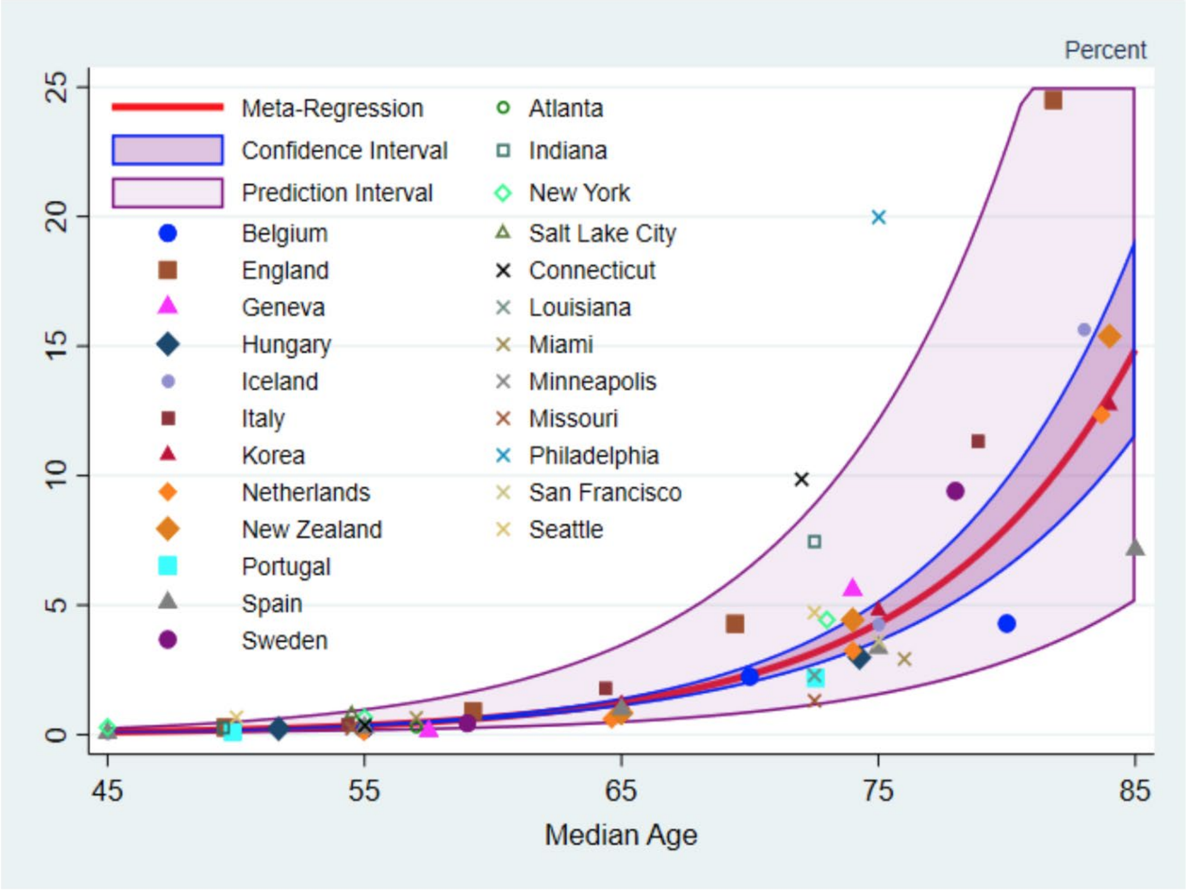
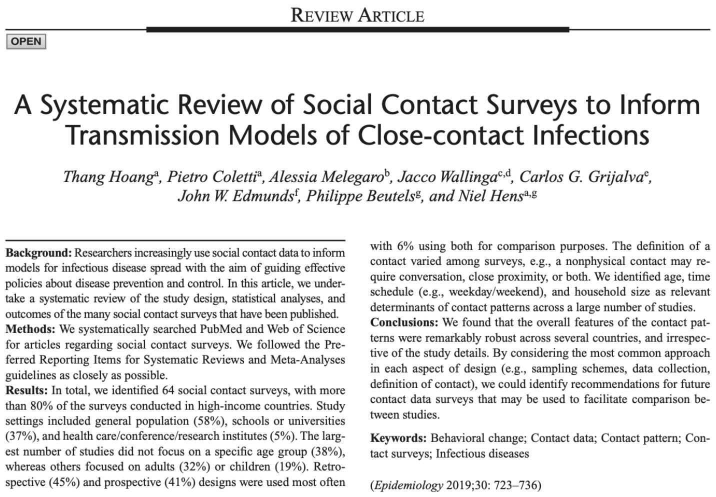


Figure 4: Benchmark analysis of the link between age and IFR

Mixing patterns



REVIEW ARTICLE

OPEN

A Systematic Review of Social Contact Surveys to Inform Transmission Models of Close-contact Infections

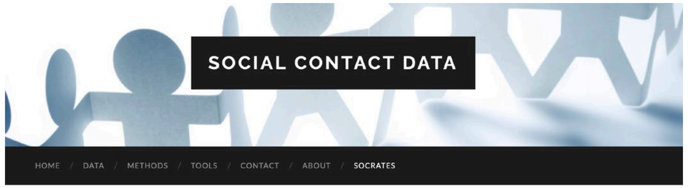
Thang Hoang[a], Pietro Coletti[a], Alessia Melegaro[b], Jacco Wallinga[c,d], Carlos G. Grijalva[e], John W. Edmunds[f], Philippe Beutels[g], and Niel Hens[a,g]

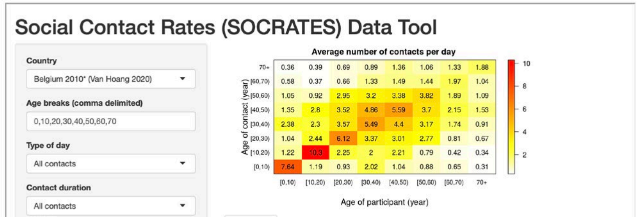
Background: Researchers increasingly use social contact data to inform models for infectious disease spread with the aim of guiding effective policies about disease prevention and control. In this article, we undertake a systematic review of the study design, statistical analyses, and outcomes of the many social contact surveys that have been published.
Methods: We systematically searched PubMed and Web of Science for articles regarding social contact surveys. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines as closely as possible.
Results: In total, we identified 64 social contact surveys, with more than 80% of the surveys conducted in high-income countries. Study settings included general population (58%), schools or universities (37%), and health care/conference/research institutes (5%). The largest number of studies did not focus on a specific age group (38%), whereas others focused on adults (32%) or children (19%). Retrospective (45%) and prospective (41%) designs were used most often with 6% using both for comparison purposes. The definition of a contact varied among surveys, e.g., a nonphysical contact may require conversation, close proximity, or both. We identified age, time schedule (e.g., weekday/weekend), and household size as relevant determinants of contact patterns across a large number of studies.
Conclusions: We found that the overall features of the contact patterns were remarkably robust across several countries, and irrespective of the study details. By considering the most common approach in each aspect of design (e.g., sampling schemes, data collection, definition of contact), we could identify recommendations for future contact data surveys that may be used to facilitate comparison between studies.

