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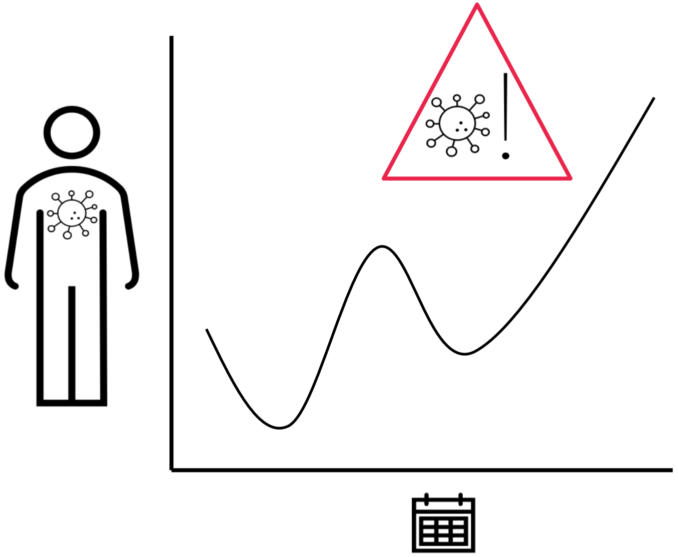
Early Warning Signals
in Epidemiological data

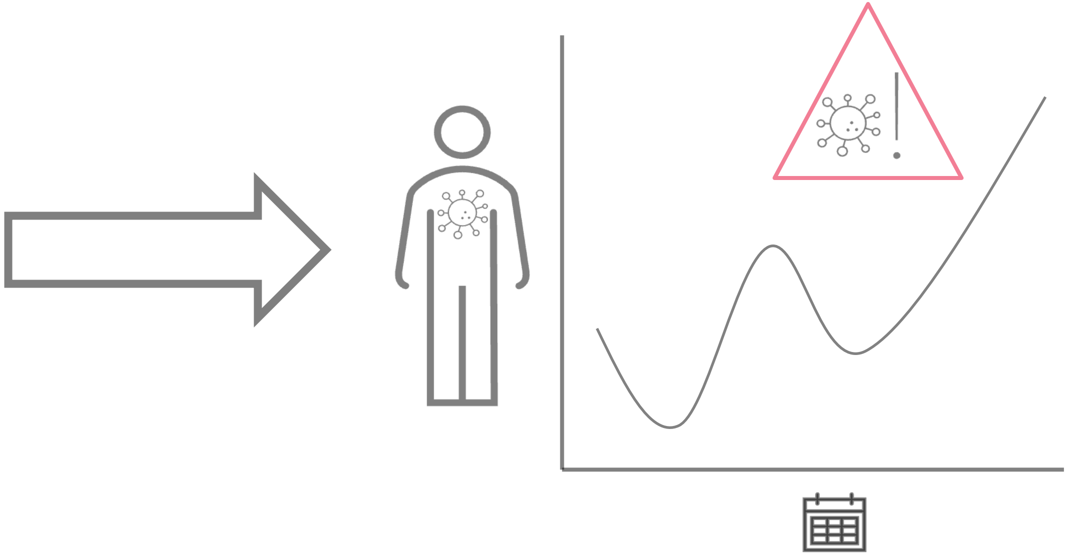


INPUT Research meeting

Bern, 16 September 2022

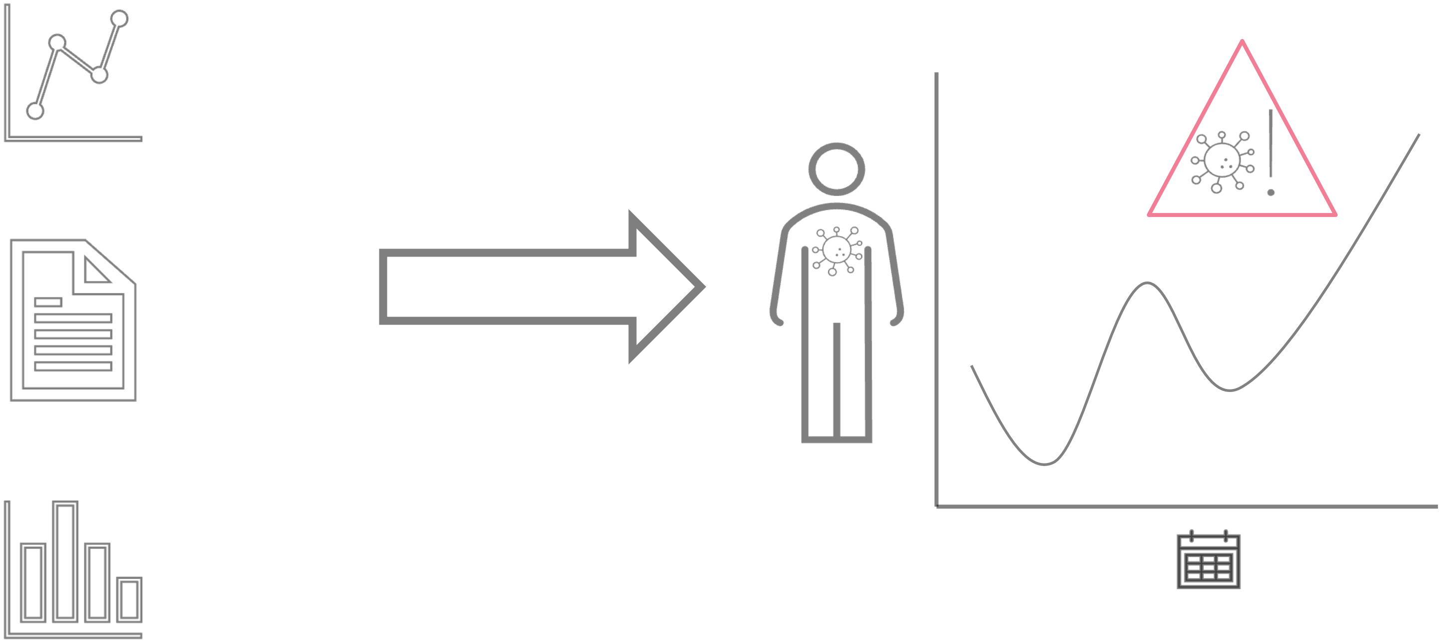
Several types of data

Predict epidemic waves



Several types o ict epidemic waves

Early Warning Signals



Several types o ict epidemic waves

Early Warning Signals

I. Introduction to dynamical systems and bifurcations

II. The theory behind Early Warning Signals (EWS)

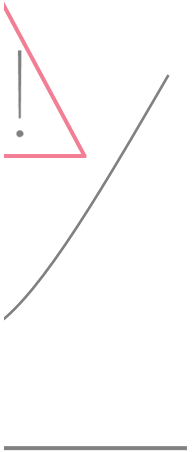
III. Examples of EWS

IV. Applications of EWS to COVID-19

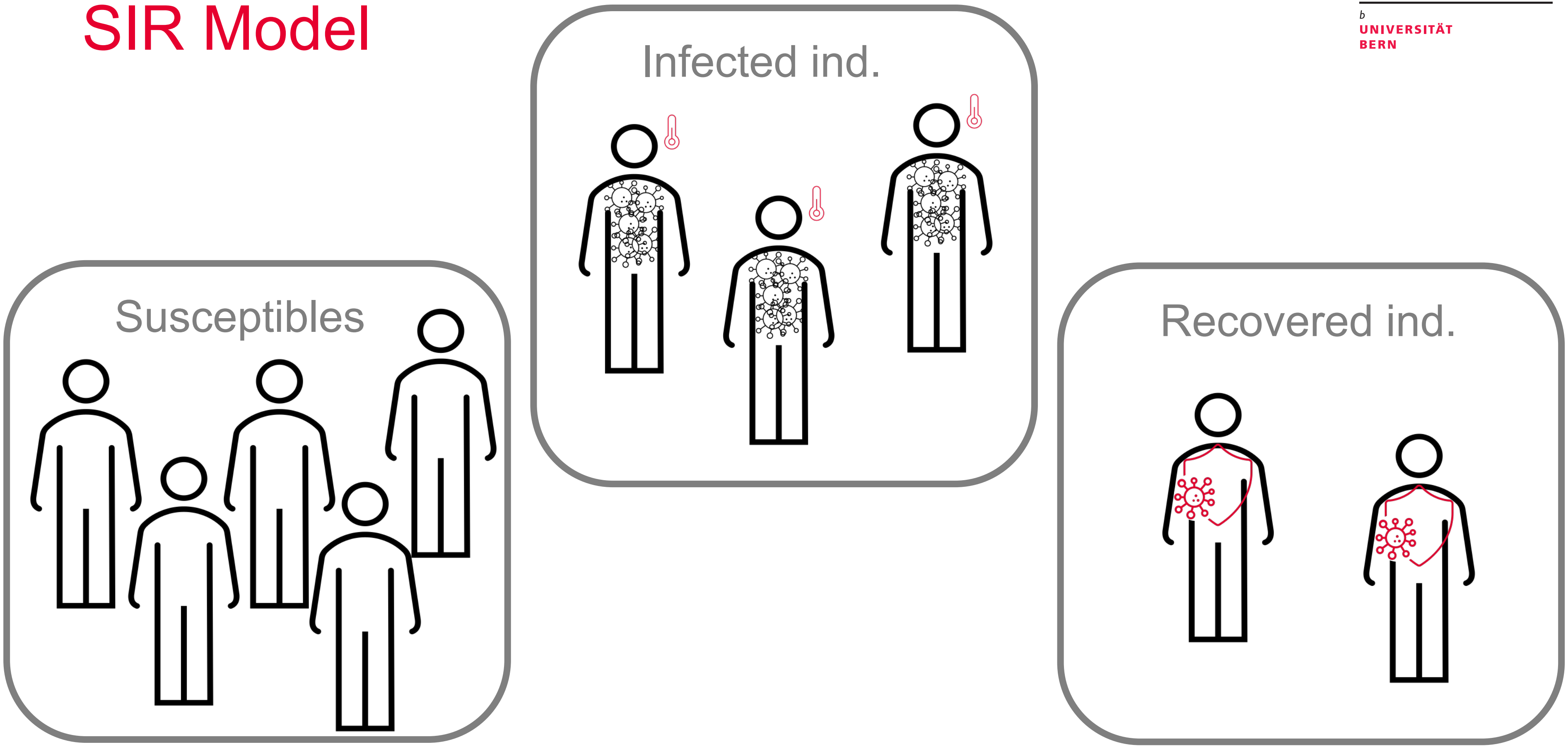
V. Challenges of EWS for COVID-19

VI. EWS in the MCID project

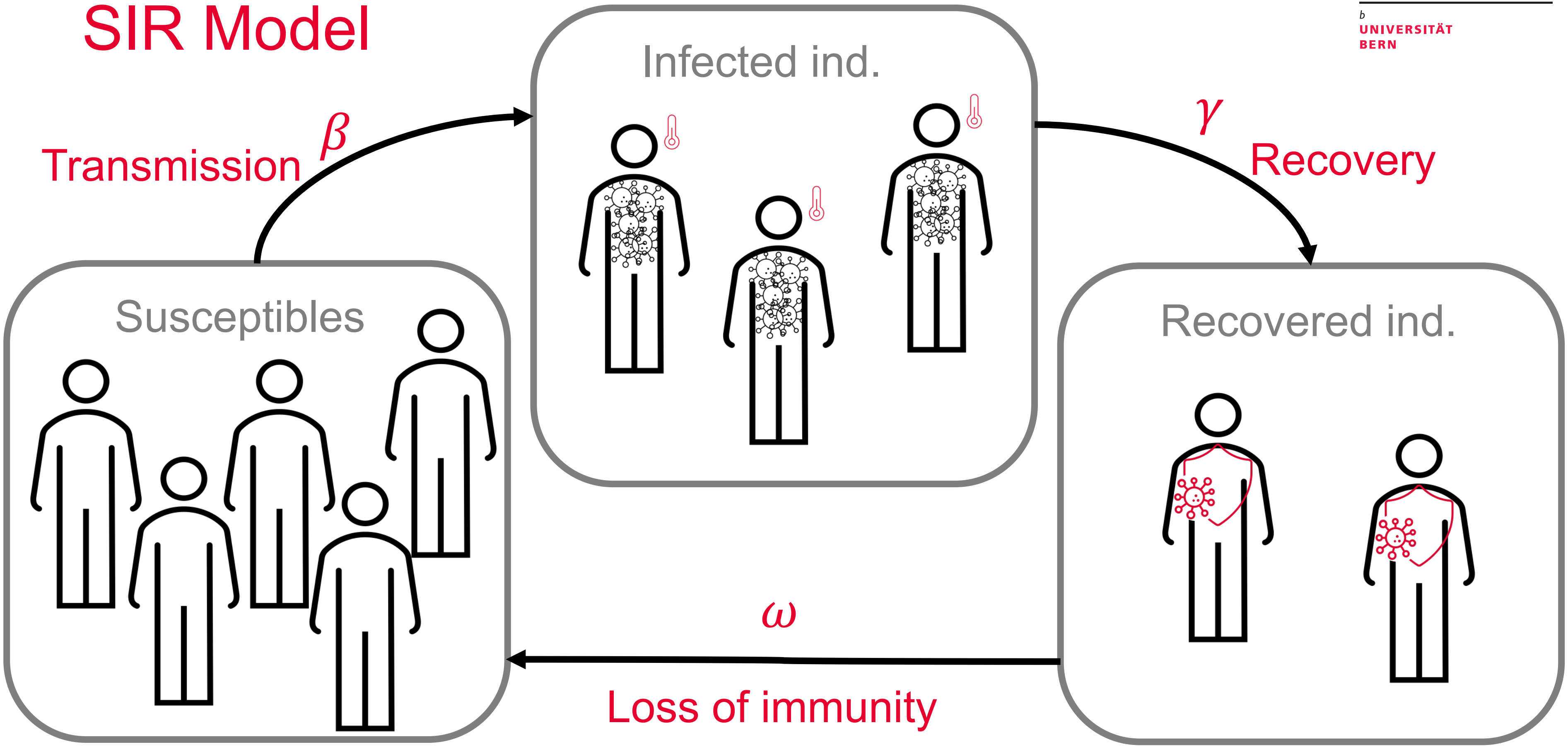
VII. Discussion



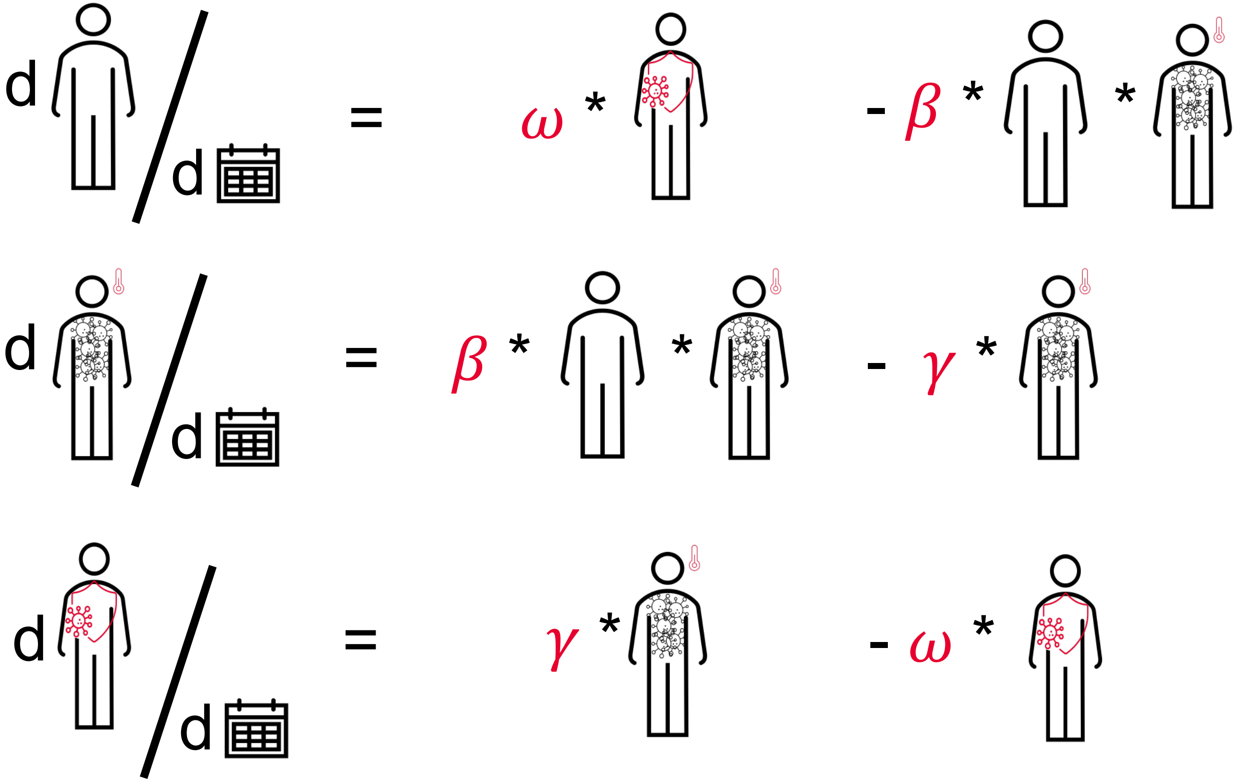
SIR Model



SIR Model

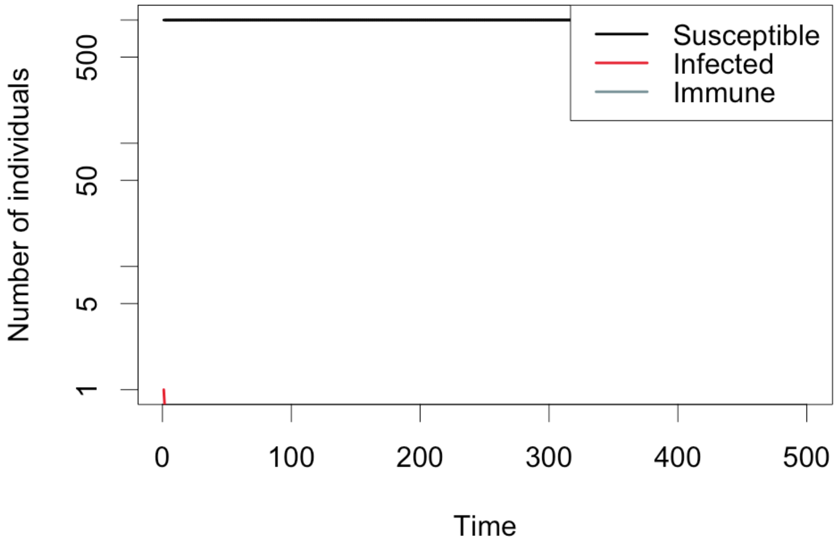

Infected ind.
β
Transmission
γ
Recovery
Susceptibles
Recovered ind.
ω
Loss of immunity

