How to remove the testing bias in CoV-2 statistics

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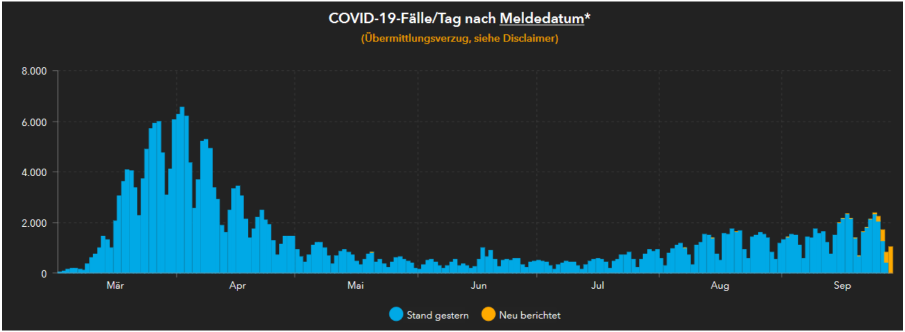
1. Introduction

- Statistics gained a lot in reputation during the Covid-19 pandemic
- Almost everybody studies “the curve”
  - Is it becoming flatter?
  - What are infections per 100.000 inhabitants over the last seven days?
  - When should public health authorities react? As of 35 or 50?
- An example: new infections per day from February 2020 to today



1. Introduction

- Our questions
  - What do these numbers mean?
  - What does it mean that we talk about "a second wave"?
- Intuitive interpretations of "the curve"
  - the higher the number of new infections, the more severe the epidemic
  - infections go up and discussions on public health measures start
- Argument of this paper
  - Reported numbers of CoV-2 infections are not comparable over time
  - x new cases today do not have same meaning as earlier this year
  - We need enlarged SIR model to identify data needs
  - With this (simple but not public) data, intertemporally consistent severity index of an epidemic can be constructed

1. Introduction

- Why official numbers have problems
  - Relative changes of test regimes
  - With one rule, e.g.
    "test for SARS-CoV-2 in the presence of a certain set of symptoms", infection numbers would be comparable over time
  - With a relative shift in the reason ...
    - "test in the presence of symptoms"
    - "test travellers without symptoms"
    - "undertake representative testing"
    - etc ...
  - ... a comparison of the numbers over time bears no meaning
- Understanding the bias provides answer to one of the most frequently asked questions
  - What is the role of testing?
  - Do we observe a lot of reported infections only because we test a lot?
  - Is it true that "If we test half as much, we have half as many cases"
  - Is number of infections causally determined by number of tests?

1. Introduction

- Understanding the bias provides answer to one of the most frequently asked questions
  - ...
  - Is number of infections causally determined by number of tests?
- The answer in a nutshell
  - 'No' when testing by symptoms
  - 'Yes' when testing for other reasons (travellers, representative testing)
- An unbiased measure of epidemic dynamics
  - Having understood this, an unbiased severity index can be constructed
  - Logic of SIR models: count only infections WITH symptoms
  - Message: Test for CoV-2 but count Covid-19

1. Introduction

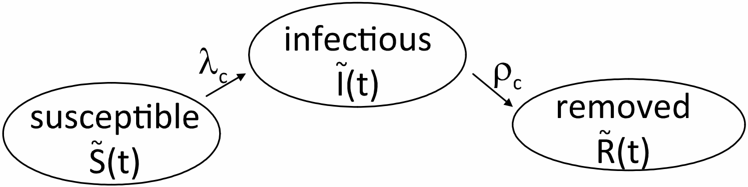
- Structure of talk
  - Extension of classic SIR model
    - for asymptomatic cases and
    - for testing
  - Results
    - reasons for the intertemporal bias
    - when reported infections rise due to tests and when they do not
    - what the positive rate tells us (nothing)
  - Conclusion
    - presents a severity index for an epidemic that corrects for the bias
    - describes the type of (very simple) data that is needed for index
    - index should be used when thinking about public health measures

2. The model

- Starting point
  - susceptible-infectious-removed (SIR) model
  - (Kermack and McKendrick, 1927, Hethcote, 2000)
- Main extensions
  - belief that true infections dynamics are not observable
  - (weekly representative testing is not feasible)
  - testing is modelled within SIR framework