Keywords: Behavioral change; Contact data; Contact pattern; Contact surveys; Infectious diseases

(*Epidemiology* 2019;30: 723–736)

(Hoang et al., Epi, 2019)





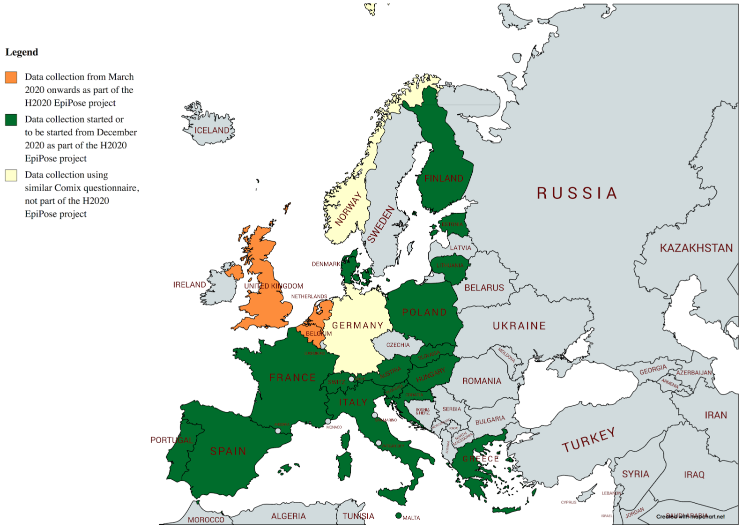
(Willem et al., 2020)

← POLYMOD

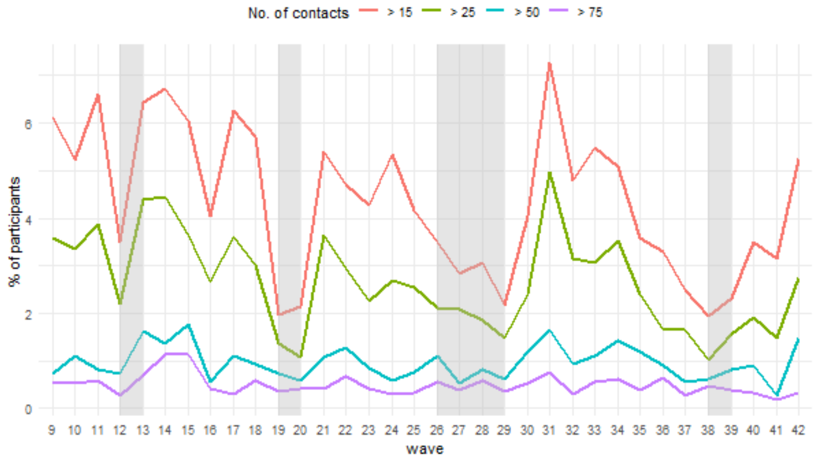
- FP6 Framework
- ERC TransMID

CoMix →

- EpiPose Consortium
- ECDC



(Verelst et al, 2021)



(Loedy et al, 2021)

Reference Model

Stochastic compartimentel model (Abrams et al., 2021)

→ integration of different data sources

- Calibration to
    - hospital admissions
    - hospital load
    - early serology
- Further calibration to growth rates
    - cases
    - genomic suveillance
- Forecasts based on CoMix data

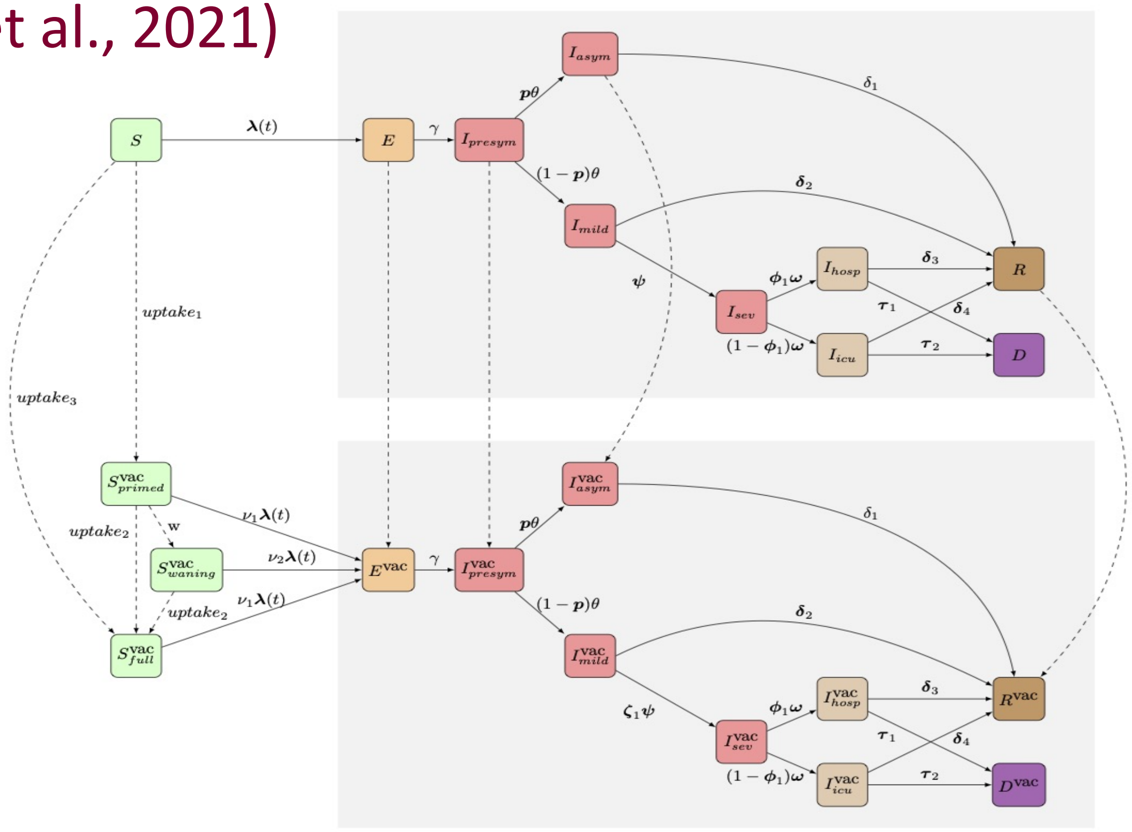


Figure 4: **Schematic overview of compartmental model including vaccination with vaccine-induced protection after 1 and 2 doses and waning immunity.** The gray boxes indicate the duplication we include for the VoC (see Figure 3).