SIR Model

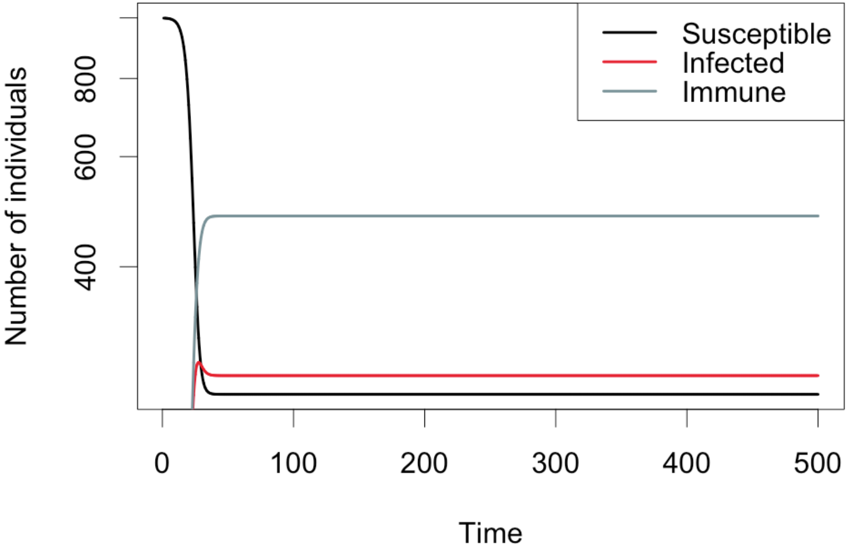


SIR dynamics

$\beta = 0.0002$
$\gamma = 0.45$
N = 1000



$\beta = 0.001$
$\gamma = 0.45$
N = 1000



SIR dynamics

$\beta = 0.0002$
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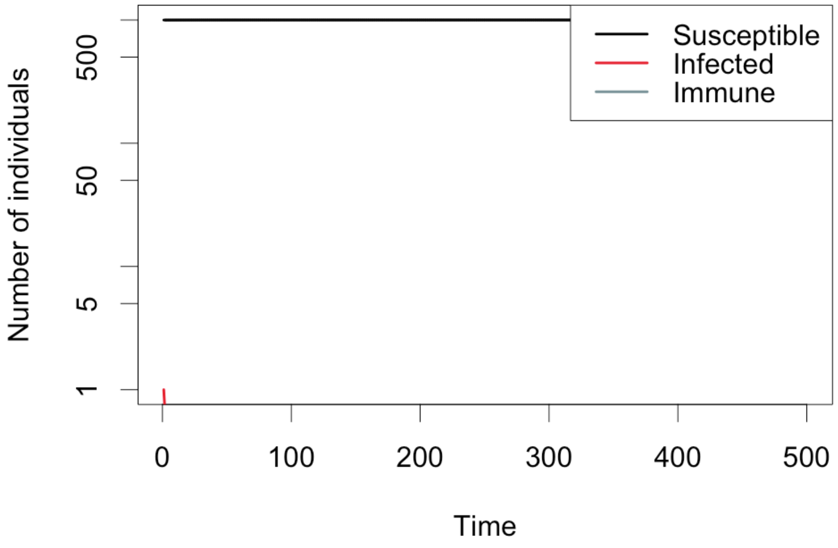
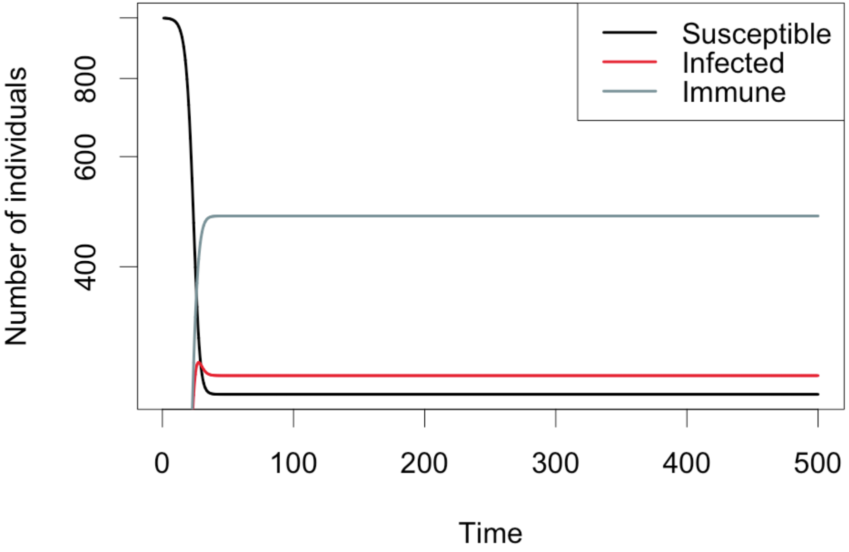
N = 1000



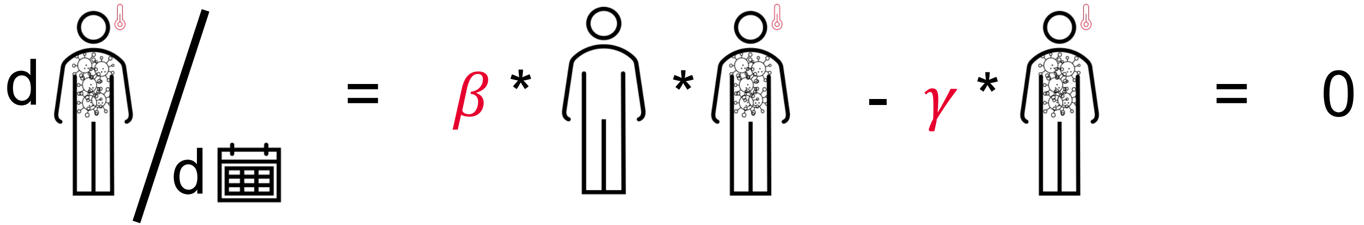
Disease free equilibrium

$\beta = 0.001$
$\gamma = 0.45$
N = 1000



Endemic equilibrium

Equilibria – where are they?



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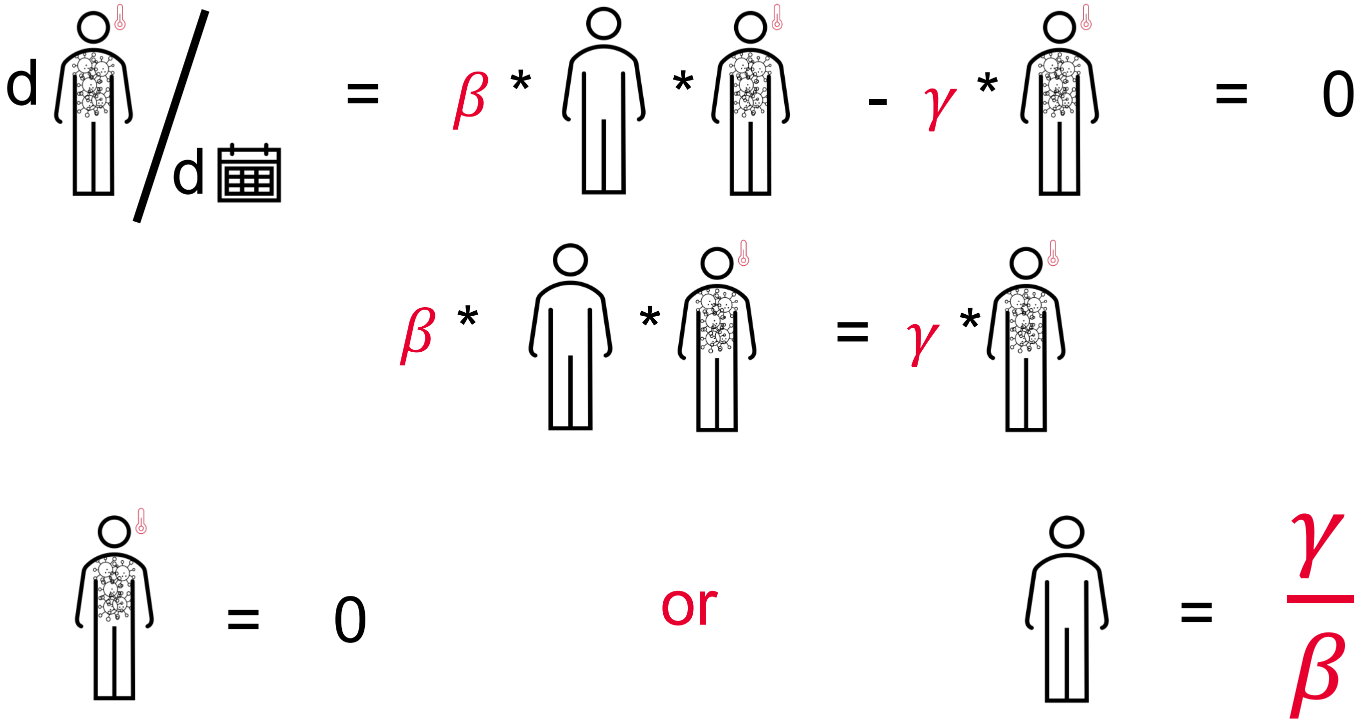
Equilibria – where are they?