2. The model

2.1. True but unobserved infection dynamics (classic SIR)



- Number of susceptible falls

$$\frac{d}{dt}\tilde{S}(t) = -\lambda_c(t)\tilde{S}(t),$$

where r is constant and $\lambda_c(t) \equiv r\tilde{I}(t)$ is individual infection rate

- Individual recovery and death rate merged to ρ_c, number of infectious individuals follows

$$\frac{d}{dt}\tilde{I}(t) = \lambda_c(t)\tilde{S}(t) - \rho_c\tilde{I}(t)$$

- Number of removed individuals (residual) rises over time

$$d\tilde{R}(t)/dt = \rho_c\tilde{I}(t)$$

2. The model

2.2. Modelling symptomatic and asymptomatic cases

- The big issue at beginning of epidemic - how large is the number of asymptomatic cases?
- Asymptomatic cases in SIR model
- Split true number of infectious individuals

$$\tilde{I}(t) = \tilde{I}_{symp}(t) + \tilde{I}_{asymp}(t)$$

- Infection process is twofold then

$$\frac{d}{dt}\tilde{I}_{symp}(t) = \lambda_c^{symp}(t)\tilde{S}(t) - \rho_c \tilde{I}_{symp}(t),$$
$$\frac{d}{dt}\tilde{I}_{asymp}(t) = \lambda_c^{asymp}(t)\tilde{S}(t) - \rho_c \tilde{I}_{asymp}(t)$$

where individual infection rates are now

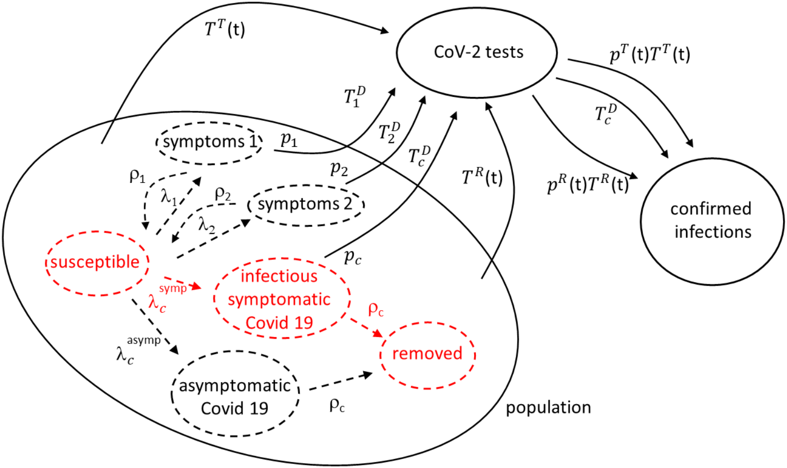
$$\lambda_c^{symp}(t) = sr\tilde{I}(t),$$
$$\lambda_c^{asymp}(t) = (1-s)\, r\tilde{I}(t)$$

and share of individuals that develop symptoms is s

2. The model

2.2. Modelling symptomatic and asymptomatic cases

An illustration (consider lower part only)



2. The model

2.3. Modelling tests for SARS-CoV-2

- Tests are undertaken for many reasons
  - Various countries have national test strategies
  - We look at three reasons for testing: symptoms, representative, travellers (and other)

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  - Disease dynamics

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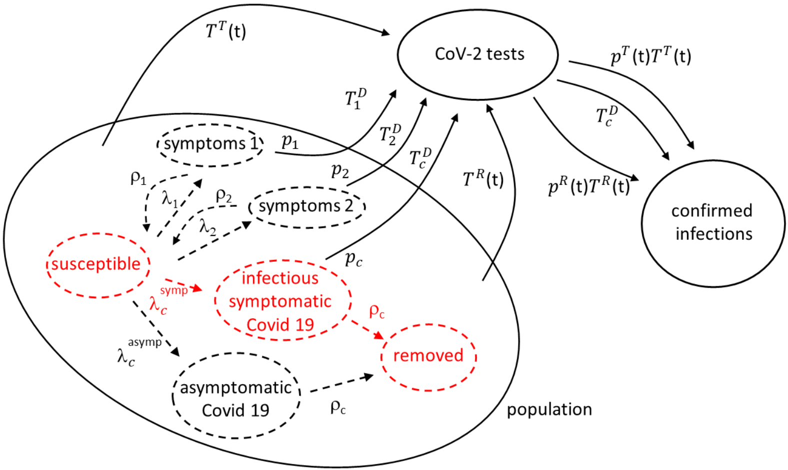
2.3. Modelling tests for SARS-CoV-2