Modelling SARS-CoV-2: a first evaluation

Scenario’s, no predictions

Spring 2020: lockdown:

- succesful exit strategy until July 2020
- prognosis: second wave

Autumn and Winter 2020-2021:

- a (too) large second wave with high tail
- a succesful management of the festive season

Modelling SARS-CoV-2: a first evaluation

Spring 2021

- the alpha wave – higher burden - press conference

Summer 2021

- projections with large uncertainty
- increasing vaccination coverage
- penetration of the delta variant

Modelling SARS-CoV-2: a first evaluation

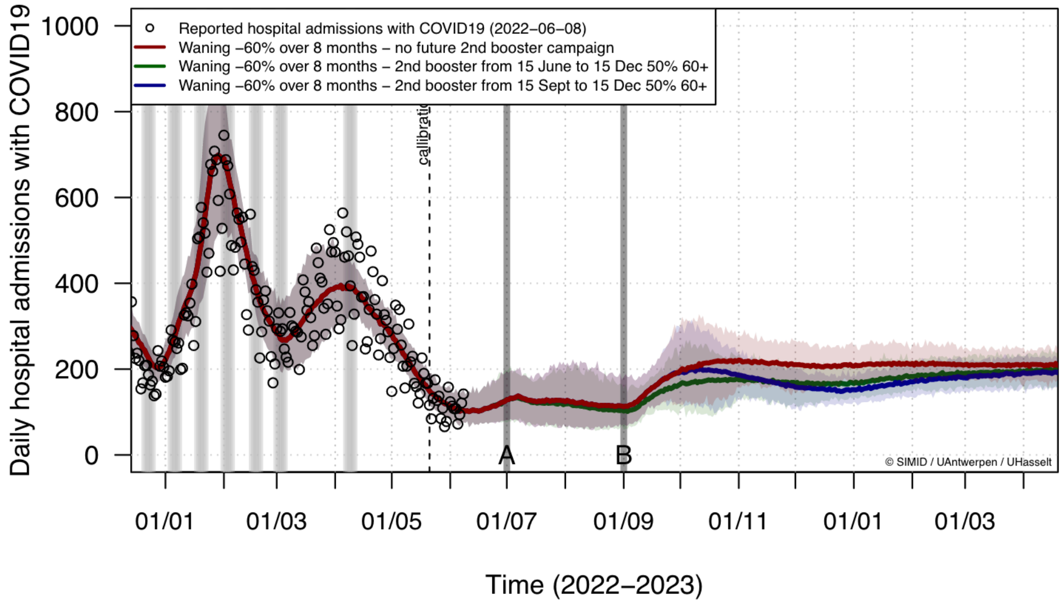
Autumn 2021

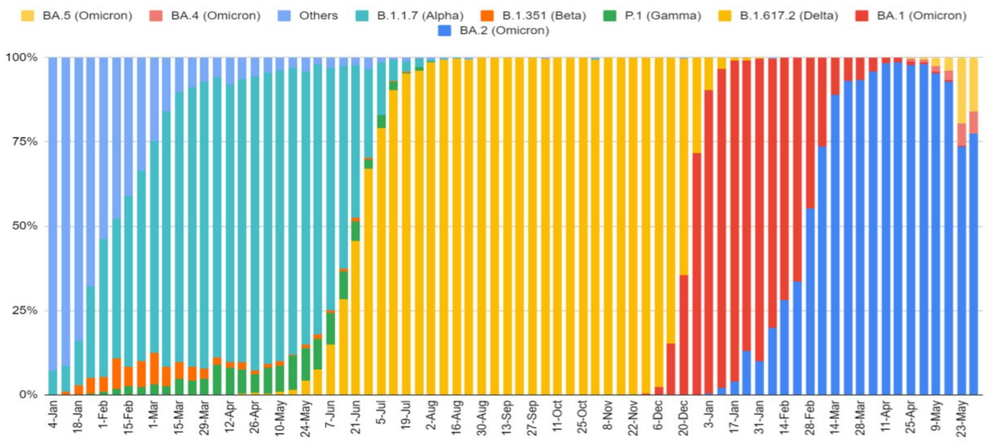
- fourth wave with regional differences ~ vaccination
- initial slower growth because of prudent behaviour
- acceleration because of perfect storm: release of measures & delta