Basic reproduction number

$$R_0 = \frac{\beta * S_0}{\gamma}$$

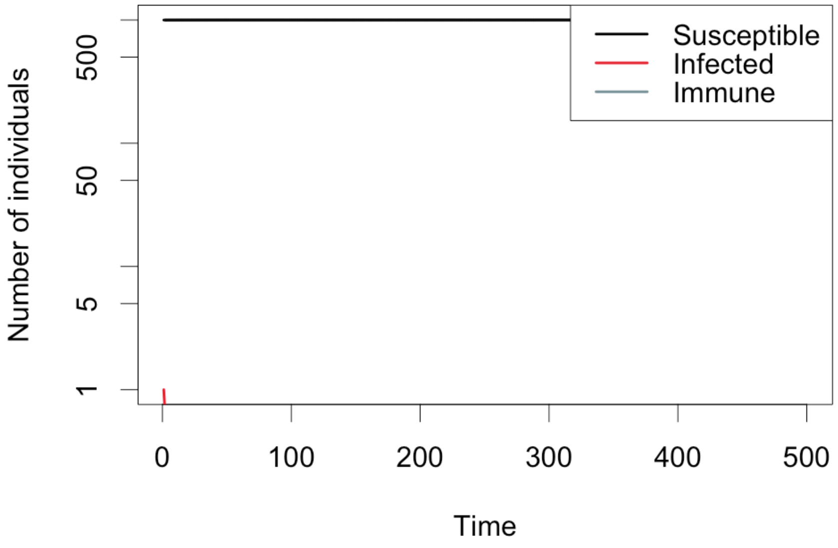
Initial number of susceptibles

$\frac{1}{\gamma}$ → duration of infectious period

SIR dynamics

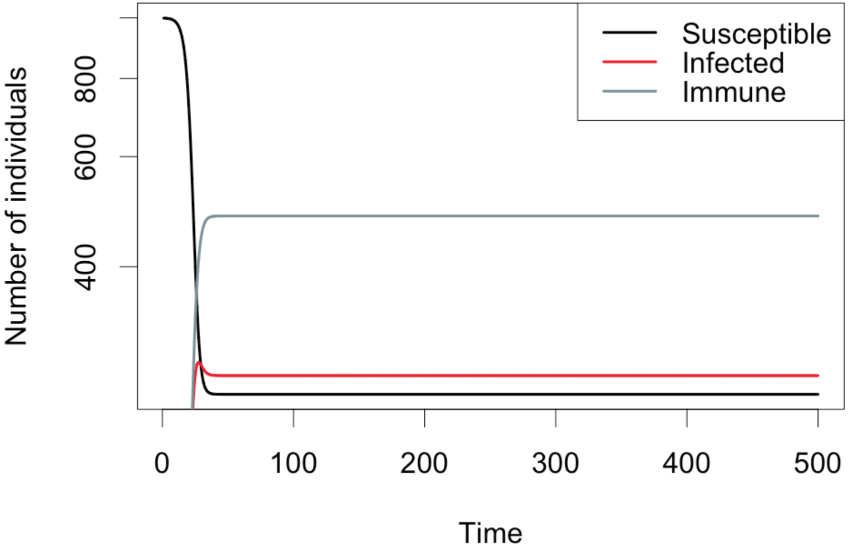
$R_0 < 1$

$R_0 = 0.44$



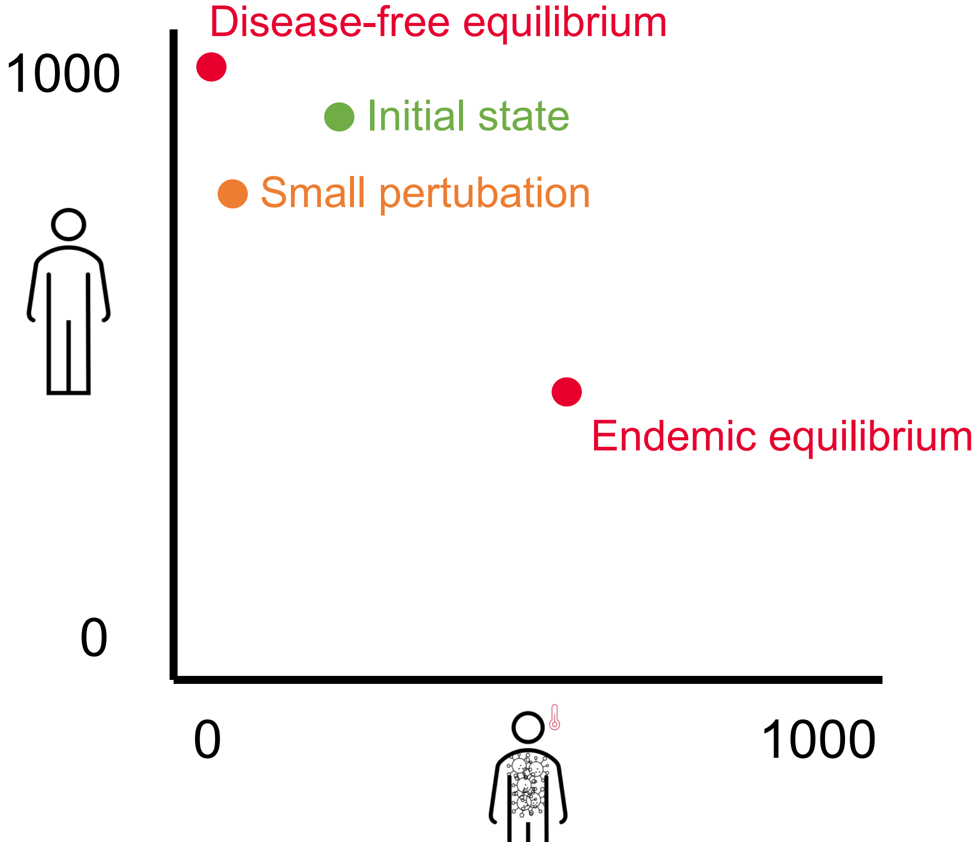
$R_0 > 1$

$R_0 = 2.2$



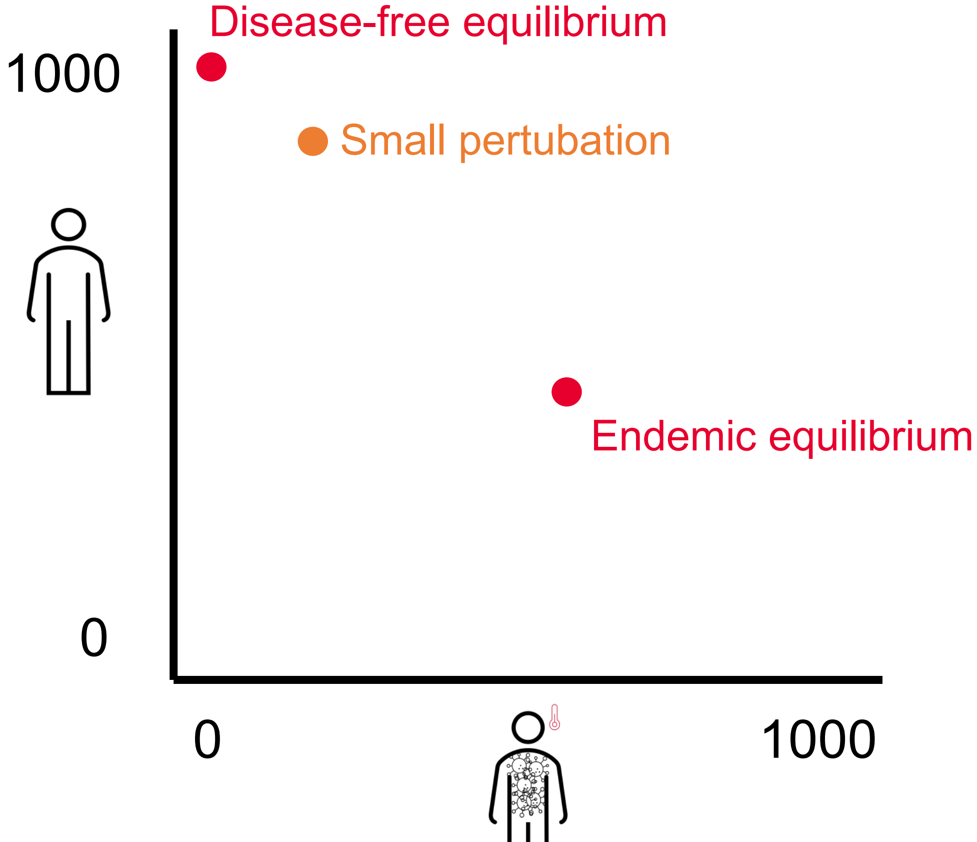
Stability of equilibria

$R_0 = 0.44$

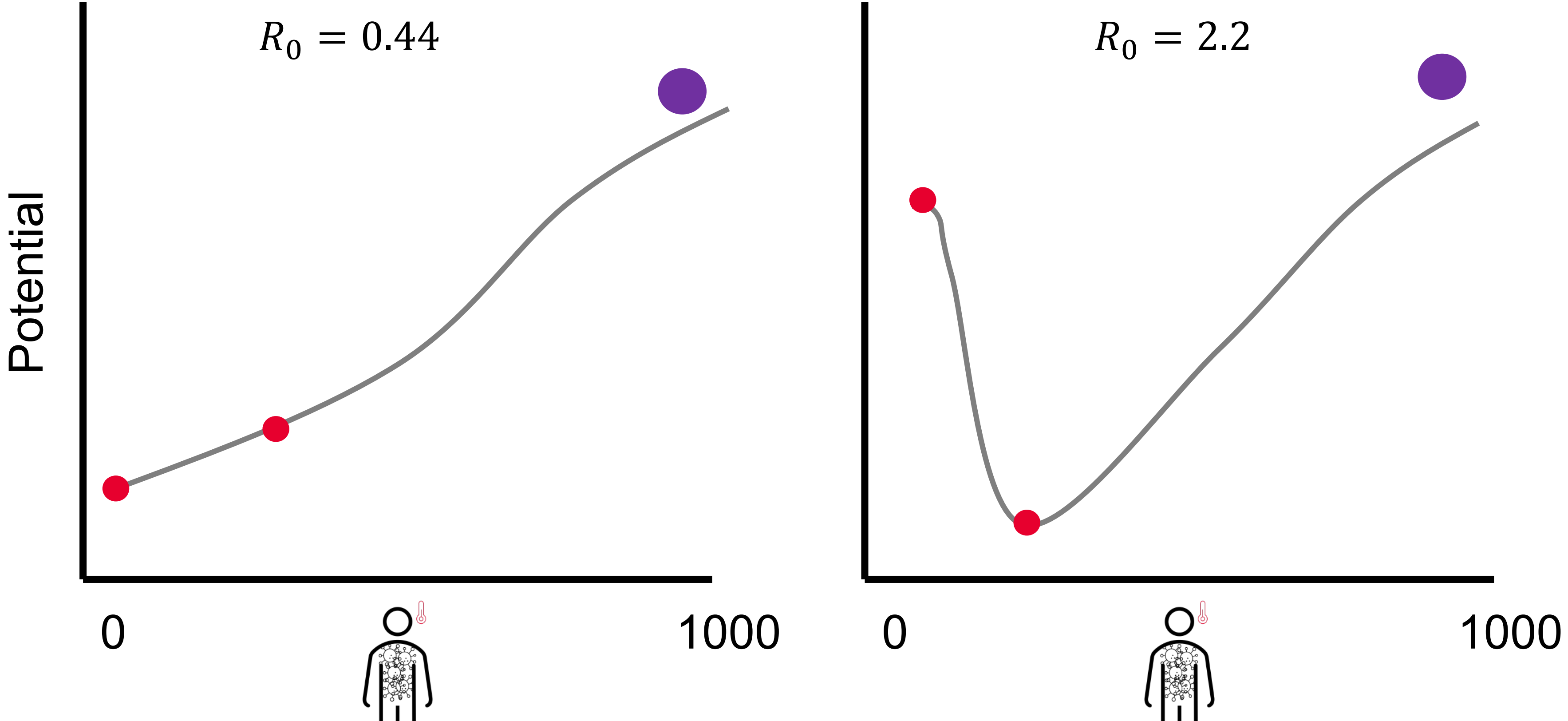


Stability of equilibria

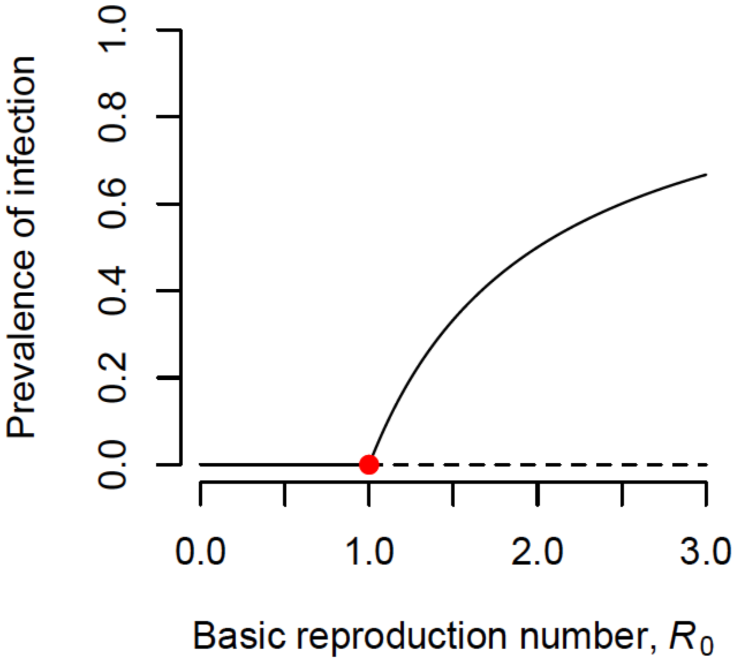
$R_0 = 2.2$



Stability of equilibria – Potential of the system

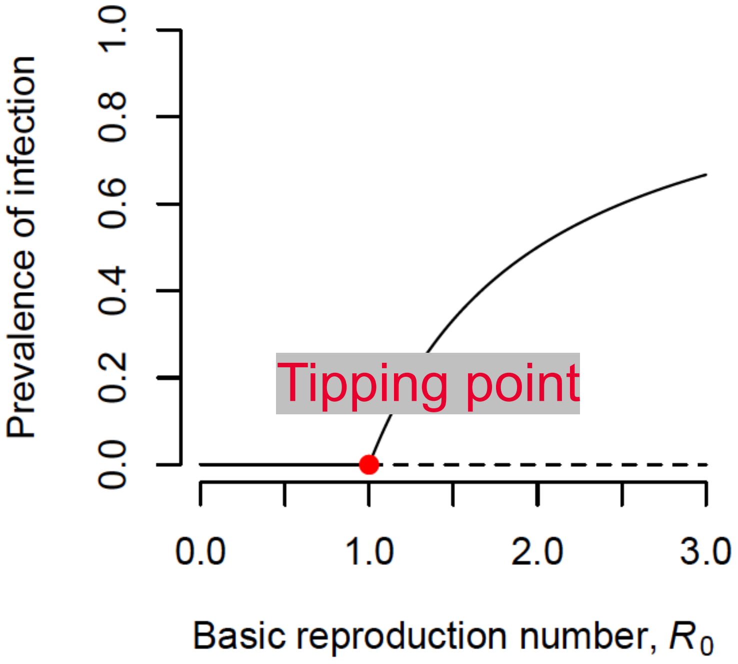


Bifurcation



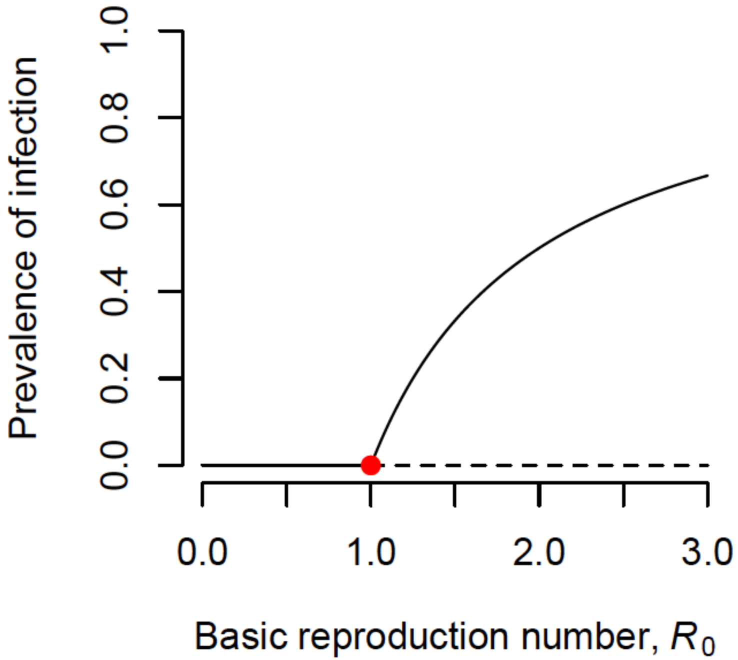
Althaus, pers. Com.

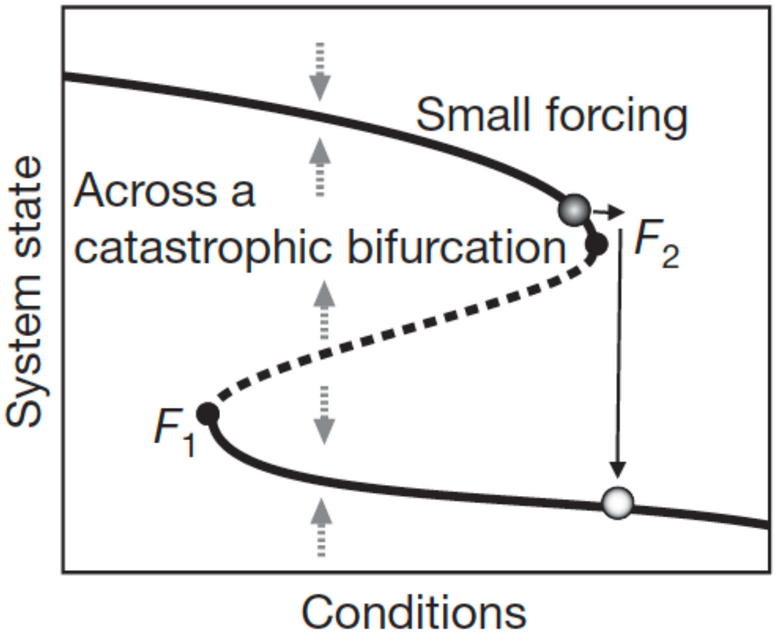
Bifurcation



Althaus, pers. Com.

Critical transitions

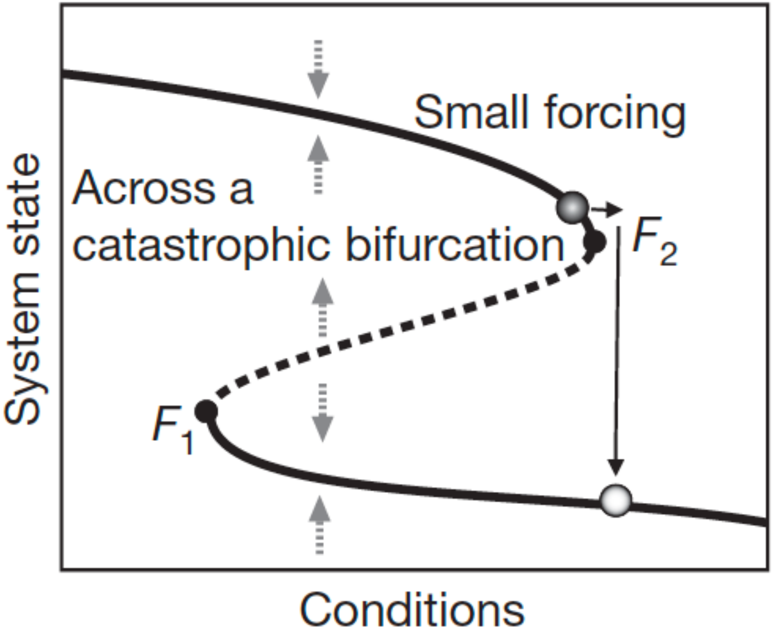




Althaus, pers. Com.

