

Modelling in Public Health

SE Scientific Communication
Summer 2019

Lukas Richter

28. June 2019

Content

- 1 Background
- 2 Statistical models
- 3 Dynamic models
- 4 Conclusion

Background

Infectious diseases are a serious **burden** for human health

Loss of QUALYs and also money

WHO: **50,000 deaths per day** due to infectious diseases

Outbreaks vs endemic infection

Different chains of **transmission**:



Modelling in Public Health

└ Background

└ Background

Background

Infectious diseases are a serious **burden** for human health

Loss of QUALYs and also money

WHO: **50,000 deaths per day** due to infectious diseases

Outbreaks vs endemic infection

Different chains of **transmission**:



QUALY = quality-adjusted life year

many are preventable (vaccines) or curable

infection is constantly maintained at a baseline level in a geographic area without external inputs (steady state) / regularly found among particular people or in a certain area.

Outbreaks



Influenza pandemic “swine flu”

Global, 2009–2010, 100,000 – 400,000 deaths

Ebola

West Africa, 2014–2016, 11,000 deaths

DRC, since 2018, 1,900 deaths

Zika Virus

Brazil, 2015–2016, estimated 1 Mio cases in Brazil only and 2,000 confirmed severe complications in newborns

Measles

Europe, 2019, ca. 6,300 cases from Jan–Apr

Austria, 2019, more than 130 cases up to this week

Modelling in Public Health

└ Background

└ Outbreaks

Outbreaks

Influenza pandemic "swine flu"

Global, 2009-2010, 100,000 - 400,000 deaths

Ebola

West Africa, 2014-2016, 11,000 deaths

DRC, since 2018, 1,900 deaths

Zika Virus

Brazil, 2015-2016, estimated 1 Mio cases in Brazil only and 2,000 confirmed severe complications in newborns

Measles

Europe, 2010, ca. 6,300 cases from Jan-Apr

Austria, 2019, more than 130 cases up to this week

Flu: this time: not more than usual season (see also Spanish flu 1918),
10-15 weeks earlier than normal

Ebola: CFR up to 40%

Measles EU: Romania, Lithuania, Italy, Poland, Bulgaria, Czech Republic,
France, Greece, Slovakia

How can modellers help?

Outbreak situations:

Exploit all available data

Inform response team in real time

Prioritise interventions

Non outbreak situations:

Evaluate health programmes (vaccination, WHO elimination targets)

Find **high impact and cost-effective** interventions

Allow **evidence** based decisions

Benefits of modelling:

Low cost! Clinical trials are expensive and seldom large enough

Often little or no data to analyse (new emerging diseases)

Modelling in Public Health

└ Background

└ How can modellers help?

How can modellers help?

Outbreak situations:

Exploit all available data

Inform response team in real time

Prioritise interventions

Non outbreak situations:

Evaluate health programmes (vaccination, WHO elimination targets)

Find **high impact and cost-effective** interventions

Allow evidence based decisions

Benefits of modelling:

Low cost! Clinical trials are expensive and seldom large enough

Often little or no data to analyse (new emerging diseases)

WHO elimination target for HIV-AIDS, Hepatitis C

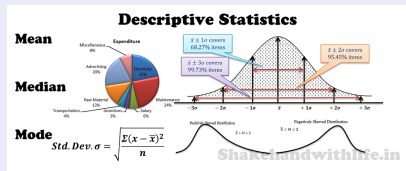
mathematical models can help to assess potential threats and impacts early in the process, and later aid in interpreting data

Public health programmes are usually implemented over a long period of time with broad benefits to many in the community.

WHO: over 30 new diseases emerged in the last 20 years

Types of models

Statistical



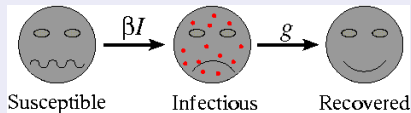
Descriptive

Regression

Bayesian statistics

Spatial models

Mathematical



Dynamic, compartmental (SIR)

Stochastic - Markov chain

Deterministic

Agent-based

2019-06-26

Modelling in Public Health

└ Background

└ Types of models

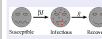
Types of models

Statistical



Descriptive
Regression
Bayesian statistics
Spatial models

Mathematical



Dynamic, compartmental (SIR)
Stochastic - Markov chain
Deterministic
Agent-based

Dynamic models: origin is in the early 20th century

Modelling: higher influence with increasing computer power

Intervention effect – Invasive Pneumococcal Disease (IPD)

Caused by ***Streptococcus pneumoniae***

90 distinct pneumococcal serotypes

Highest burden: **infants** and **elderly**

Pneumococcal conjugate **vaccine** **introduced** in 2012 in AT for children



Intervention effect – Invasive Pneumococcal Disease (IPD)

Caused by ***Streptococcus pneumoniae***

90 distinct pneumococcal serotypes

Highest burden: **infants** and **elderly**

Pneumococcal conjugate **vaccine** **introduced** in 2012 in AT for children



Vaccine effect? Direct? Indirect (elderly)?