Winter and Spring 2021-2022

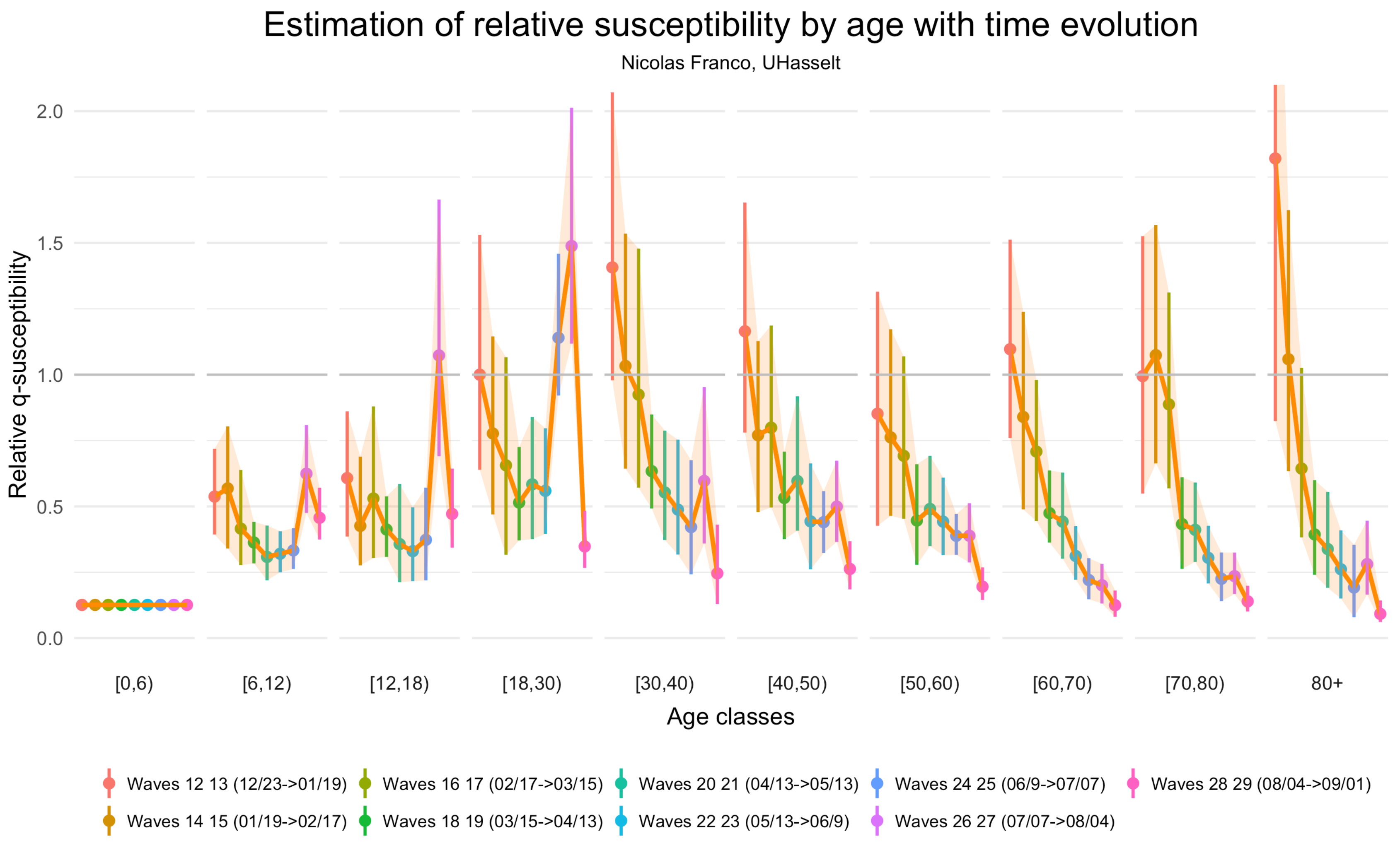
- omicron: bad and good news

Modelling SARS-CoV-2: where are we now?



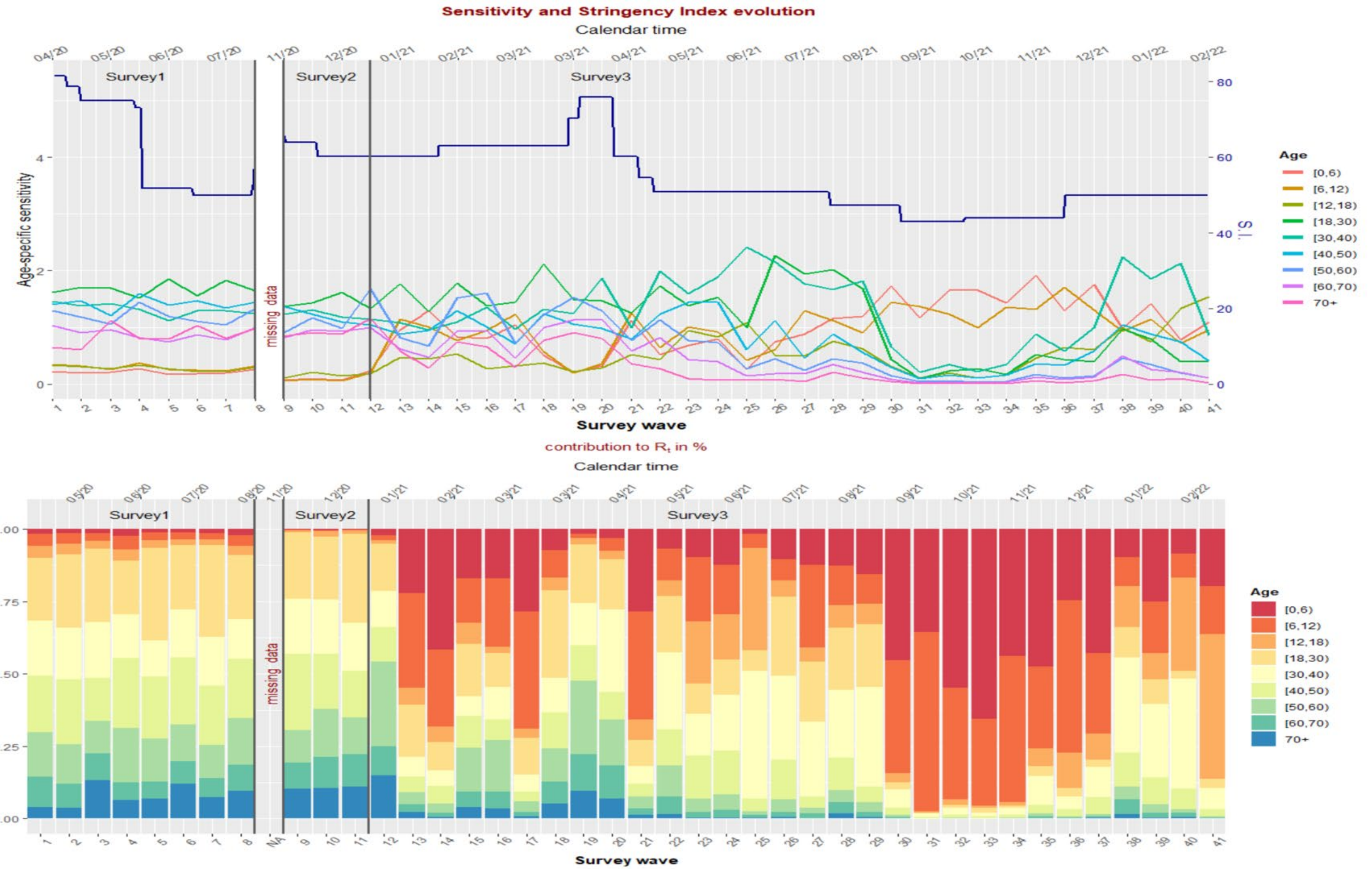


The Next Generation Approach

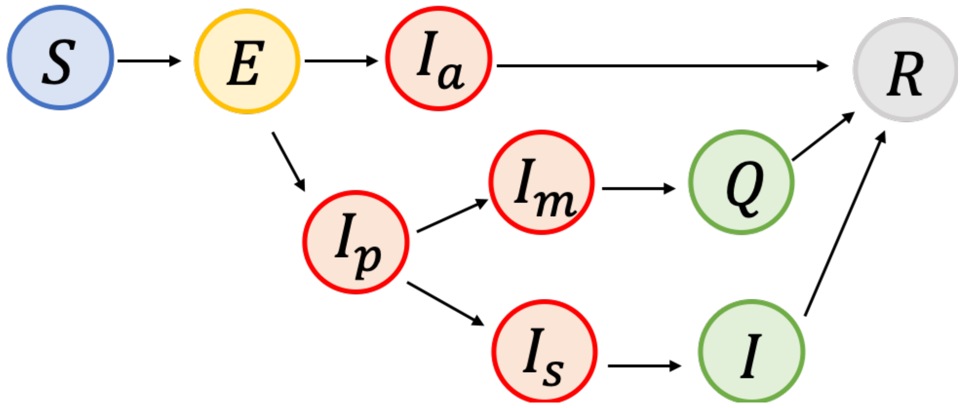


Susceptibility estimated by comparison between CoMix social contact data (using next generation approach) and positive PCR tests.
Susceptibility means here a factor influencing transmission not limited to clinical susceptibility but including effects like risk behavior and vaccination.
Results are relative numbers normalised with [0,6) class constant. Limitation: PCR tests are subject to biases.