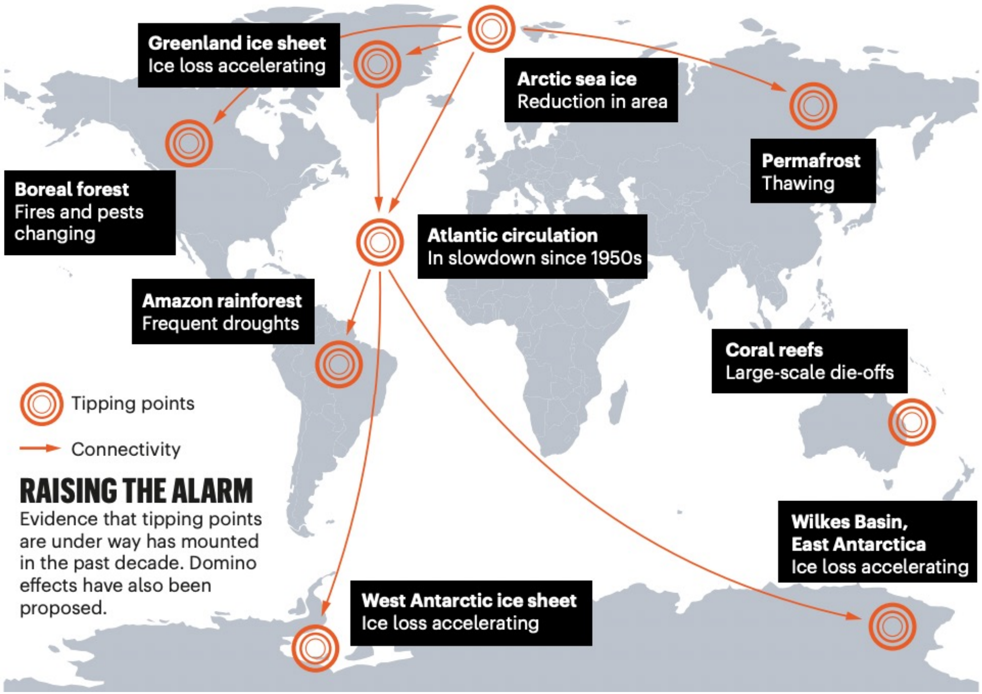
Scheffer et al, Nature, 2009

Critical transition for coral bleaching



Scheffer et al, Nature, 2009

Many examples from climate science



Lenton et al, Nature, 2019

Predicting critical transitions

Early Warning Signs predict critical transitions in a wide range of dynamical models

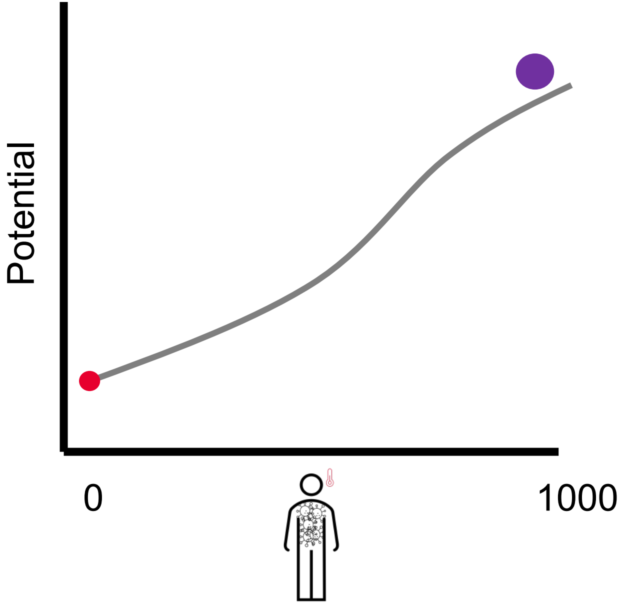
Generic properties near critical point:

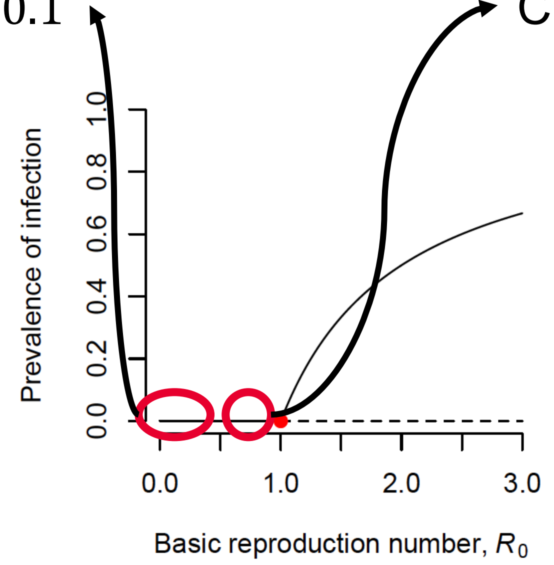
- More time to recover from a small perturbation close to a transition: critical slowing down
- Asymmetry of fluctuations increases
- Flickering between to steady states

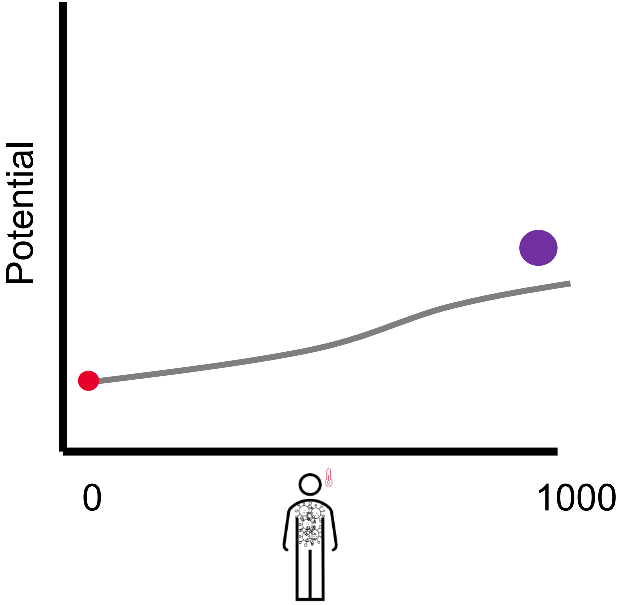
Critical slowing down

Far from bifurcation: $R_0 = 0.1$

Close to bifurcation: $R_0 = 0.95$



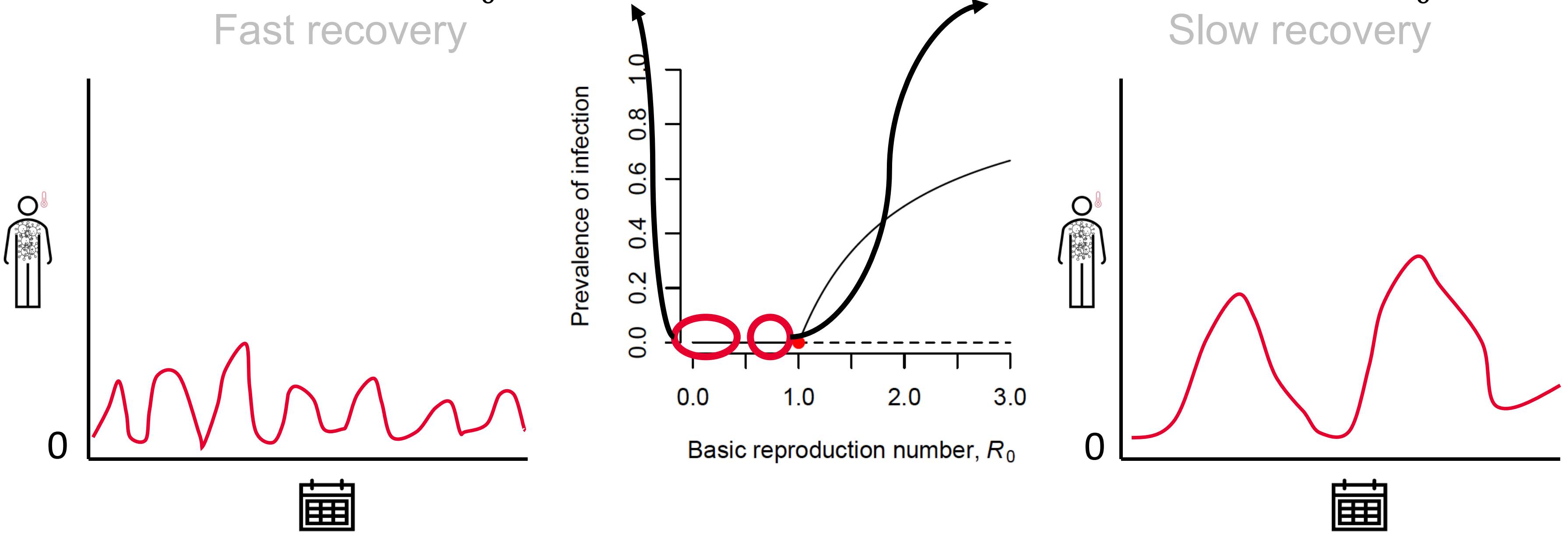




Critical slowing down – recovery rate

Far from bifurcation: $R_0 = 0.1$
Fast recovery

Close to bifurcation: $R_0 = 0.95$
Slow recovery

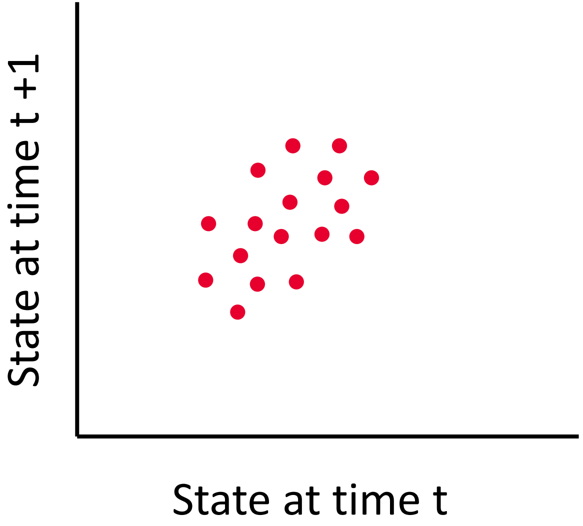


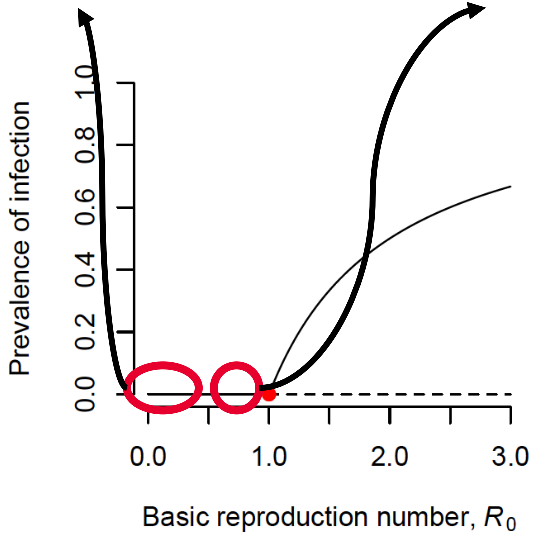
Inspired by: Dablander et al, Psych Methods, 2022

Critical slowing down – Autocorrelation

Far from bifurcation: $R_0 = 0.1$

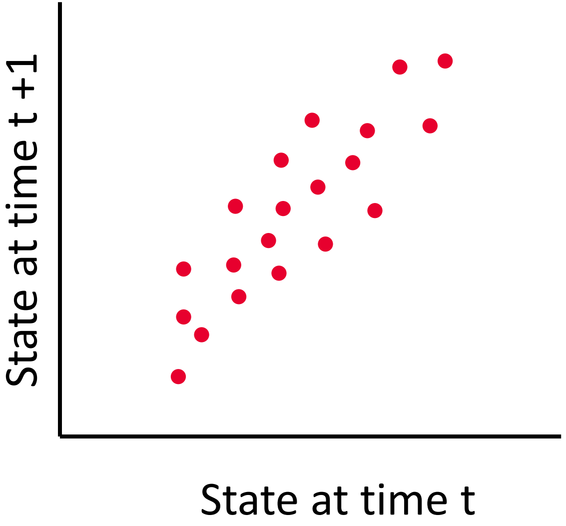
Low autocorrelation





Close to bifurcation: $R_0 = 0.95$

High autocorrelation

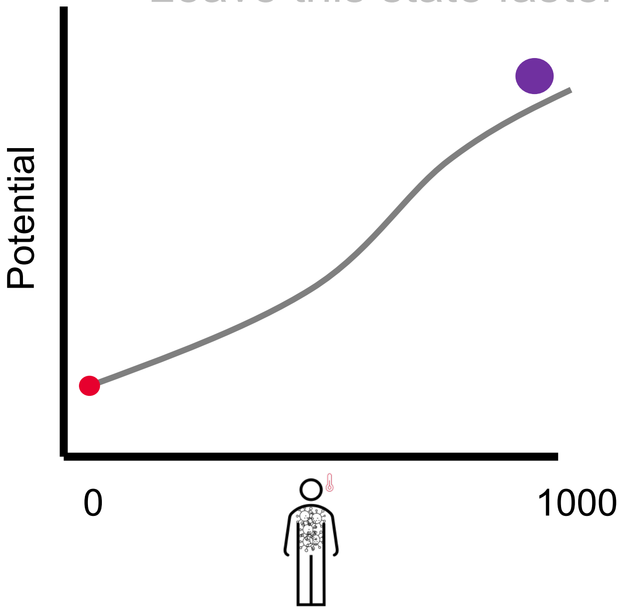


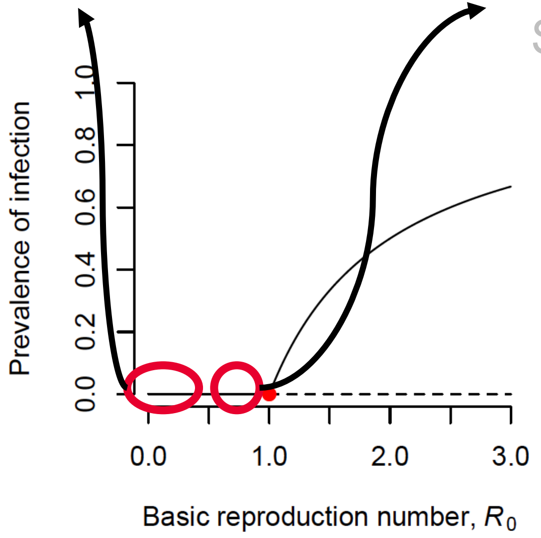
Inspired by: Dablander et al, Psych Methods, 2022

Asymmetry of fluctuations – Skewness & kurtosis

Far from bifurcation: $R_0 = 0.1$

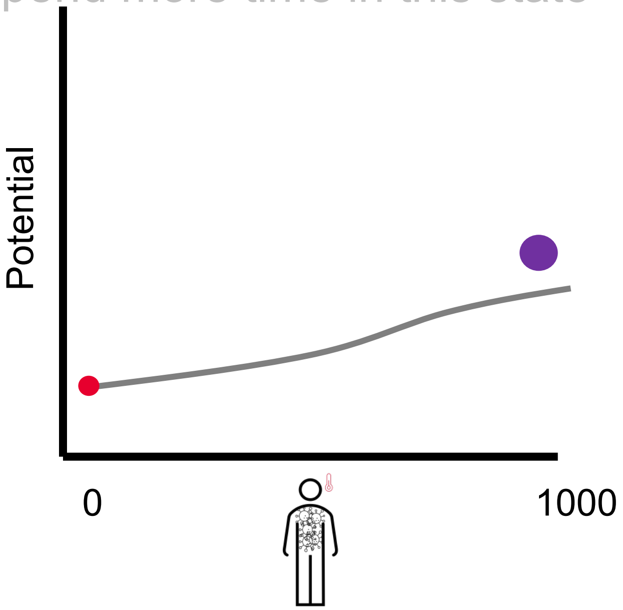
Leave this state faster





Close to bifurcation: $R_0 = 0.95$

Spend more time in this state



Different types of EWS

Due to critical slowing down increase in:

- recovery time
- Variance
- Coefficient of variation
- Autocorrelation

Due to asymmetry of fluctuations increase in:

- Skewness
- Kurtosis

Due to flickering:

- bi-modality

Scheffer et al, Nature, 2009

Different types of EWS

Due to critical slowing down increase in:

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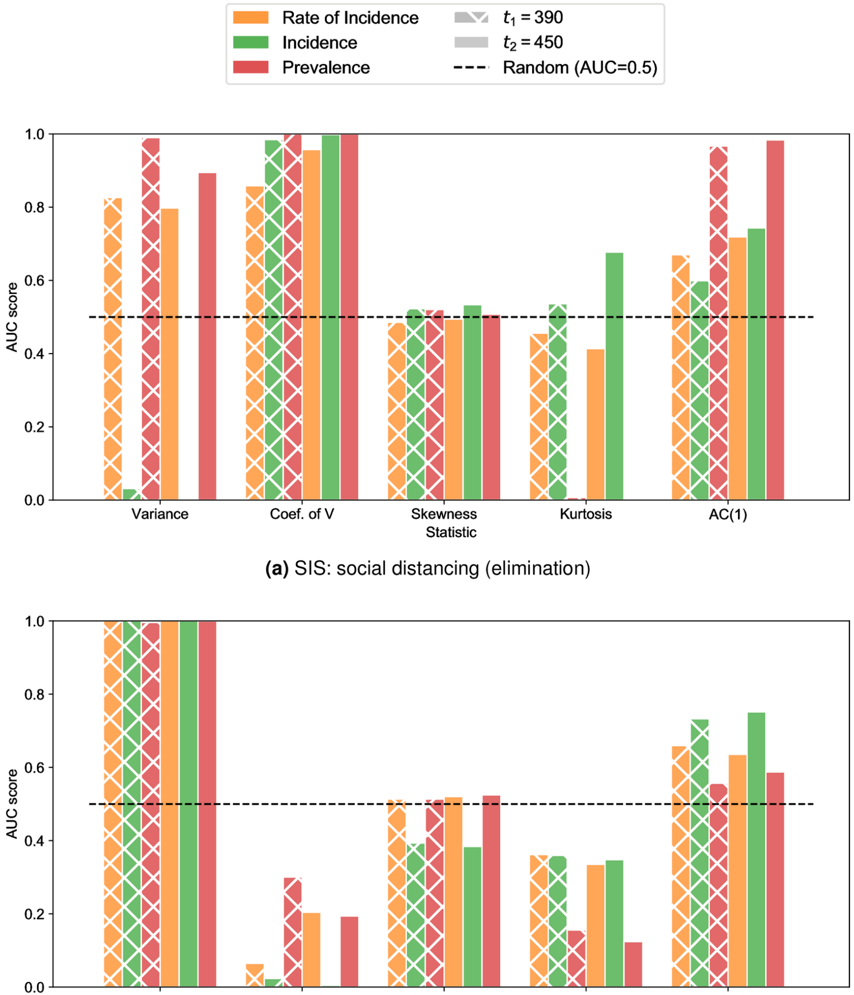
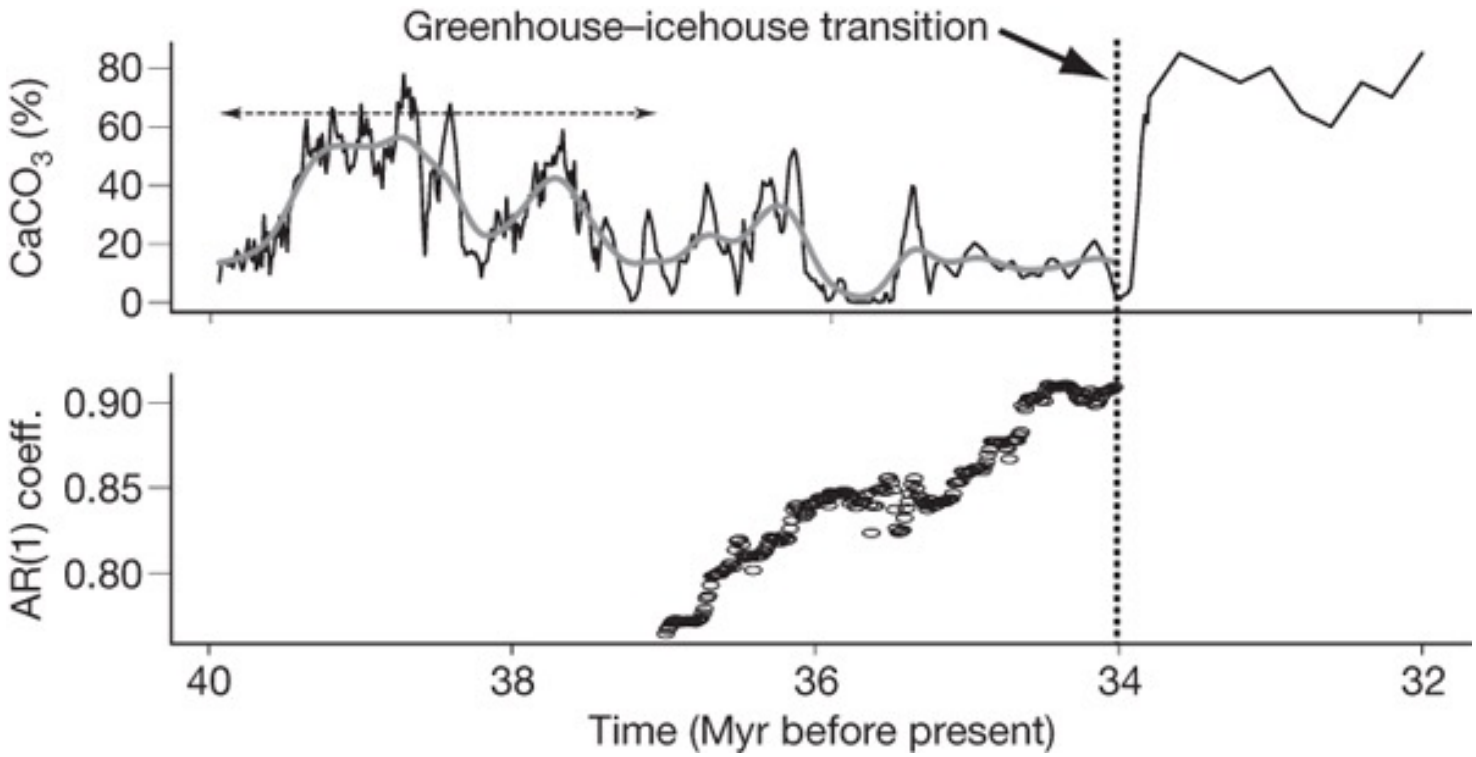


(a) SIS: social distancing (elimination)

(b) SIS (emergence)