- Tests are undertaken for many reasons
  - Various countries have national test strategies
  - We look at three reasons for testing: symptoms, representative, travellers (and other)
- Testing by symptoms
  - Disease dynamics
    - Individuals can catch many diseases (sets of symptoms)
    - Number of individuals with sets of symptoms i is $D_i(t)$
    - Arrival rate λ_i and recovery rate ρ_i
    - Symptomatic SARS-CoV-2 occurs with rate $\lambda_c^{\text{symp}}(t)$ and removal with rate ρ_c
    - The number of symptomatic SARS-COV-2 individuals is $\tilde{I}_{\text{symp}}(t)$
    - ($\rightarrow$ figure next slide)

2. The model

2.3. Modelling tests for SARS-CoV-2

An illustration (consider symptom part now)



- Testing by symptoms (cont'd)
  - Number of tests and number of reported infections
    - With probability p_i a GP performs a test, given symptoms i
    - Probability to get tested with symptomatic SARS-CoV-2 infection is p_c
    - The number of tests (caused by symptoms) at time t is

$$\begin{aligned} T^D(t) &= \Sigma_{i=1}^n T_i^D(t) + T_c^D(t) \\ &= \Sigma_{i=1}^n p_i D_i(t) + p_c \tilde{I}_{\text{symp}}(t) \end{aligned}$$

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\end{aligned}
$$

    - The number of tests $T^D(t)$ is (the first variable that is) observed!

2. The model

2.3. Modelling tests for SARS-CoV-2

- Testing travellers or for scientific reasons
  - Theses tests are not related to symptoms (!)
  - The number of tests is chosen by public authorities, scientists, available funds, capacity considerations and other
  - Number is independent of infection-characteristics of the population
  - Number of representative testing denoted by $T^R(t)$, number of tests for travelers is $T^T(t)$

2. The model

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  - Number of representative testing denoted by $T^R(t)$, number of tests for travelers is $T^T(t)$
  - Representative test is positive with probability $p^R(t)$
  - Probability satisfies $p^R(t) = \frac{\tilde{I}(t)}{P}$ (P is population size)
  - Probability that a test of travellers is positive is "some" $p^T(t)$

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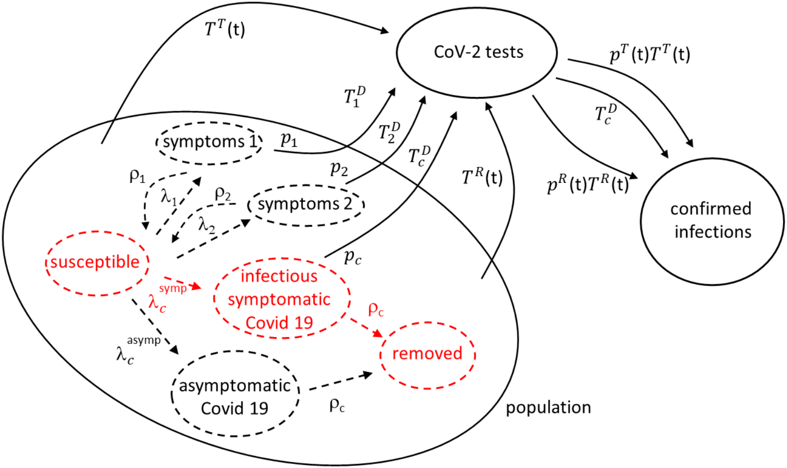
- Total overall number of tests

$$T(t) = T^D(t) + T^R(t) + T^T(t)$$

2. The model

2.3. Modelling tests for SARS-CoV-2

An illustration (consider entire figure now)