The Next Generation Approach

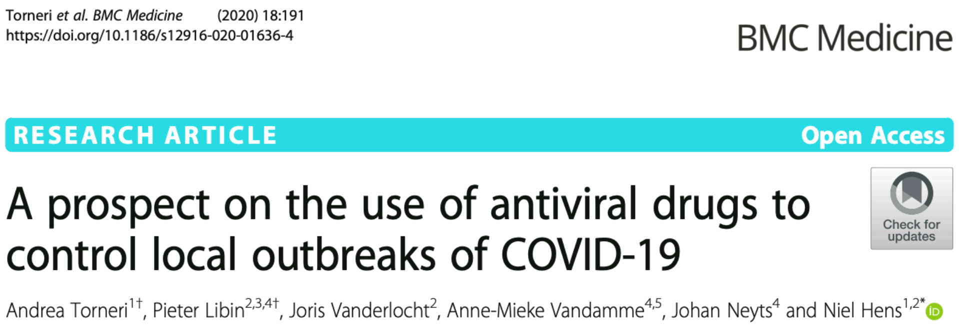


Contact process models



Epidemic dynamics

S = susceptible
E = exposed
I_a= asymptomatic
I_p= presymptomatic
I_m= mild symptoms
I_s= severe symptoms
Q = quarantine
I = isolation
R = removed



Infectives are assumed to spread the infection according to a nonhomogeneous Poisson Process of rate:

$$r(t)=\underbrace{\lambda(t)}_{\text{Contact rate}}\underbrace{\omega(t)}_{\text{Infectiousness}}$$

Key assumption: Infectiousness described by viral load

Contact process models

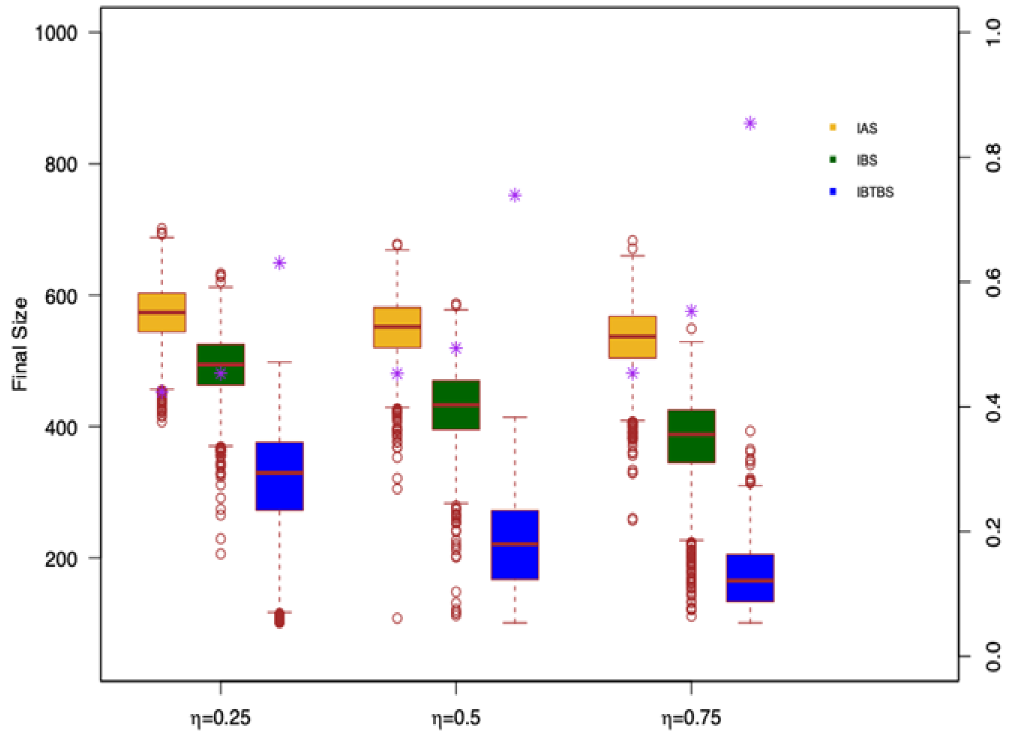
We compare three control measures based on contact tracing:

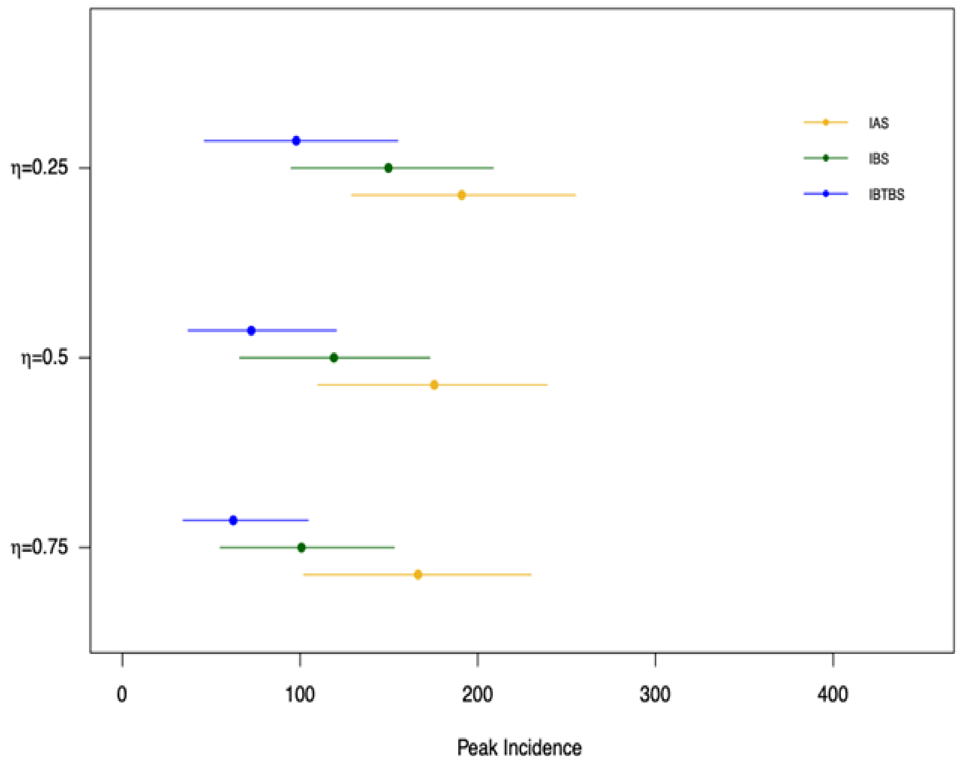
- **Monitoring** ("IAS"): traced individuals are monitored and quarantined/isolated when showing symptoms

- **Testing** ("IBS"): traced individuals are tested and quarantined/isolated if testing positive.