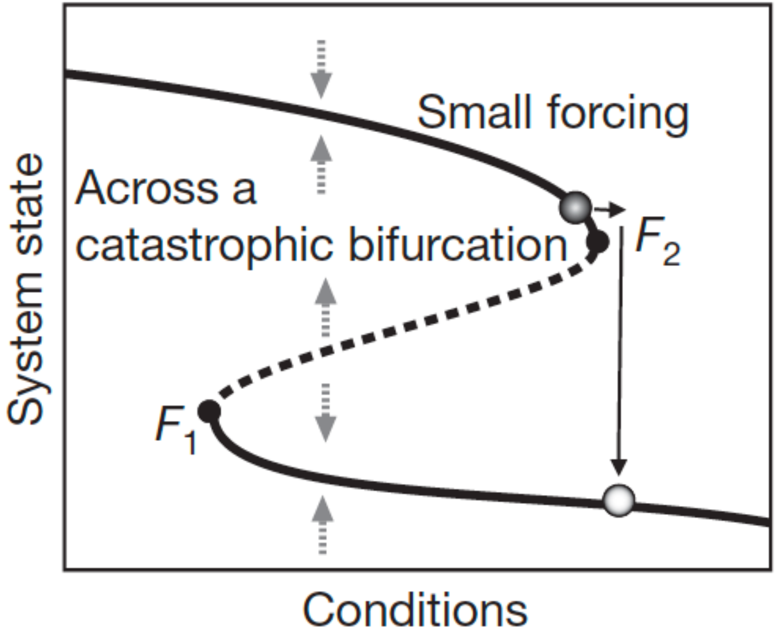
Southall et al, Plos Comp. Bio., 2020

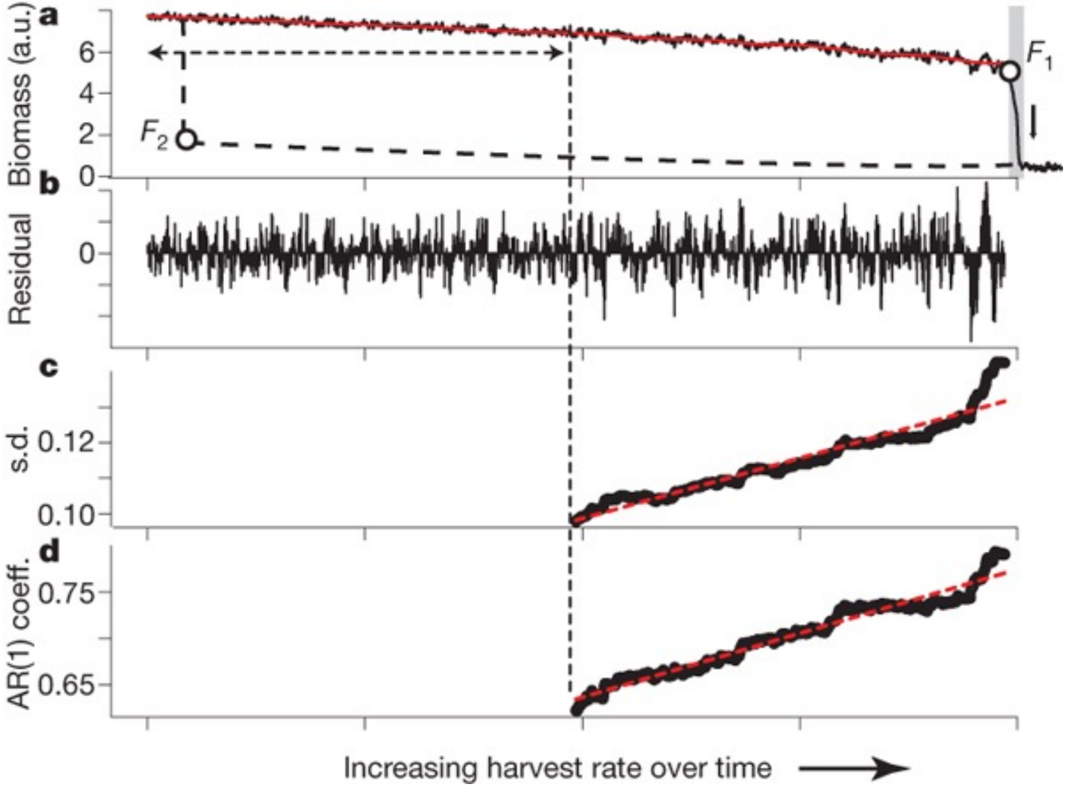
Greenhouse-icehous transition



Scheffer et al, Nature, 2009

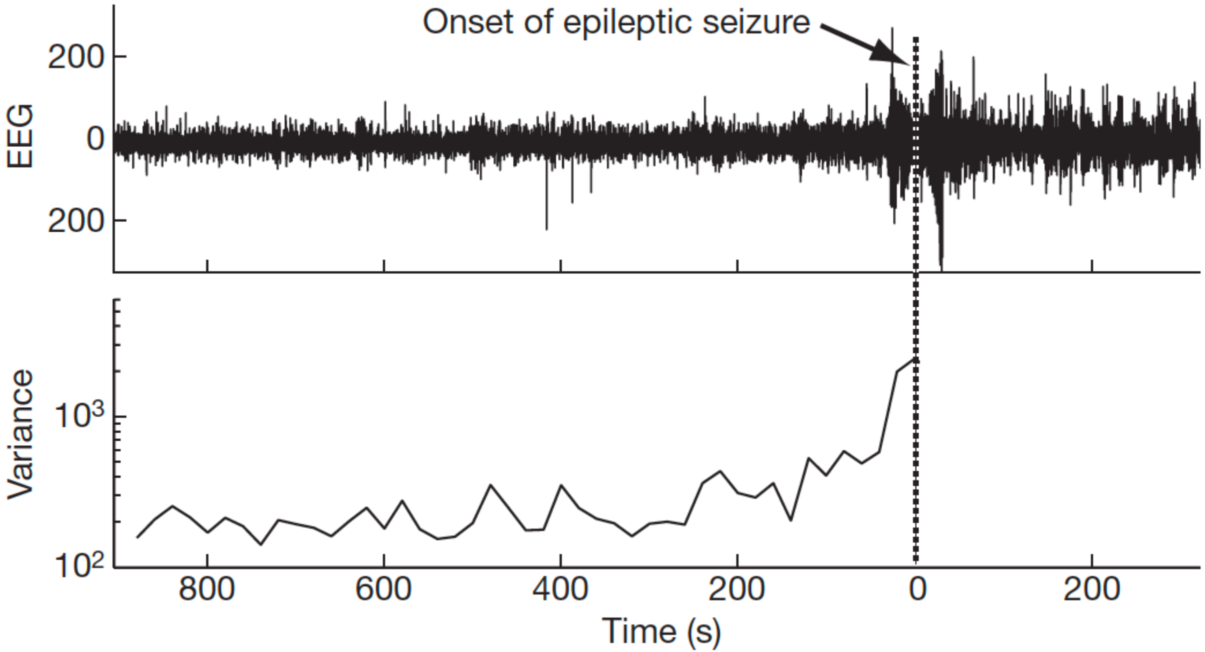
Critical transition in harvast





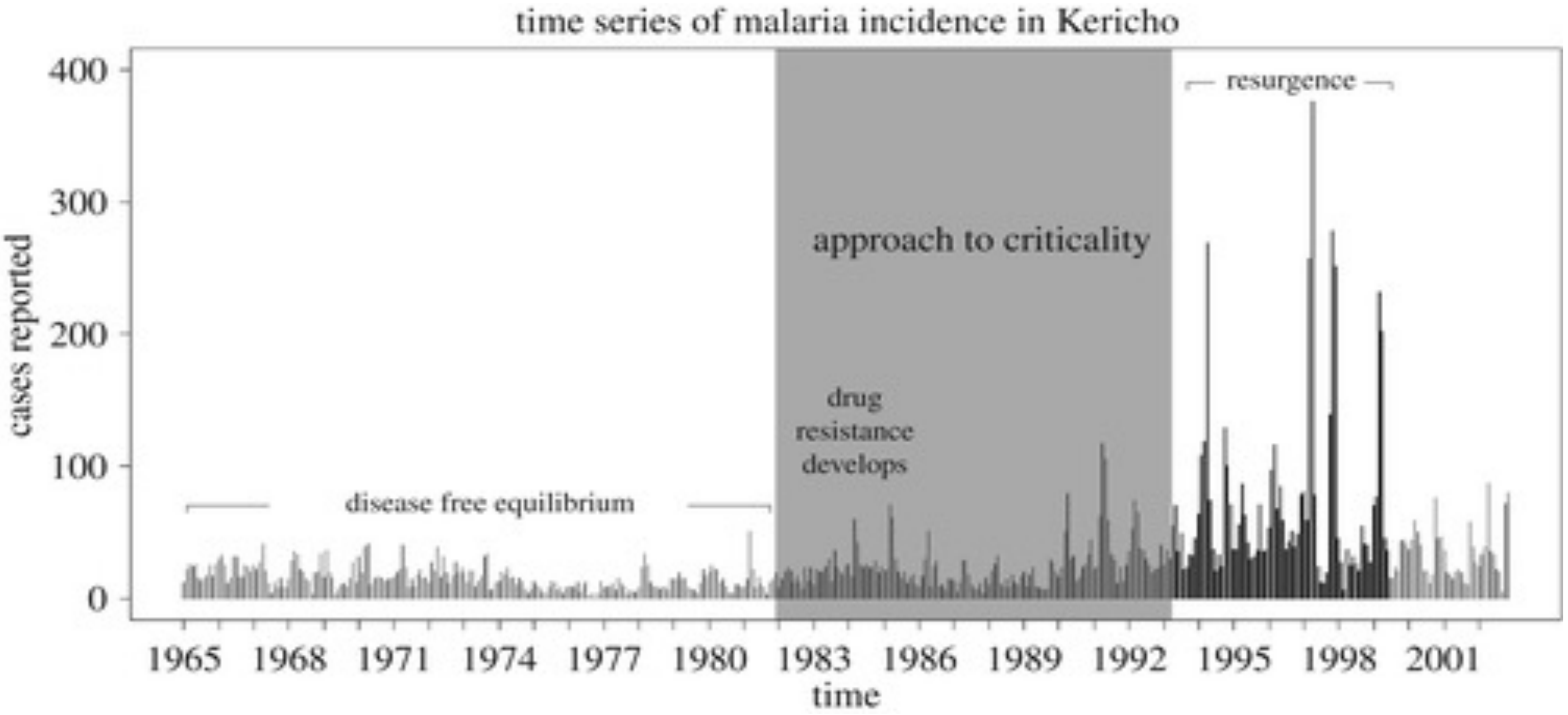
Scheffer et al, Nature, 2009

Epileptic seizure

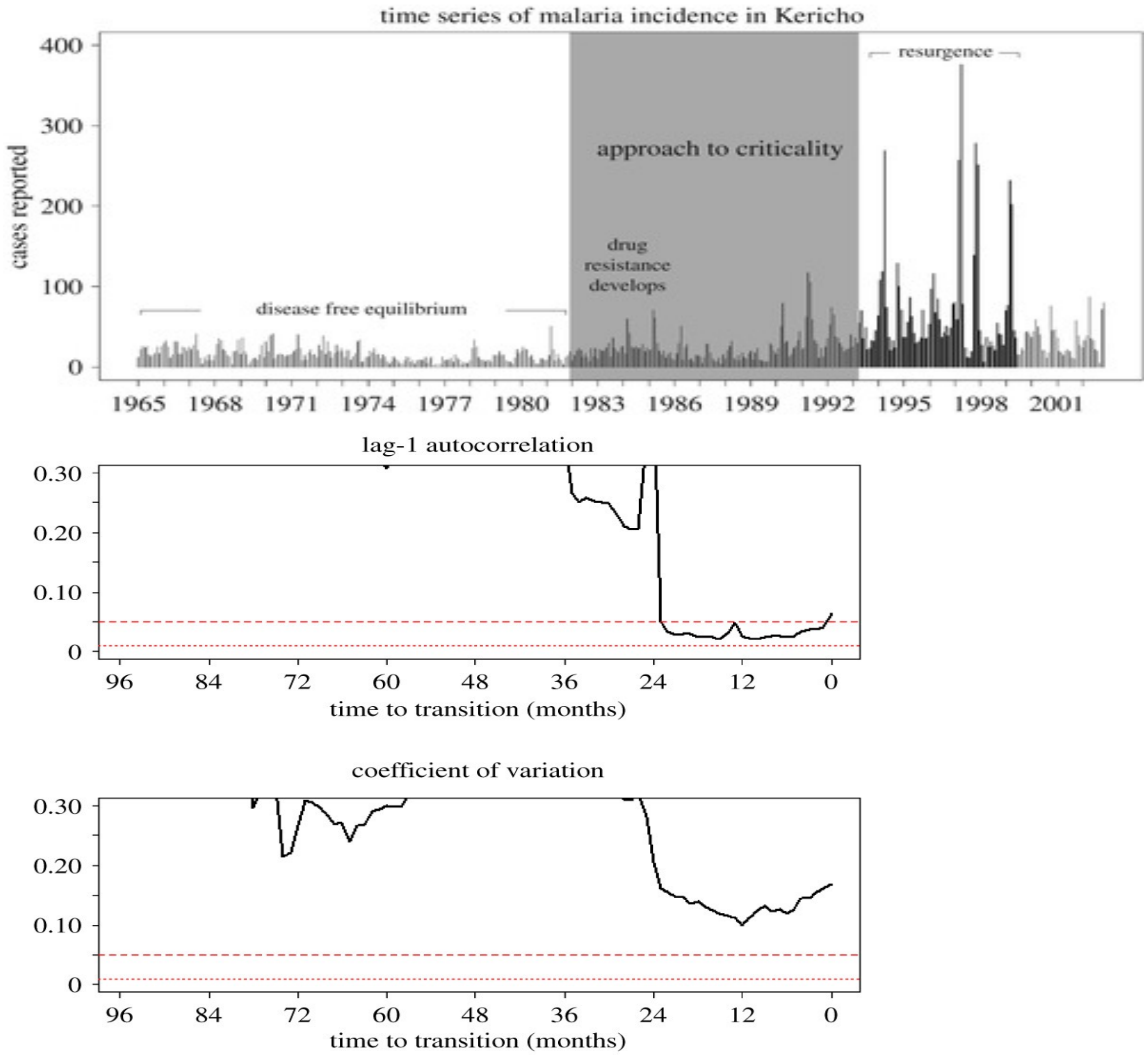


Scheffer et al, Nature, 2009

Resurgence of Malaria



Harris et al, R. Soc. B, 2020



Harris et al, R. Soc. B, 2020

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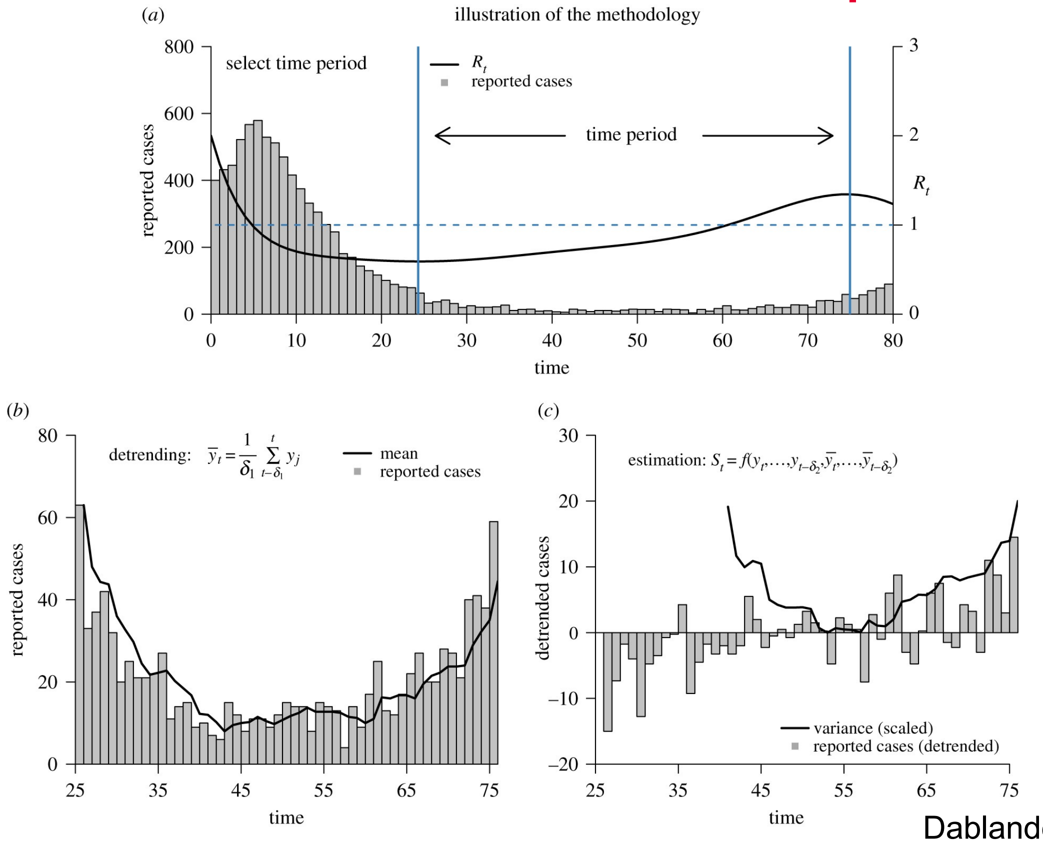
EWS for case data of COVID-19

First Author	Main result	DOI
Dablander	Overlapping time-scales obscure EWS.	https://doi.org/10.1098/rspb.2021.1809
Proverbio	EWS can be useful for active monitoring of epidemic dynamics, but that their performance is sensitive to certain features of the underlying dynamics.	https://doi.org/10.1371/journal.pcbi.1009958
O`brien	EWSs offer the opportunity for policymakers to improve the accuracy of urgent intervention decisions but best characterize hypothesized critical transitions.	https://doi.org/10.1098/rsbl.2021.0487

Detecting the second wave in Europe



Dablander et al, proc. R. Soc. B., 2022

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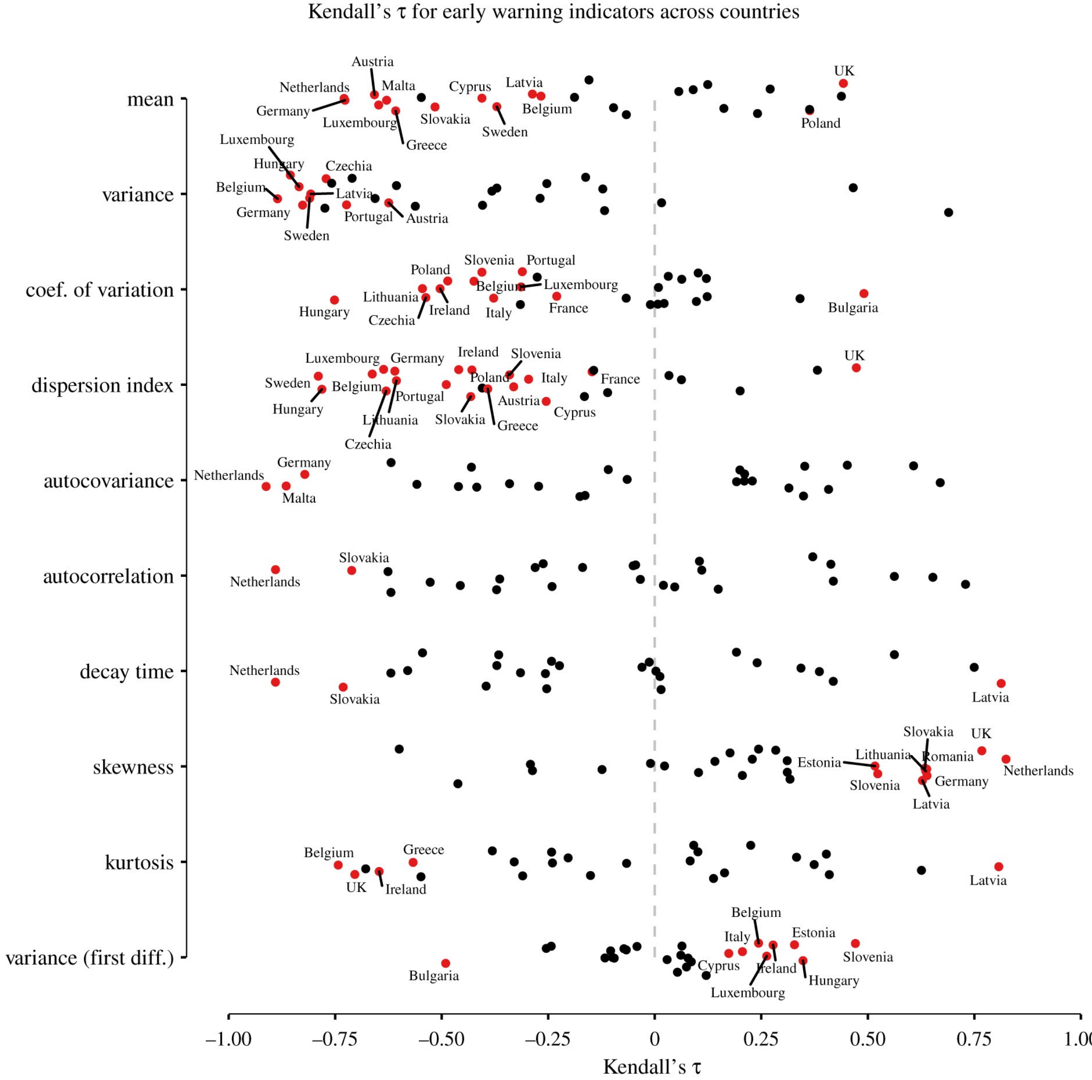

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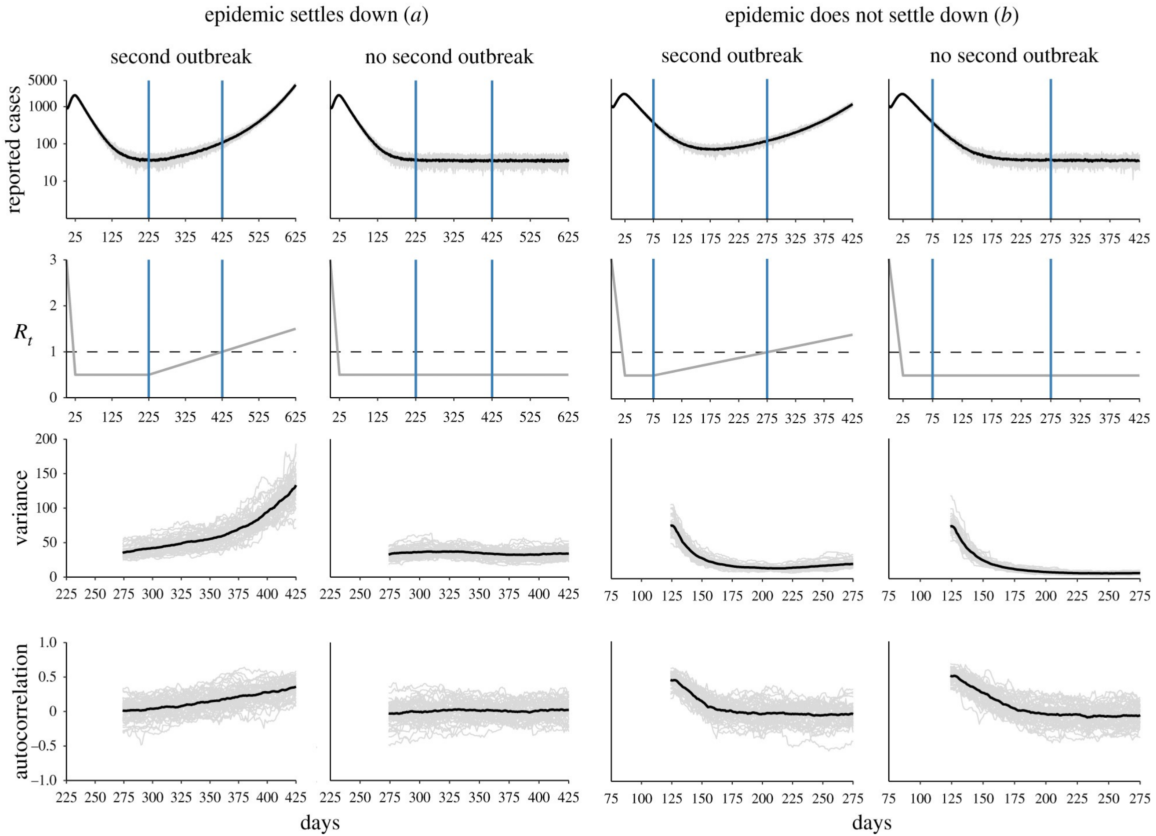
Dablander et al, proc. R. Soc. B., 2022

Detecting the second wave in Europe



Dablander et al, proc. R. Soc. B., 2022

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EWS for other COVID-19 related data

First Author	Type of data	Main result	DOI
Bari	Google search queries & mobility data	Only very pre-liminary results	https://doi.org/10.1007/s13278-021-00723-5
Li	Visits to points of interest	Detects the behavioural response of the population to the COVID-19 pandemic	10.1109/ACCESS.2021.3058568
Lopreite	Twitter data	Unexpected levels of concerns about pneumonia had been raised for several weeks before the frst cases of infection were ofcially announced	https://www.nature.com/articles/s41598-021-81333-1

EWS are not unique to critical transitions

EWS without Critical Transitions	Critical Transitions without EWS
EWS can occur prior to smooth transitions between stable states (Drake & Griffen, 2010; Kéfi et al., 2013).	Strong external perturbations can lead to transitions without EWS (Ditlevsen & Johnsen, 2010; van Nes et al., 2016).
EWS can occur when there is no transition (e.g., Wagner & Eisenman, 2015).	EWS may not occur prior to critical transitions in systems with non-smooth potentials (Hastings & Wysham, 2010).
	Not all variables in a system generally express EWS equally strongly or at all (Boerlijst et al., 2013; Patterson et al., 2021).
	EWS may not occur under correlated or extrinsic noise (Dakos et al., 2012b; O'Regan & Burton, 2018; Qin & Tang, 2018).

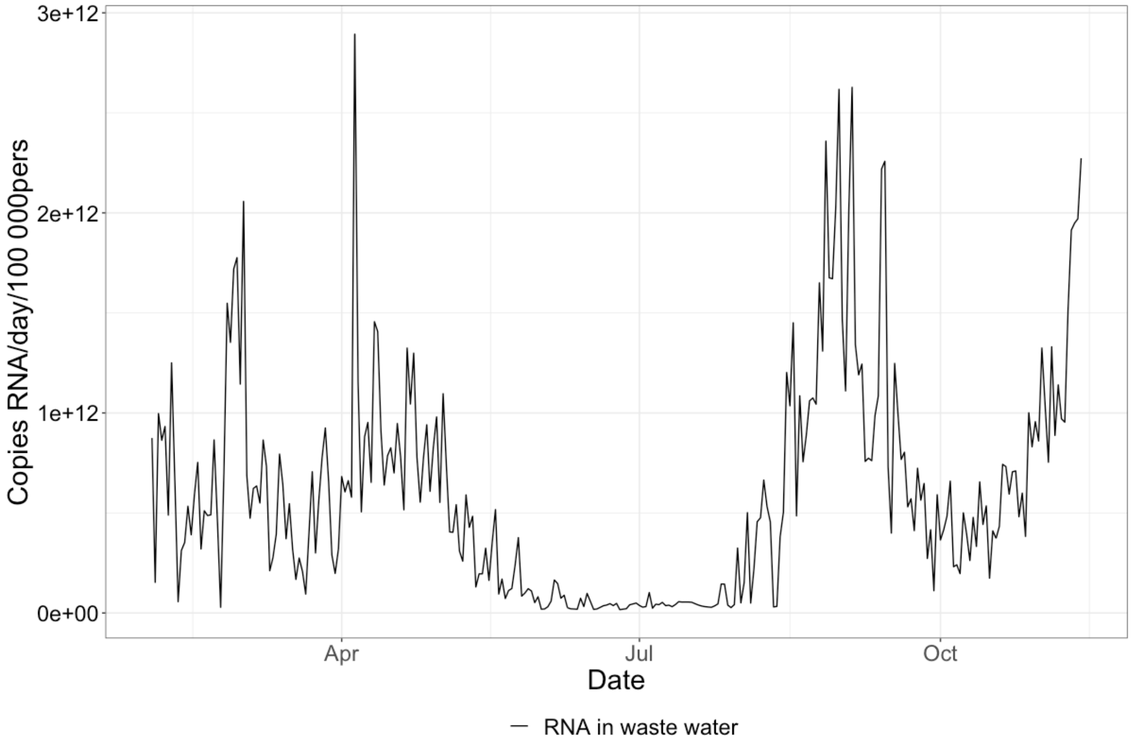
Dablander et al, Psych Methods, 2022

Other challenges

- Seasonality of the data
- Type of detrending used
- Availability of negative control data
- Overlapping time scales
- Co-occuring variants with different R_0 values