- Number of reported infections can be split into reasons for testing

$$I\left(t\right)=\Sigma_{i=1}^{n}I_{i}\left(t\right)+I_{c}+I^{R}\left(t\right)+I^{T}\left(t\right)$$

- Testing by symptoms
  - The probability that a "normal" test is positive is zero

$$I_{i}=0$$

  - The probability that a CoV-2 infected individual has a positive test is 1

$$I_{c}\left(t\right)=T_{c}^{D}\left(t\right)$$

2. The model

2.4. The number of reported infections

- (again) Number of reported infections can be split into reasons for testing

$$I(t) = \Sigma_{i=1}^{n} I_i(t) + I_c + I^R(t) + I^T(t)$$

2. The model

2.4. The number of reported infections

- (again) Number of reported infections can be split into reasons for testing
$$I(t) = \Sigma_{i=1}^{n} I_i(t) + I_c + I^R(t) + I^T(t)$$
- Testing for other reasons

2. The model

2.4. The number of reported infections

- (again) Number of reported infections can be split into reasons for testing
$$I(t) = \Sigma_{i=1}^{n} I_i(t) + I_c + I^R(t) + I^T(t)$$
- Testing for other reasons
    - Representative tests yield positive outcome with probability $p^R(t)$
    - This probability satisfies
    $$p^R(t) = \frac{\tilde{I}(t)}{P}$$
    and reflects the true number $\tilde{I}(t)$ of infections (symptomatic and asymptomatic)
    - The probability that a test of travellers is positive is denoted by $p^T(t)$
    - It depends on a multitude of determinants (region traveled to and behaviour of the traveller)
    - It is exogenous in our model

2. The model

2.4. The number of reported infections

- Total reported infections
  - Reported infections come from testing CoV-2 individuals with symptoms, from representative testing and from travellers

$$I(t) = T_c^D + p^R(t)\,T^R(t) + p^T(t)\,T^T(t)$$

  - This is also the expression displayed in figure between 'CoV-2 tests' and 'confirmed infections'
  - Employing expression relating $T_c^D(t)$ to $\tilde{I}_{\text{symp}}(t)$ from above and probability $p^R(t)$, we get

$$I(t) = p_c \tilde{I}_{\text{symp}}(t) + \frac{\tilde{I}(t)}{P} T^R(t) + p^T(t)\,T^T(t)$$

3. Biased and unbiased infection numbers

- **Definition:** Numbers of reported infections are intertemporally unbiased if they are proportional to the true (but unobserved) infection dynamics

3. Biased and unbiased infection numbers

3.1. Unbiased reporting

- Testing by symptoms is unbiased
  - With $T^R(t) = T^T(t) = 0$,

$$I(t) = I^D(t) = p_c \tilde{I}_{\text{symp}}(t)$$

  - When reported number of infections $I(t)$ goes up, one would be certain that the unobserved number of symptomatic CoV-2 infections $\tilde{I}_{\text{symp}}(t)$ would go up as well
  - The more infections are reported, the more severe the epidemic
  - Tests do *not* have a causal effect on the number of reported infections!
  - Tests are endogenous and driven by symptoms

3. Biased and unbiased infection numbers

3.1. Unbiased reporting

- Representative testing is unbiased
  - With $T_c^D = T^T(t) = 0$,

$$I(t) = \frac{\tilde{I}(t)}{P} T^R(t)$$

  - Number of reported infections, $I(t)$, does rise in the number of tests, $T^R(t)$
  - Ratio of positive cases to the number of tests (positive rate) yields the share of infections in the population,

$$\frac{I(t)}{T^R(t)} = \frac{\tilde{I}(t)}{P}$$

  - Representative testing provides a measure of overall infections (symptomatic and asymptomatic)

3. Biased and unbiased infection numbers

3.2. Biased reporting

- Illustrating a bias
  - Several types of testing are being undertaken simultaneously :-(
  - Consider first symptomatic and representative testing ($T^T(t) = 0$)

$$I(t) = p_c \tilde{I}_{\text{symp}}(t) + \frac{\tilde{I}(t)}{P} T^R(t)$$

  - Representative testing $T^R(t)$ goes up, reported cases $I(t)$ increase but
    - no change in the true number $\tilde{I}_{\text{symp}}(t)$ of symptomatic cases
    - no change in the true number $\tilde{I}(t)$ of symptomatic and asymptomatic cases
  - Don't build your plans on confirmed number of cases $I(t)$