- **Testing + Antivirals** ("IBTBS"): traced individuals are tested. If positive they are quarantined/isolated and an antiviral drug is administered to them.

Contact process models





A control measure based on testing (green and blue) reduce final size (left panel) and peak incidence (right panel) compare to a monitoring strategy. In addition, the use of antiviral (blue) as prophylaxis compound is computed to have a big impact in controlling local outbreaks.

Contact process models

Limitations:

- The model is based on a homogenous population
- We inform the antiviral effect using a study for Remdesivir in a murine model
- Not accounting for difficulties in administering Remdesivir
- Longitudinal data on the effect of antiviral on the viral load will be informative, especially when the drug is administered in the early phase of infection

School simulator

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Comment on this paper

Controlling SARS-CoV-2 in schools using repetitive testing strategies

Andrea Torneri, Lander Willem, Vittoria Colizza, Cécile Kremer, Christelle Meuris, Gilles Darcis, Niel Hens, Pieter Libin

doi: https://doi.org/10.1101/2021.11.15.21266187

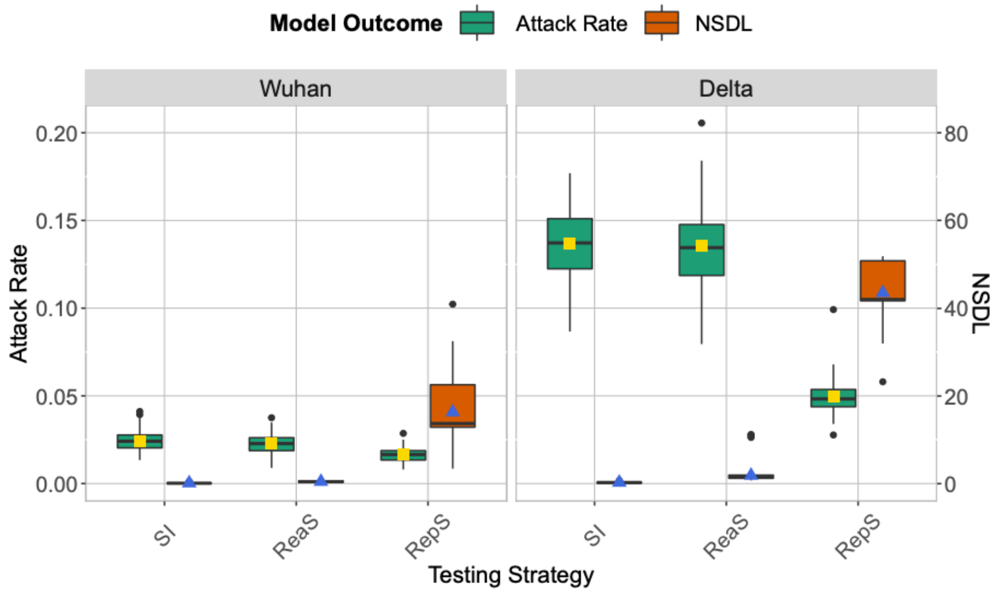


Figure 1: We show the base scenario for the Wuhan strain (left panel) and Delta VoC (right panel) for a moderate seeding of 5 seeds per week. In each panel we consider three testing strategies: symptomatic testing (SI), symptomatic testing in combination with reactive screening (ReaS) and repetitive screening (RepS). For each of the testing strategies we show a boxplot of the attack rate (green boxplot) and NSDL (orange boxplot) together with their mean values (respectively, yellow and blue dots).

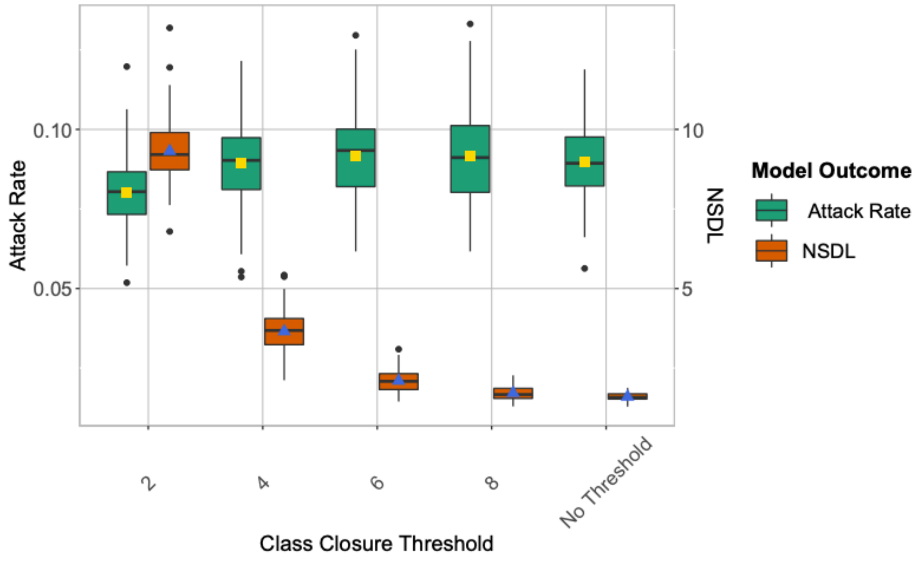
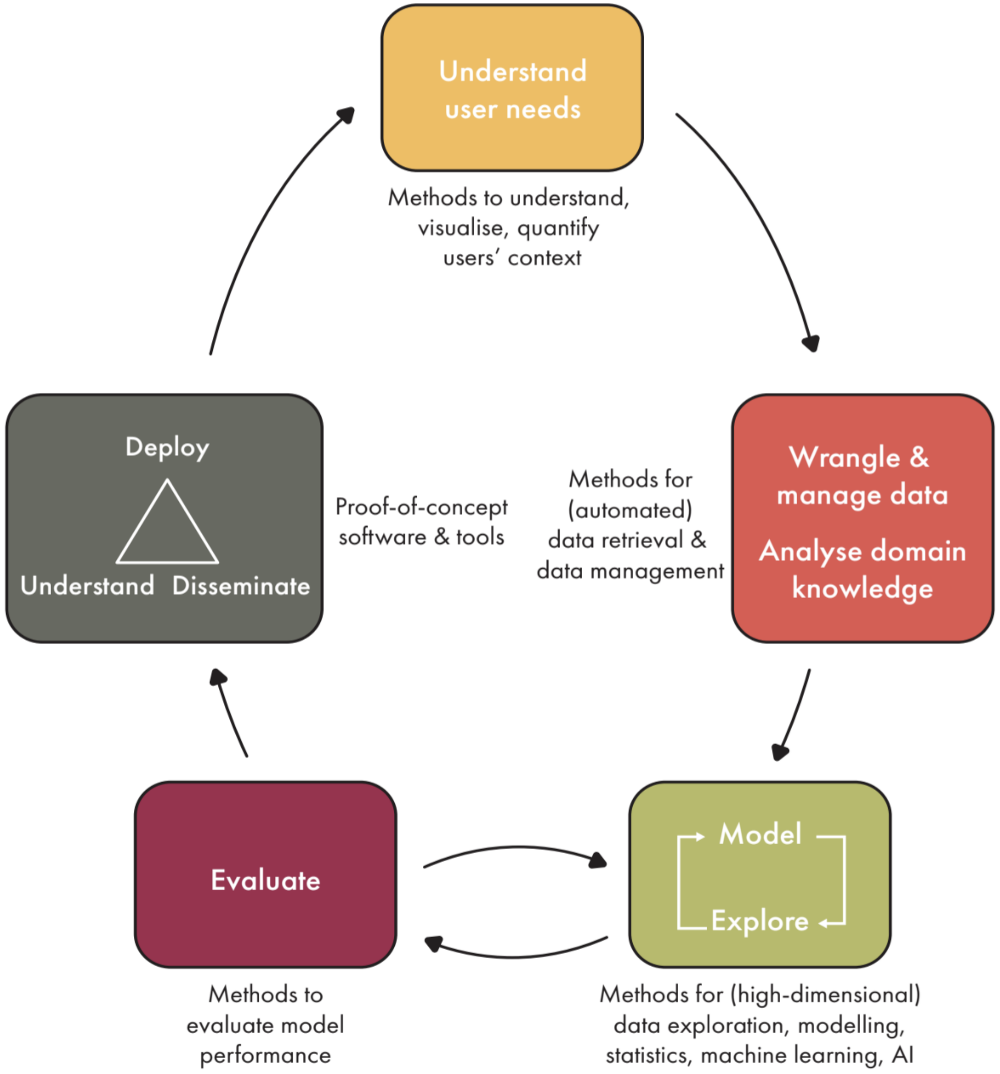