EWS in the MCID C-19 monitoring project

Preliminary analysis of Waste-water data



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Step 1

Case numbers

Waste water

Hospitalizations

Sentinella data

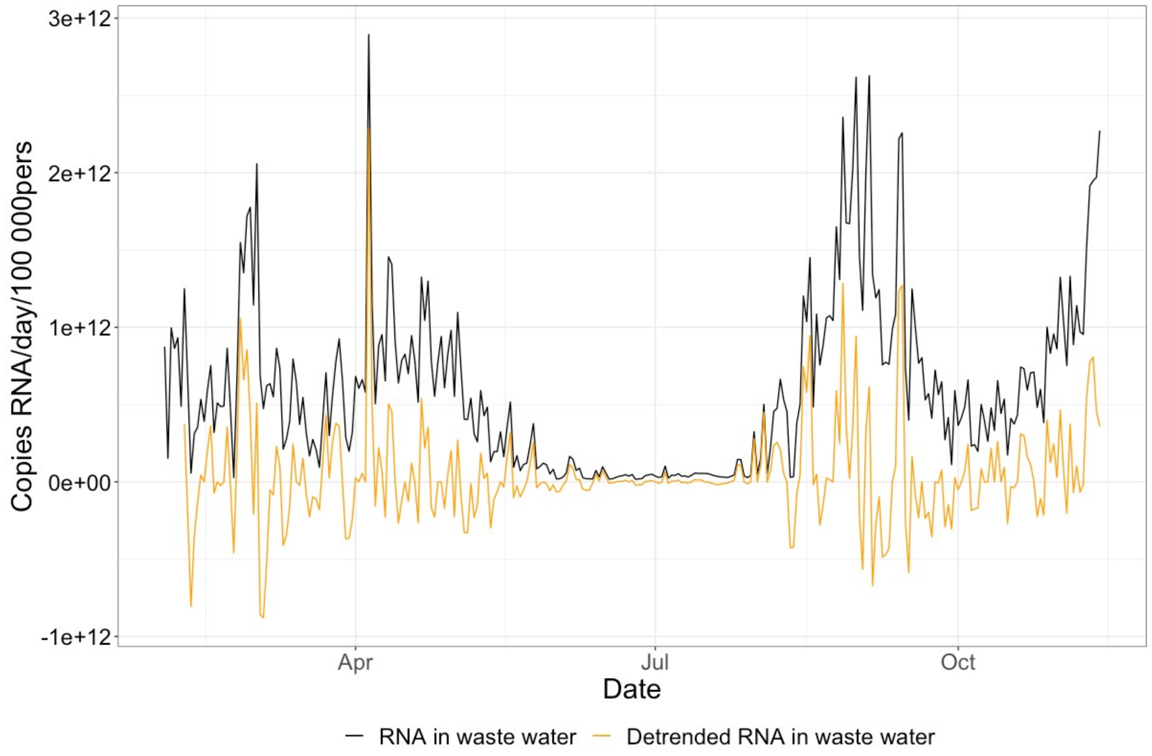
EHRs

Algorithm to determine EWS from single data source

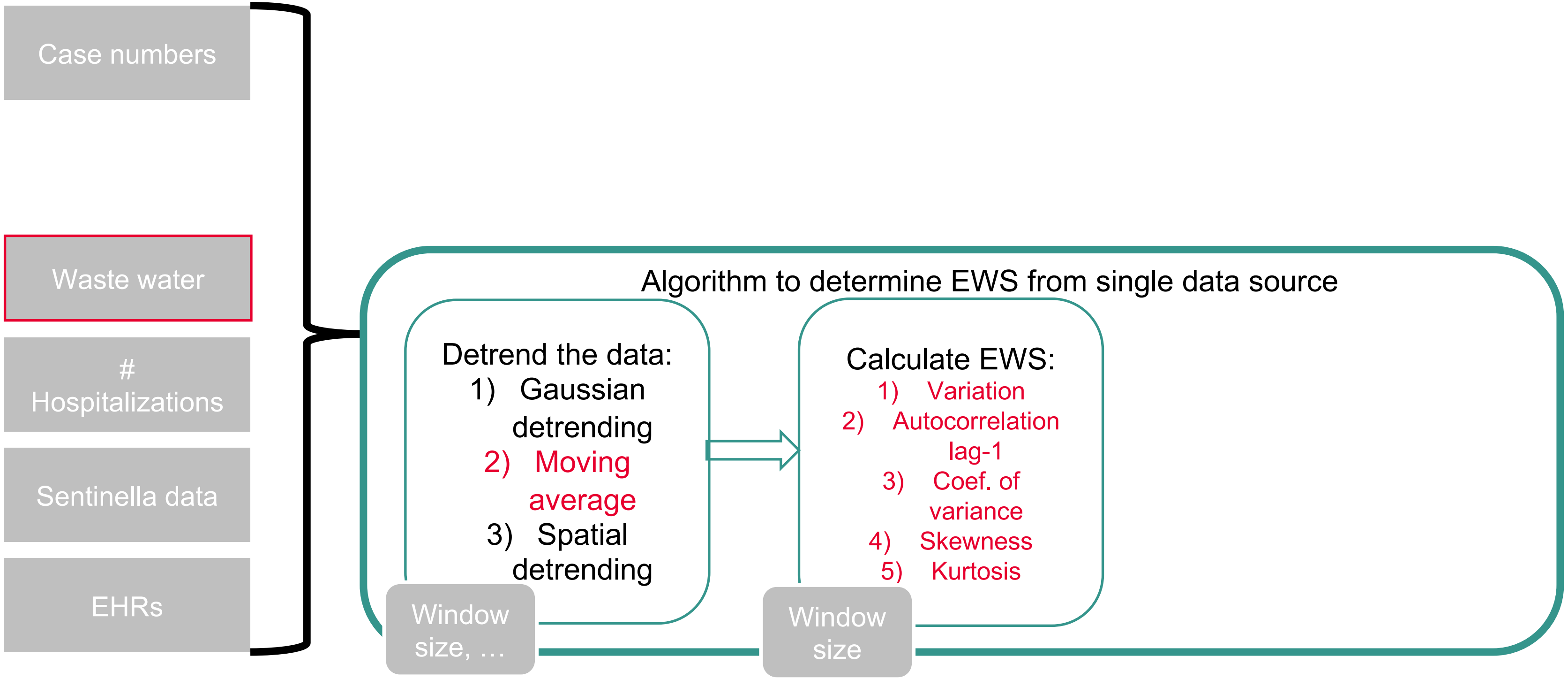
Detrend the data:
1) Gaussian detrending
2) Moving average
3) Spatial detrending

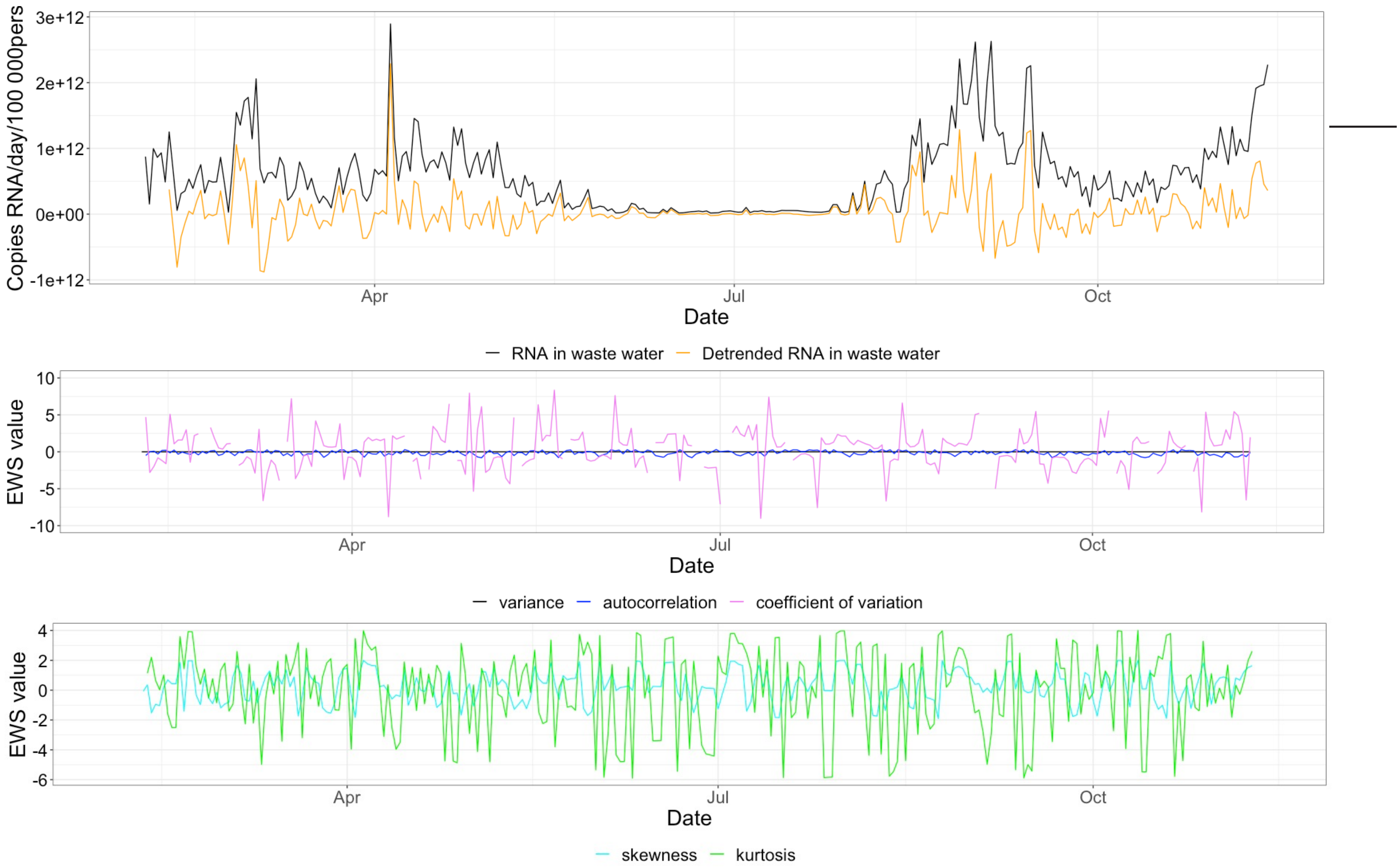
Window size, …

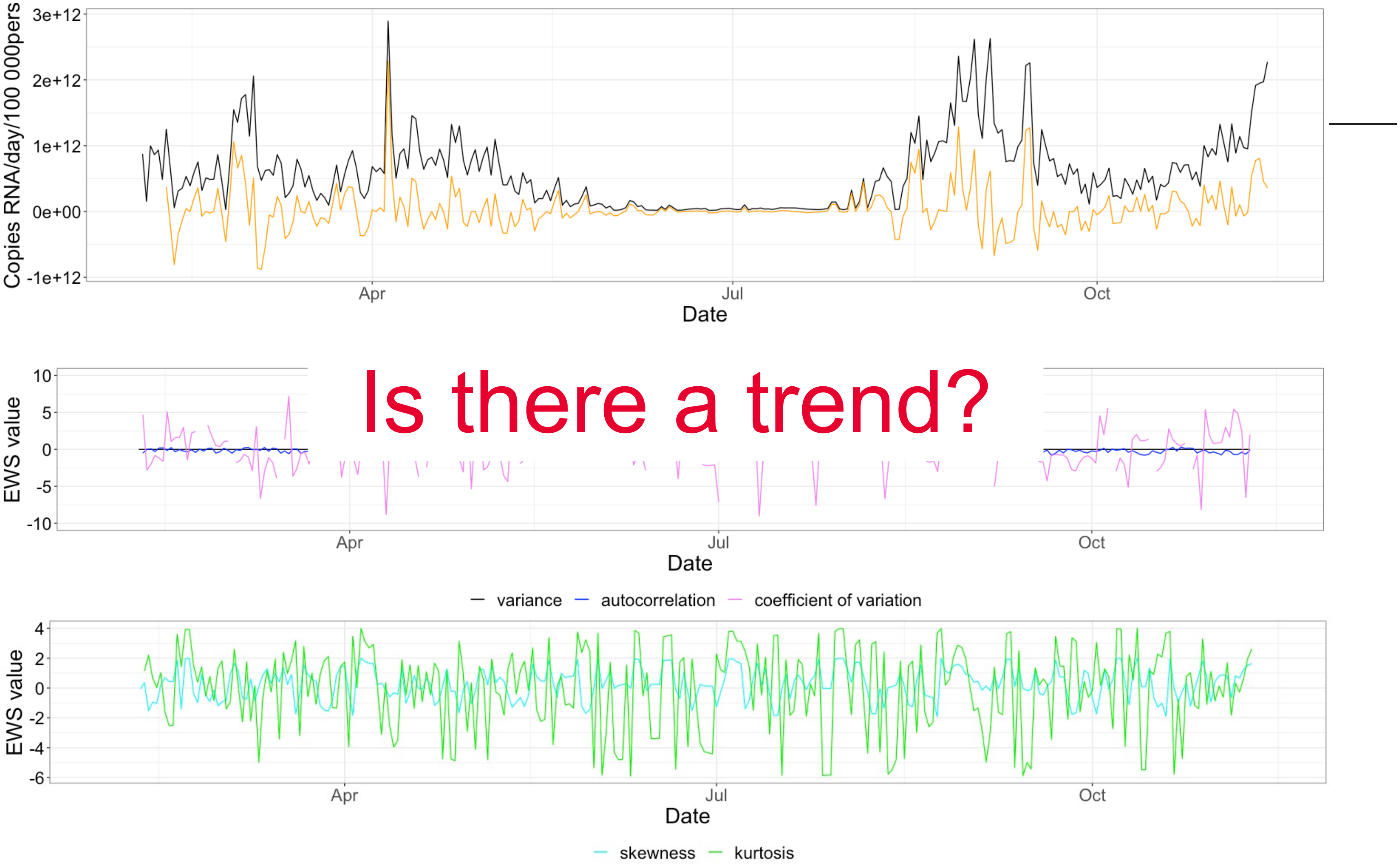
Preliminary analysis of Waste-water data



Step 2

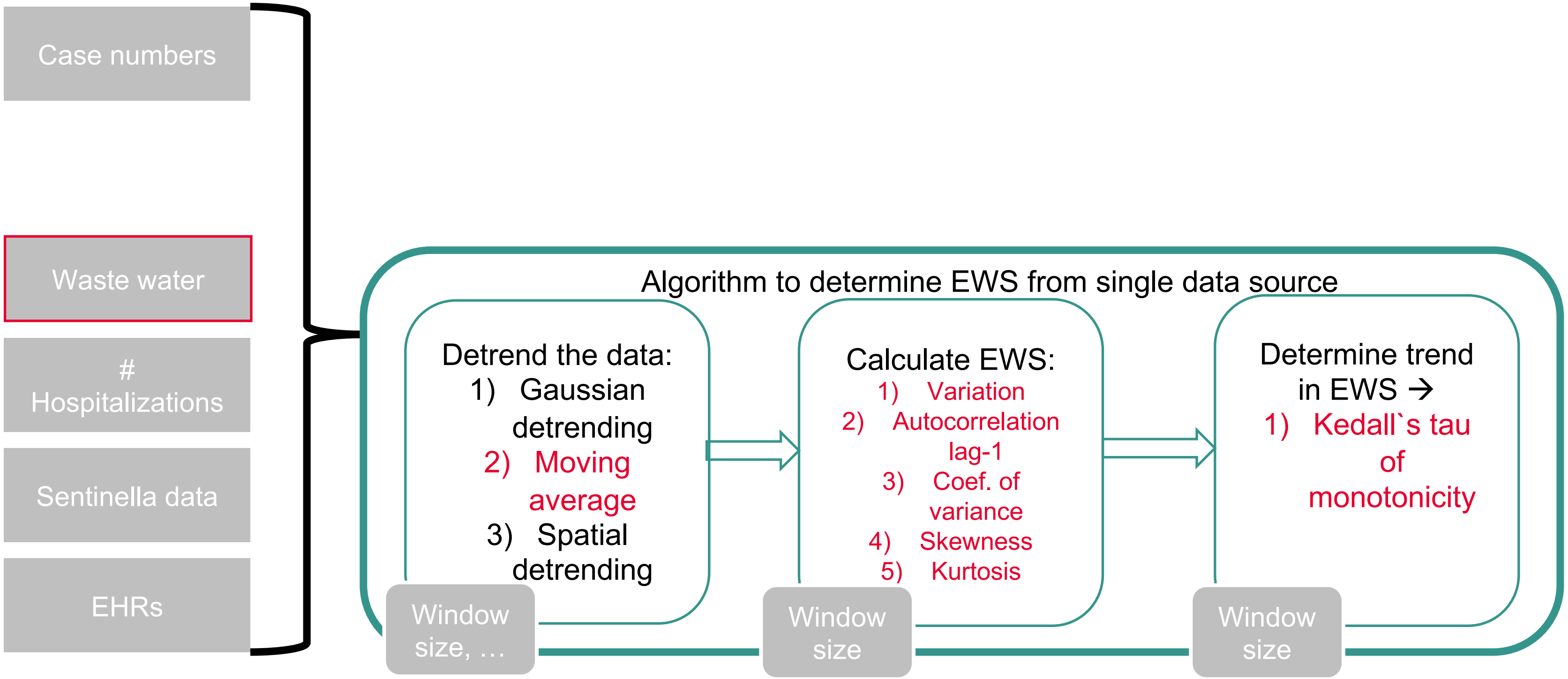

Case numbers
Waste water
Hospitalizations
Sentinella data
EHRs
Algorithm to determine EWS from single data source
Detrend the data:
1) Gaussian detrending
2) Moving average
3) Spatial detrending
Window size, …
Calculate EWS:
1) Variation
2) Autocorrelation lag-1
3) Coef. of variance
4) Skewness
5) Kurtosis
Window size


3e+12
2e+12
1e+12
0e+00
-1e+12
Copies RNA/day/100 000pers
Apr
Jul
Oct
Date
RNA in waste water
Detrended RNA in waste water
10
5
0
-5
-10
EWS value
Apr
Jul
Oct
Date
variance
autocorrelation
coefficient of variation
4
2
0
-2
-4
-6
EWS value
Apr
Jul
Oct
Date
skewness
kurtosis



Is there a trend?