3. Biased and unbiased infection numbers

3.2. Biased reporting

- A numerical example of a bias
  - Simultaneous testing due to symptoms and testing travellers
  - Reported cases are

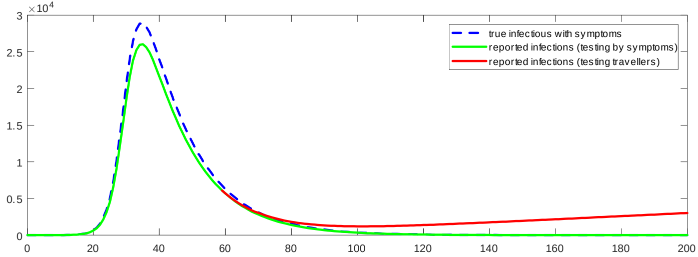
$$I(t) = p_c \tilde{I}_{\text{symp}}(t) + p^T(t)\, T^T(t)$$

  - Scenario we study
    - No testing of travellers took place at the beginning of the pandemic
    - At some later point (as of $t = 60$ in our figure below), travellers are tested
    - The number of tests per day, $T(t)$, increases linearly in time

3. Biased and unbiased infection numbers

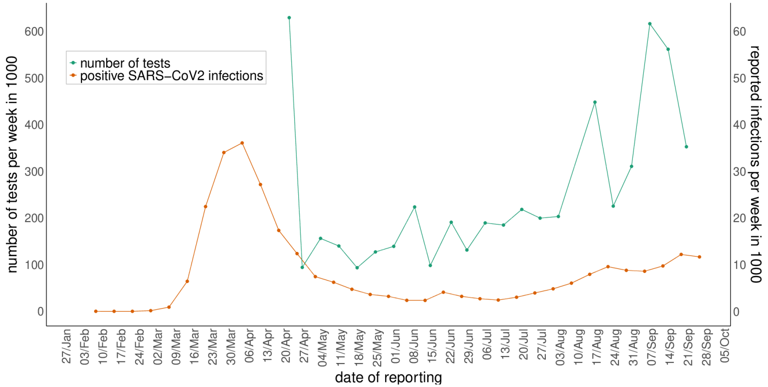
3.2. Biased reporting

- True epidemiological dynamics (blue), correct reporting (green) and an example of a bias (red) of the reported number of infections



- We see a "second wave" where there is no second wave
  - reported numbers of infections go up
  - true infection dynamics go down

- An empirical non-application to Germany



3. Biased and unbiased infection numbers

3.3. Two non-applications

- An empirical non-application to Germany
  - We observe the number of tests $T(t)$
  - We oberve the number of infections $I(t)$
  - Question: Can we conclude anything about $\tilde{I}_{\text{symp}}(t)$ or $\tilde{I}(t)$?
  - Technically speaking, we have two equations ...

$$T(t) = \Sigma_{i=1}^{n} p_i D_i(t) + p_c \tilde{I}_{\text{symp}}(t) + T^R(t) + T^T(t)$$

$$I(t) = p_c \tilde{I}_{\text{symp}}(t) + \frac{\tilde{I}(t)}{P} T^R(t) + p^T(t) T^T(t)$$

    ... in too many unknowns
  - True infection dynamics $\tilde{I}_{\text{symp}}(t)$ or $\tilde{I}(t)$ cannot be understood

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  ... in too many unknowns
  - True infection dynamics $\tilde{I}_{\text{symp}}(t)$ or $\tilde{I}(t)$ cannot be understood
  - Houston, we have a problem

3. Biased and unbiased infection numbers

3.3. Two non-applications

- The positive rate
  - Positive rate is the ratio of confirmed infections to number of tests

$$s^{\text{pos}}(t) \equiv \frac{I(t)}{T(t)}$$

  - Often discussed in media and elsewhere (e.g. Our World in Data, 2020)
  - In our model, positive rate is

$$s^{\text{pos}}(t) = \frac{p_c \tilde{I}_{\text{symp}}(t) + \frac{\tilde{I}(t)}{P} T^R(t) + p^T(t)\, T^T(t)}{\Sigma_{i=1}^n p_i D_i(t) + p_c \tilde{I}_{\text{symp}}(t) + T^R(t) + T^T(t)}$$