Figure 2: We show the repetitive testing strategy in the context of the Delta VoC for a moderate seeding of 5 seeds per week, where we consider different class closure thresholds, and no school closure threshold. This experiment shows that a higher class closure threshold has little effect on the attack rate, yet it significantly reduces the NSDL.

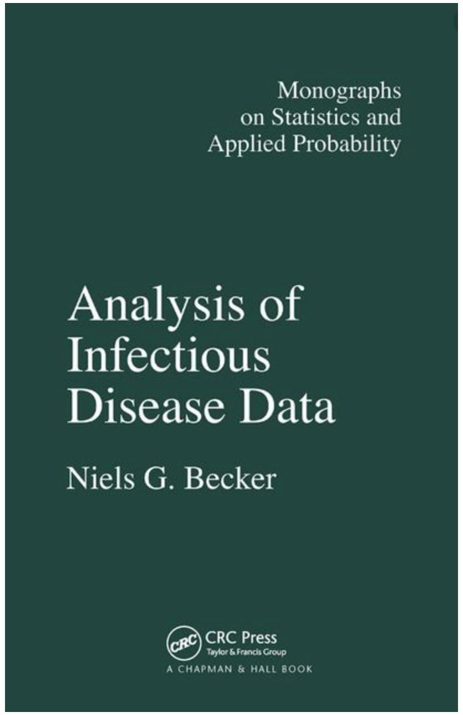
Data science cycle



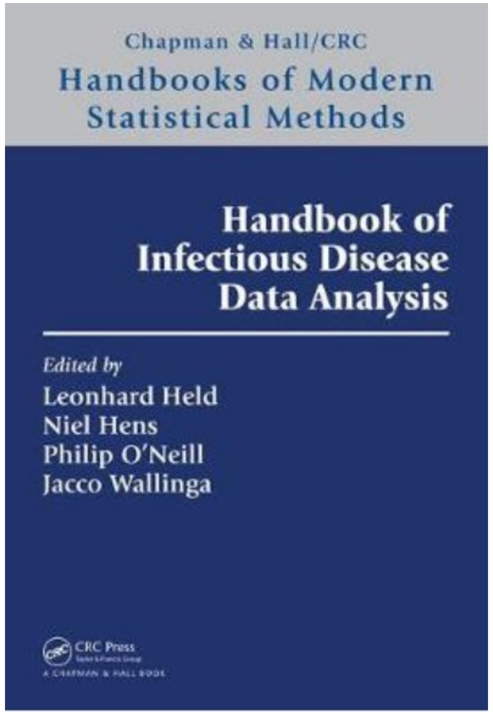
Data Science Cycle
(Bron: Data Science Institute, UHasselt)

Data collection & analysis

- Difficulties
  - interdepencies
  - incomplete data
- Observational studies
  - biases
  - association not causation
  - …
- Scientific principles
  - conjecture versus refutation
  - Bradford Hill criteria – confidence
  - → Robert Koch & microbiology



Becker (1989)



Held et al. (2019)

Lessons learned

Methodology

- learning from the past
- heterogeneity is key
- validation is key
- optimizing NPIs
- …

Multi- & interdisciplinary research is key

Peacetime research

- (inter)national collaborations should be forched in peacetime

examples

- demography and newly emerging pathogens ~ nursing home populations
- behavioural epidemiology ~ chronic conditions and acute infections