Step 3


Case numbers
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Detrend the data:
1) Gaussian detrending
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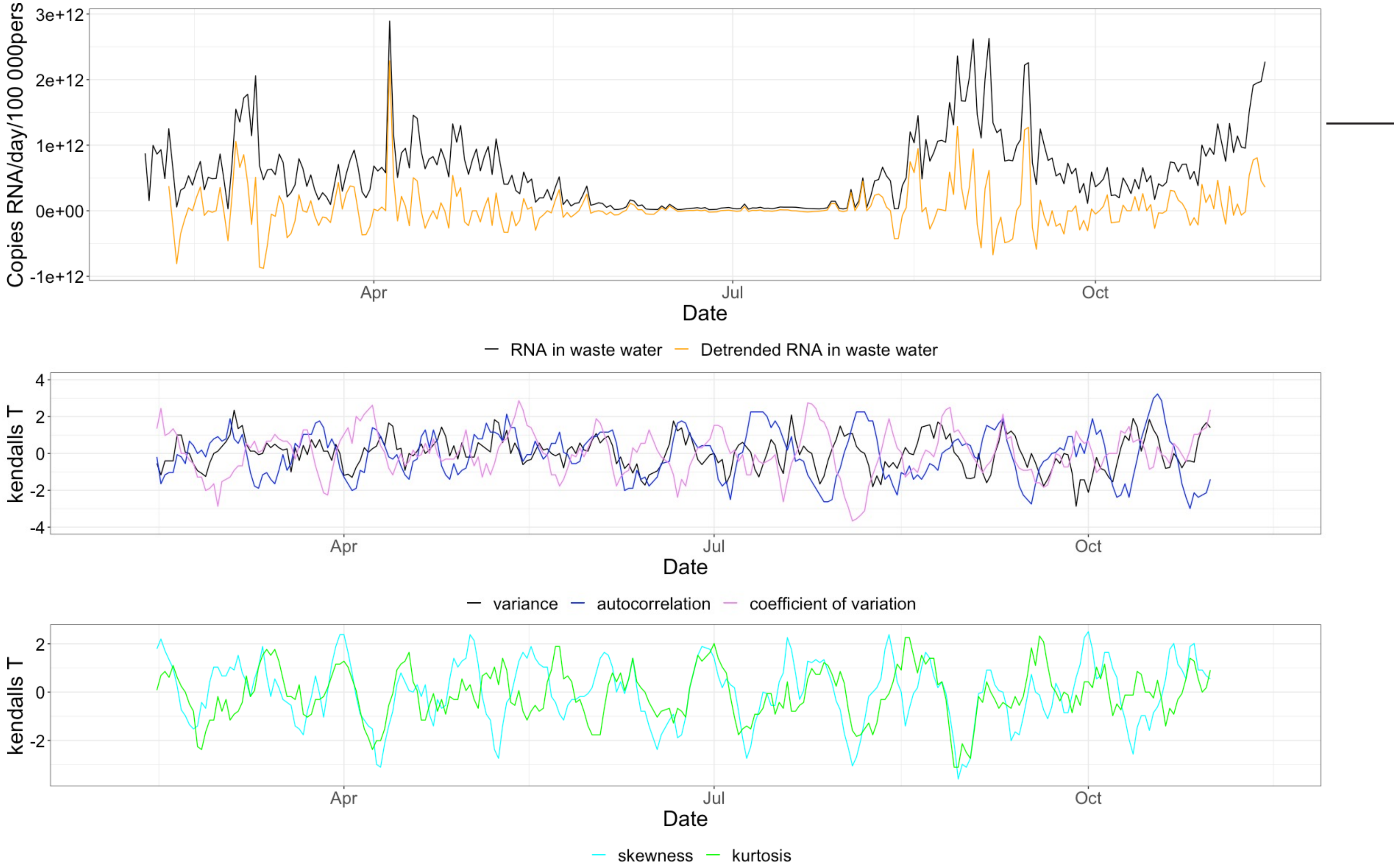
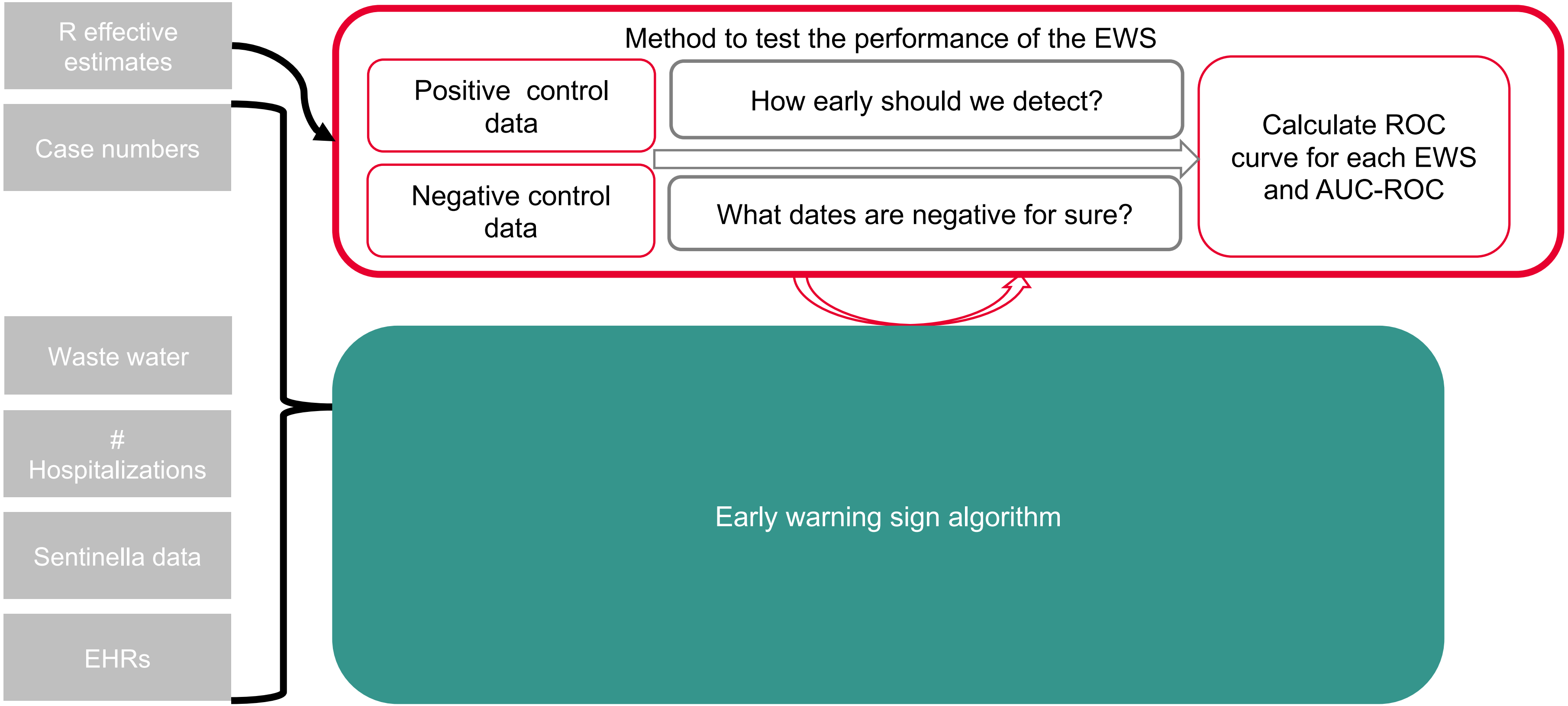
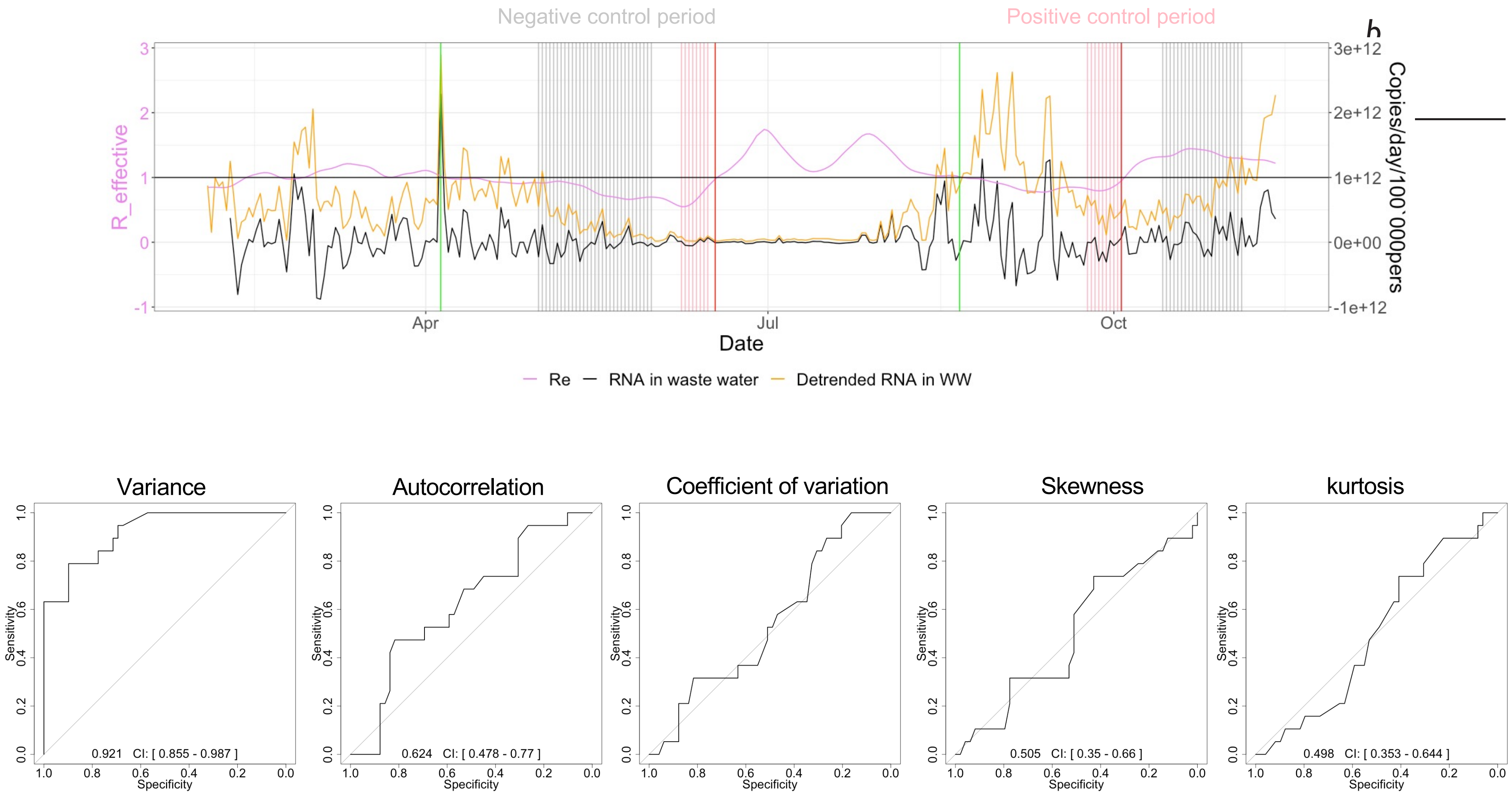
3) Spatial detrending
Calculate EWS:
1) Variation
2) Autocorrelation lag-1
3) Coef. of variance
4) Skewness
5) Kurtosis
Determine trend in EWS →
1) Kedall`s tau of monotonicity
Window size, …
Window size
Window size

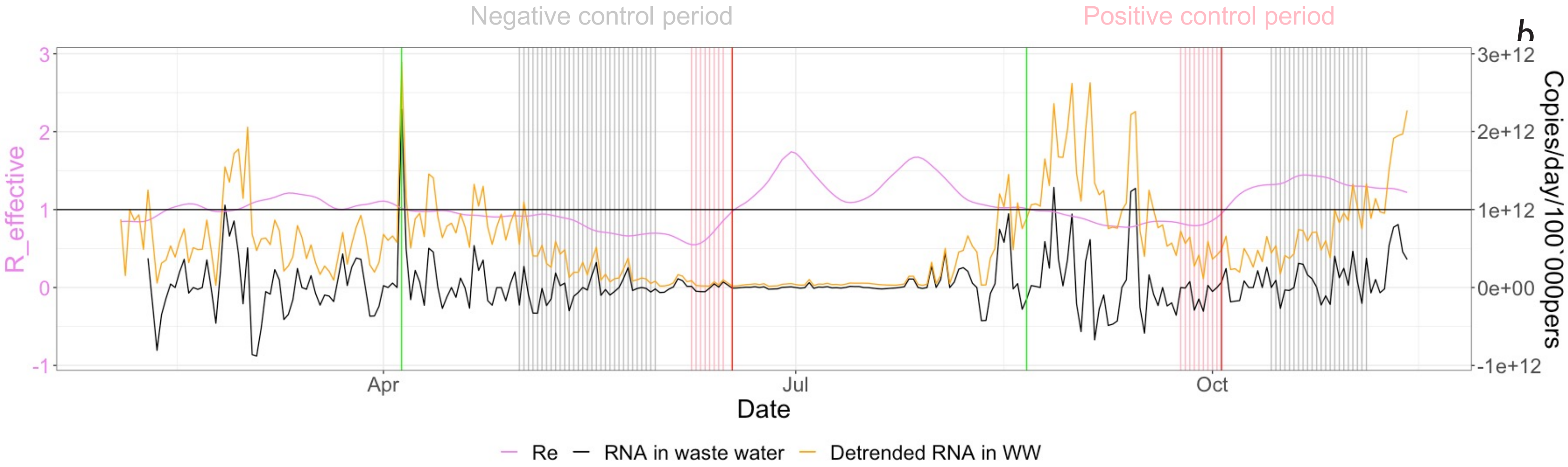


Copies RNA/day/100 000pers
3e+12
2e+12
1e+12
0e+00
-1e+12
Apr
Jul
Oct
Date
RNA in waste water
Detrended RNA in waste water
kendalls T
4
2
0
-2
-4
Apr
Jul
Oct
Date
variance
autocorrelation
coefficient of variation
kendalls T
2
0
-2
Apr
Jul
Oct
Date
skewness
kurtosis

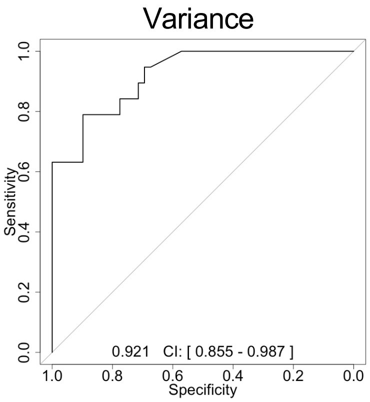
What value predicts a transition?




Negative control period
Positive control period
b
R_effective
Copies/day/100`000pers
3
2
1
0
-1
3e+12
2e+12
1e+12
0e+00
-1e+12
Apr
Jul
Oct
Date
Re
RNA in waste water
Detrended RNA in WW
Variance
0.921 CI: [0.855 - 0.987]
Autocorrelation
0.624 CI: [0.478 - 0.77]
Coefficient of variation
Skewness
0.505 CI: [0.35 - 0.66]
kurtosis
0.498 CI: [0.353 - 0.644]
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0



Negative control period
Positive control period
R_effective
3
2
1
0
-1
3e+12
2e+12
1e+12
0e+00
-1e+12
Copies/day/100`000pers
Apr
Jul
Oct
Date
Re
RNA in waste water
Detrended RNA in WW



Variance
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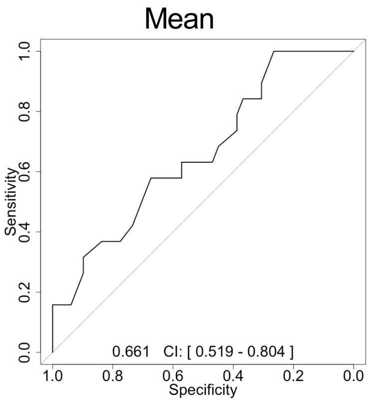

Mean
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
0.661 CI: [0.519 - 0.804]

Challenges and possible solutions

1. Too few data, especially in times where there are no transitions.
2. The thruth is unknown, Re estimates also depend on the data.
3. The power of the analysis is low.

1. Possible solutions:
   a) Use data from multiple locations.
   b) Use EHR, which were collected long before COVID started.
   c) Validate the methods and test their performance with simulated data using the transmission model
2. Use the Re estimates from our transmission model rather than those calculated directly from case data.
3. Possible solutions:
   a) Combine several types of EWS.
   b) Combine EWSs from multiple data sources.
   c) Consider a different type of warning sign
      1. distribution of passing a threshold?
      2. Deeplearning on simulated data and then apply to real data?

Resources

b
UNIVERSITÄT
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https://fabiandablander.com/