Modelling in Public Health

└ Statistical models

└ Intervention effect – Invasive Pneumococcal Disease (IPD)

s. pneumoniae: bacteria

Serotypes: Only a small number account for IPD

Risk: <2 and 50+

can result in: meningitis, bacterial pneumonia, sepsis

vaccine: covering 10 serotypes (PCV10)

3 doses in the first year (3rd, 5th, 12th month)

Caused by *Streptococcus pneumoniae*

90 distinct pneumococcal serotypes

Highest burden: **infants and elderly**

Pneumococcal conjugate vaccine introduced in 2012 in AT for children



Vaccine effect? Direct? Indirect (elderly)?

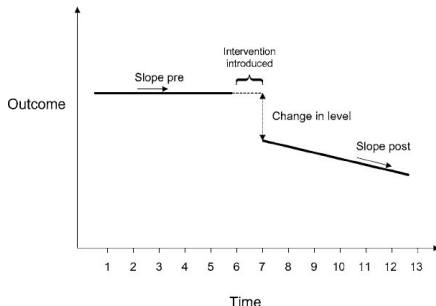
IPD – A Segmented Regression Model

Serfling-like Model

$$\begin{aligned}\log(Y_t) = & \beta_0 + \beta_1 t + \beta_2 \sin\left(\frac{2\pi t}{12}\right) + \beta_3 \cos\left(\frac{2\pi t}{12}\right) \\ & + \beta_5 (t - t_0)^+ + \mathbb{1}_{t-t_0>0} \left[\beta_4 + \beta_6 \sin\left(\frac{2\pi t}{12}\right) + \beta_7 \cos\left(\frac{2\pi t}{12}\right) \right] \\ & + \log(pop_t)\end{aligned}$$

with

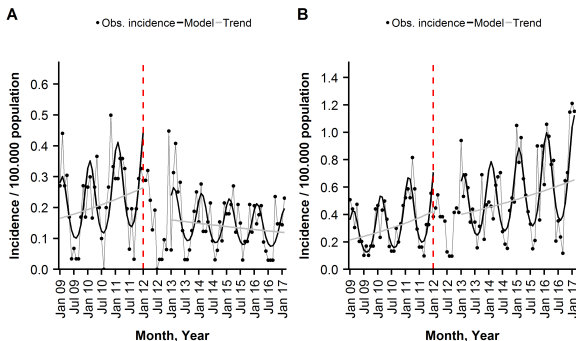
$$(x)^+ = \begin{cases} x, & \text{if } x > 0, \\ 0, & \text{otherwise.} \end{cases}$$



Richter et al., 2019

IPD – Results

Figure: Monthly incidence of (A) **vaccine type IPD** (B) **non vaccine type IPD**, among the **≥ 50 years old**, observed and modelled, Austria



Mathematical modelling – Zika Virus

Humans infected by **mosquitos**
daytime-active *Aedes* family

Latin American Zika epidemic (Feb 2016)

Summer Olympics in Rio

Global transmission (75 countries)

e.g. *A. albopictus* **found in AT** in 2012

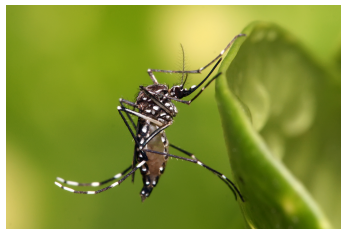
Mostly **flu-like** or **no** symptoms

Dangerous for **foetuses and neonates**

Brain malformations

Microcephaly (small head)

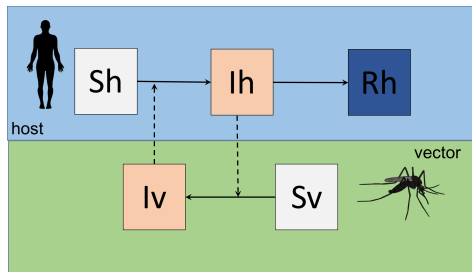
Figure: *Aedes aegypti*



Source: Muhammad Mahdi Karim,
<https://commons.wikimedia.org/w/index.php?curid=9556152>

Transmission model of Zika Virus

Vars	Description
S_h	Susceptible Humans
I_h	Infected/Infectious humans
R_h	Humans recovered from infection (with lifelong immunity)
S_v	Susceptible vectors
E_v	Exposed vectors



adapted from
<https://www.reconlearn.org/> and Ferguson et al., 2016

Transmission model of Zika Virus

Humans/Host

$$\frac{dS_h}{dt} = \mu_h N_h - \frac{\beta_h b}{N_h} S_h I_v - \mu_h S_h$$

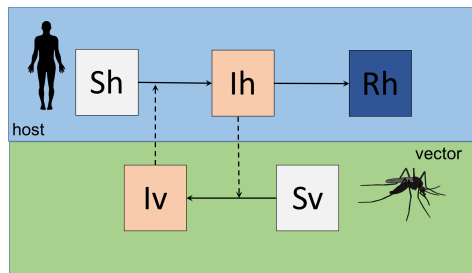
$$\frac{dI_h}{dt} = \frac{\beta_h b}{N_h} S_h I_v - (\gamma_h + \mu_h) I_h$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \mu_h I_h$$