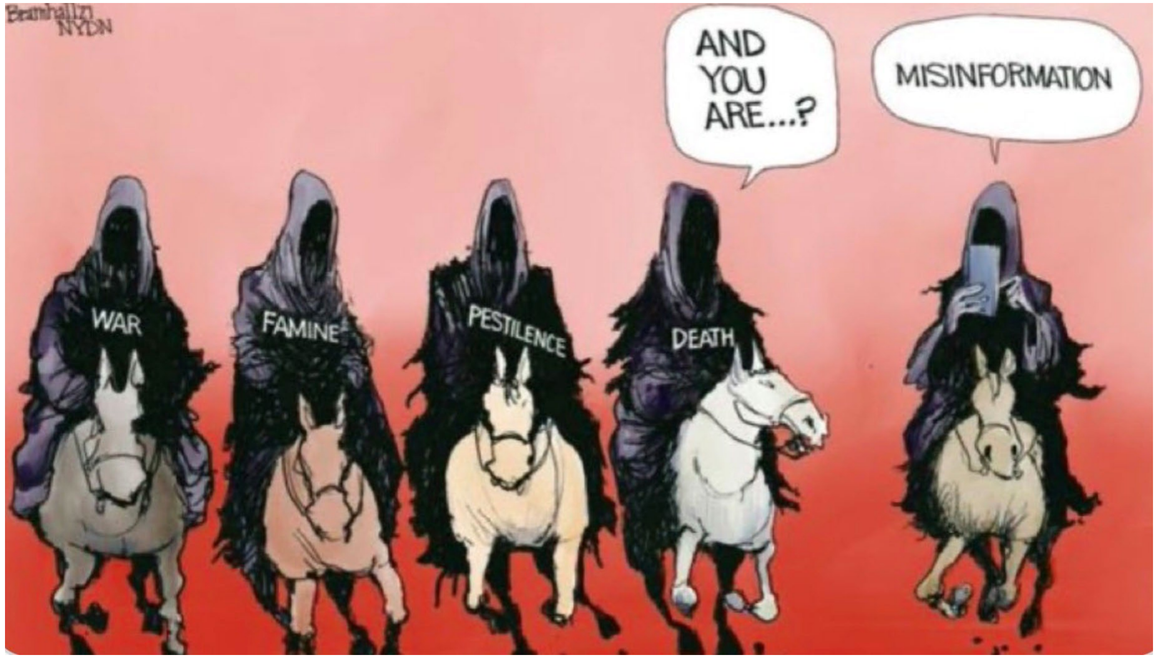
Better data

- realtime data
- well-designed surveys
- serosurveillance
- genomic surveillance
- …

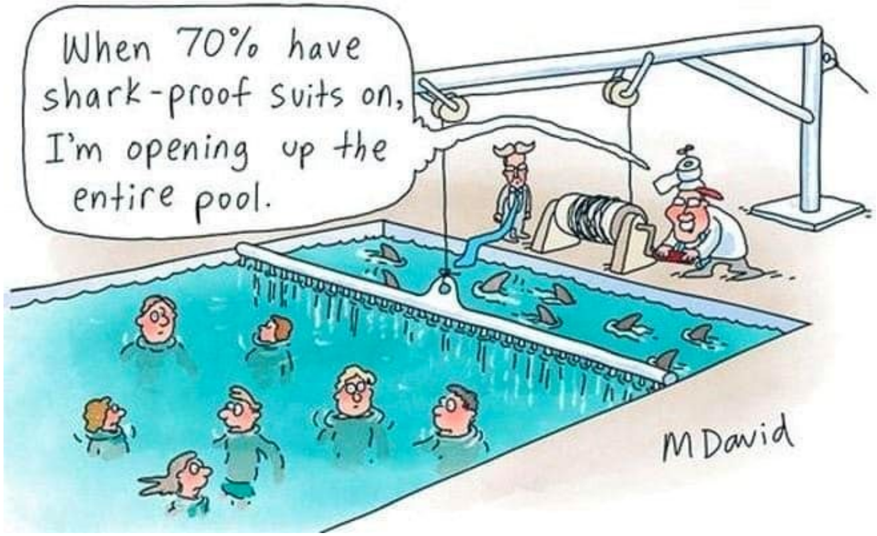
Open Science

Lessons learned

Faulty & misinformation: (non-)intential?



Outdated information



Societal choices

Lessons learned

Faulty & misinformation: (non-)intential?

Elements:

- uncertainty
- lack of scientific foundation
- lack of nuance
- mix of (in)correct arguments
- science advances
- speed trumps perfection
- ...

PROCEEDINGS B

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Research

Cite this article: King AA, Domenech de Cellès M, Magpantay FMG, Rohani P. 2015 Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. *Proc. R. Soc. B* **282**: 20150347. http://dx.doi.org/10.1098/rspb.2015.0347

Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola

Aaron A. King[1,2,3,4], Matthieu Domenech de Cellès[1], Felicia M. G. Magpantay[1] and Pejman Rohani[1,2,4]

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[4]Fogarty International Center, National Institutes of Health, Bethesda, MD 20892, USA

As an emergent infectious disease outbreak unfolds, public health response is reliant on information on key epidemiological quantities, such as transmission potential and serial interval. Increasingly, transmission models fit

Review

MDM
Medical Decision Making

Medical Decision Making
1–7

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The Use and Misuse of Mathematical Modeling for Infectious Disease Policymaking: Lessons for the COVID-19 Pandemic

Lyndon P. James, Joshua A. Salomon, Caroline O. Buckee, and Nicolas A. Menzies

Mathematical modeling has played a prominent and necessary role in the current coronavirus disease 2019 (COVID-19) pandemic, with an increasing number of models being developed to track and project the spread of the disease, as well as major decisions being made based on the results of these studies. A proliferation of models, often diverging widely in their projections, has been accompanied by criticism of the validity of modeled analyses and uncertainty as to when and to what extent results can be trusted. Drawing on examples from COVID-19 and other infectious diseases of global importance, we review key limitations of mathematical modeling as a tool for interpreting empirical data and informing individual and public decision making. We present several approaches that have been used to strengthen the validity of inferences drawn from these analyses, approaches that will enable better decision making in the current COVID-19 crisis and beyond.

Keywords
COVID-19, infectious diseases, mathematical modeling, uncertainty, validation

Paradigma shift?

Rapid Science

- Time pressure
- Context
- Assumptions
- 'early evidence'
- Uncertainty
- …
- Example: role of children

‘Slow’ Science

- More details
- Country comparisons
- Generalisability
- …
- Example: behaviour

Preparedness

- International community
- Interdisciplinary research
- Peace-time efforts
- …
- Example: demography & disease transmission

Further perspectives

Research themes

- further evaluation and perspectives of the management of SARS-CoV-2
- further development of an eco-system of models
- AI & pandemic preparedness (e.g. Reymond et al. 2022)
- …

Education and science communication

Need for consortia/baseline capacity

Pathogen ‘X’ (see e.g. MPX)

Further debate

Perspectives for debate:

- Clinical versus epidemiological perspectives
- Individual versus population perspective
- Activism versus science
- ‘Freedom’
- …

Knowing history would be a good starting point …

Bradford Hill (1965)

Bradford Hill (1965):

All scientific work is incomplete – whether it be observation or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.


REFLECTIONS ON THE INVISIBL©FREDERIK DE WILDE_2020. Inspired by the scientific work of Prof. dr. Niel HENS (UH, UA).

References

Sources:

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- www.simid.be

socrates:
- www.socialcontactdata.org

blog:
- covid-en-wetenschap.github.io

Citizen science projects:

Large Corona Study

Infectieradar

COLLABORATORS & FUNDERS