3. Biased and unbiased infection numbers

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- What does the positive rate tell us?
  - Rising positive rate $\Rightarrow$ epidemic 'gets worse', i.e. $\tilde{I}(t)$ or $\tilde{I}_{\text{symp}}(t)$ rise?
  - With representative testing only ($T_c^D = T^T(t) = 0$),

$$s^{\text{pos}}(t) = \frac{I(t)}{T^R(t)} = \frac{\tilde{I}(t)}{P}$$

  - When observed positive rate $s^{\text{pos}}(t)$ rises, number of unobserved infections $\tilde{I}(t)$ is higher

3. Biased and unbiased infection numbers

3.3. Two non-applications

- Does conclusion hold more generally?
  - Assume tests only due to symptoms and travelling
  - With $T^R(t) = 0$, positive rate reads

$$s^{\text{pos}}(t) = \frac{p_c \tilde{I}_{\text{symp}}(t) + p^T(t)\, T^T(t)}{\Sigma_{i=1}^n p_i D_i(t) + T^T(t)}$$

  - With more tests for travellers, positive rate might rise or fall,

$$\frac{ds^{\text{pos}}(t)}{dT^T(t)} > 0 \Leftrightarrow \Sigma_{i=1}^n p_i D_i(t) > \frac{p_c}{p^T(t)} \tilde{I}_{\text{symp}}(t)$$

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- What does this mean?
  - Technically it has the usual structure
  - Increase a summand ($T^T(t)$ here) that appears in numerator and denominator, sign of derivative depends on the other summands and own factor $p^T(t)$

3. Biased and unbiased infection numbers

3.3. Two non-applications

- What does this mean?
  - Epidemiological content
    - Positive ratio can rise or fall when we increase the number of tests for travellers
    - Positive rate rises if the number of "useless tests", $\Sigma_{i=1}^{n} p_i D_i(t)$ (negative tests ordered by doctor due to symptoms) exceeds the number of tests undertaken because of symptoms related to CoV-2, $p_c \tilde{I}_{\text{symp}}(t)$ (positive tests orderd by doctor) divided by the probability that a traveller test is positive
    - Condition is quantitatively not obvious
- It don't mean a thing
  - In any case, a rising positive rate does NOT imply a 'worse' epidemic state
  - $T^T(t)$ and the positive rate going up is not informative about the dynamics of $\tilde{I}_{\text{symp}}(t)$ or $\tilde{I}(t)$
  - The positive rate is not informative

3. Biased and unbiased infection numbers

3.4. An unbiased severity index

- The index is simple ....
  - Index needed for the severity of an epidemic which is comparable over time
  - Index should reflect the number of individuals with symptoms
  - Index is simply $I^D(t)$ – number of Covid-19 cases with symptoms
  - [An alternative would of course consist in representative testing]

3. Biased and unbiased infection numbers

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  - Index is simply $I^D(t)$ – number of Covid-19 cases with symptoms
  - [An alternative would of course consist in representative testing]
- ... and data requirements are minimal
  - Classify tests by reason for testing
    - No major general nation-wide agreement needed
    - Any region, any Bürgermeister or Landrat or any local health authority could start (?)
  - Improve data availability on Covid-19 cases (national and regional)
  - Health authorities should put resources into provision of Covid-19 information and stop pushing CoV-2 infection numbers
  - The latter holds true also for the media

4. Conclusion

- Starting point: True epidemic dynamics are unobservable
- Consequence: We need to model testing
- Finding
  - Changes in testing biases CoV-2 statistics
  - Reported numbers of CoV-2 cases are not comparable over time
  - "massive Ausweitung von Tests in Deutschland geplant"
  - Yes please – but don't count this – sort tests by reason for test!
- Way out
  - Count the number of CoV-2 cases with symptoms
  - In other words:

Count the number of Covid-19 cases, not the number of CoV-2 infections

Thank you!