Vectors

$$\frac{dS_v}{dt} = \mu_v N_v - \frac{\beta_v b}{N_h} I_h S_v - \mu_v S_v$$

$$\frac{dI_v}{dt} = \frac{\beta_v b}{N_h} I_h S_v - \mu_v I_v$$



adapted from
<https://www.reconlearn.org/> and Ferguson et al., 2016

Zika Virus - Modelling Outcome

Herd immunity after first epidemic

Epidemic will **re-occur** every 15-20 yrs

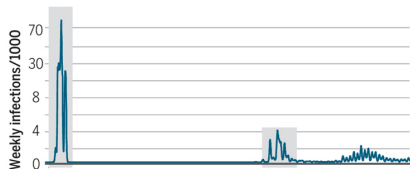
An epidemic will last about 3-5 yrs

Shorter on local scale: 6 months

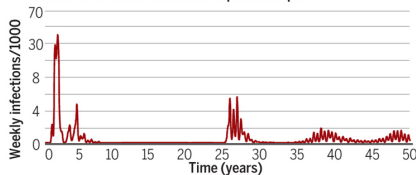
Develop **new interventions** before new large-scale outbreaks occur

Zika epidemic simulations

No intervention



With intervention to reduce mosquito life span



Ferguson et al., 2016

Other Applications

Sexually transmitted
infections (STI)

Ebola

Malaria

Influenza mortality

Foodborne outbreaks

Tuberculosis

Hepatitis C elimination

Conclusion

Modelling plays an **increasingly important** role in helping to guide the most high **impact** and **cost-effective** preventions.

It can be a **critical tool** for guiding public health action.

Model limitations.

Decision makers **benefit** - so does the population.

Still a number of **challenges** in achieving a successful interface between modelling and public health actors.

[illegible]



Any questions?

References

- [1] Craig R. Ramsay et al. "Interrupted Time Series Designs in Health Technology Assessment: Lessons from Two Systematic Reviews of Behavior Change Strategies". In: *International Journal of Technology Assessment in Health Care* 19.4 (2003), pp. 613–623. ISSN: 0266-4623. pmid: 15095767.
- [2] Lukas Richter et al. "Invasive Pneumococcal Diseases in Children and Adults before and after Introduction of the 10-Valent Pneumococcal Conjugate Vaccine into the Austrian National Immunization Program". In: *PloS One* 14.1 (2019), e0210081. ISSN: 1932-6203. DOI: 10.1371/journal.pone.0210081. pmid: 30629620.
- [3] Neil M. Ferguson et al. "Countering the Zika Epidemic in Latin America". In: *Science* 353.6297 (July 22, 2016), pp. 353–354. ISSN: 0036-8075, 1095-9203. DOI: 10.1126/science.aag0219. pmid: 27417493. URL: <https://science.sciencemag.org/content/353/6297/353> (visited on 06/19/2019).
- [4] J. Nielsen et al. "European All-Cause Excess and Influenza-Attributable Mortality in the 2017/18 Season: Should the Burden of Influenza B Be Reconsidered?" In: *Clinical Microbiology and Infection* (Feb. 18, 2019). ISSN: 1198-743X. DOI: 10.1016/j.cmi.2019.02.011. URL: <http://www.sciencedirect.com/science/article/pii/S1198743X19300588> (visited on 04/08/2019).
- [5] Polonsky Jonathan A. et al. "Outbreak Analytics: A Developing Data Science for Informing the Response to Emerging Pathogens". In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 374.1776 (July 8, 2019), p. 20180276. DOI: 10.1098/rstb.2018.0276. URL: <https://royalsocietypublishing.org/doi/10.1098/rstb.2018.0276> (visited on 06/18/2019).
- [6] R. E. Serfling, I. L. Sherman, and W. J. Houseworth. "Excess Pneumonia-Influenza Mortality by Age and Sex in Three Major Influenza A2 Epidemics, United States, 1957-58, 1960 and 1963". In: *American Journal of Epidemiology* 86.2 (Sept. 1967), pp. 433–441. ISSN: 0002-9262. DOI: 10.1093/oxfordjournals.aje.a120753. pmid: 6058395.
- [7] C. J. E. Metcalf, W. J. Edmunds, and J. Lessler. "Six Challenges in Modelling for Public Health Policy". In: *Epidemics. Challenges in Modelling Infectious Disease Dynamics* 10 (Mar. 1, 2015), pp. 93–96. ISSN: 1755-4365. DOI: 10.1016/j.epidem.2014.08.008. URL: <http://www.sciencedirect.com/science/article/pii/S1755436514000620> (visited on 06/23/2019).