Covid 19
Can we continue living our lives with the virus among us?

What we know, what we don´t know, what to expect, how to act

Introduction (what happened)

- **First the virus in a short timetable**
  - The first infections were & it was explained where it came from and that people around where being tested
  - The first persons died, it was mentioned the reason, mostly elderly and with pre existing conditions
  - More and more measurements were taken and ´Flatten the curve´was introduced
  - The country was locked down. We are waiting fot the peak to come! Herd immunity was introduced
  - Herd immunity disappeared and not the R was introduced
  - Now the pressure on hospitals is getting back to ´normal´ and the country start to open up!
- **However, until a vaccine is there we have to obey a certain way of living.**
  - 1.5 meter distance, Wearing Masks, No group gatherings etc.
- **Are we doing the right thing?**

A 1.5 m society is not a solution & opening up slowly for everyone will not take care of the underlying risk that is still there!

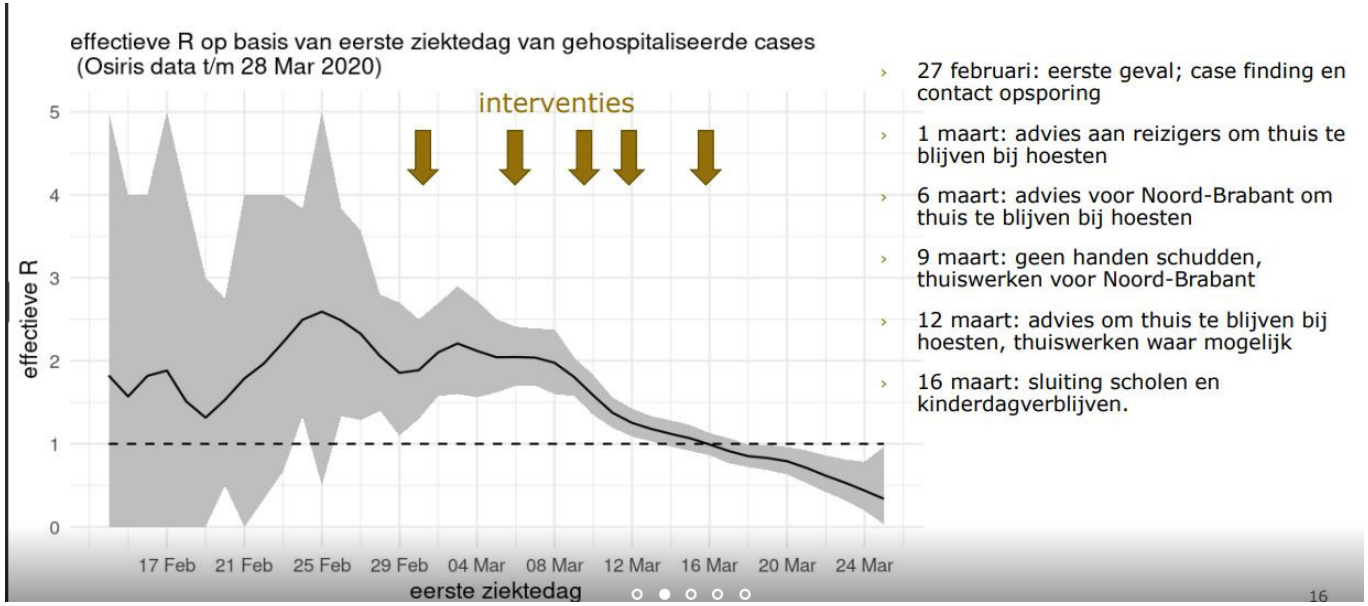
A quick recap (what did the analysis tell us?)

- Many countries came in some sort of lock down. To control the virus the R, Repetitive number is introduced. R < 1 means the virus is under control (slide 5)
- We acted on time, possibly to soon. Waiting longer could have caused a big wave of infection, possibly taking out the healthcare system (slide 6,7)
- Are we done? Can we move on or losen up now? (slide 8)
- We made an estimation on the possible impact on society based on age!
  - You need to know the risk among the population! (slide 9-10)
  - 3 scenario´s where constructed. (Slide 11)
  - The results shows clearly a big difference in impact between the age! (Slide 12)
- If we take into account the pre- existing condition the results until 50 are no reason to keep the country closed for this group!

We need to act! What is the right approach!?

- **Should we focus on herd immunity? This was one of the first ideas of Governments!**
  - Although It is not clear yet if herd immunity will be effective but it doesn´t hurt to start with it.
  - It is still not 100% proven it creates immunity but experts believe it will at least make sure the cells in your body recognize the virus and act. So you can still become ill but less!
  - The faster we reach herd immunity the faster we can let go of strict measurements!
- **Should we keep our social distancing by creating new rules?**
  - Social distancing is there for one purpose only. Protect the healthcare system from collapsing
  - Creating boundaries and a whole new way of life. The 1.5 m society.
    This will result in a fundamental change in how we experience freedom. Is that what we want?
  - Or… Can we find an alternative way without big restrictions!
- **What danger are we facing if we wait too long or make the rules too strict?**
  - People will losen up and a second wave will hit us where the impact will be much much bigger!
  - Economies will collapse (The 1929 Great Depression started similar)
  - We are not creating immunity
  - Other countries like China will take a major position in the geopolitics

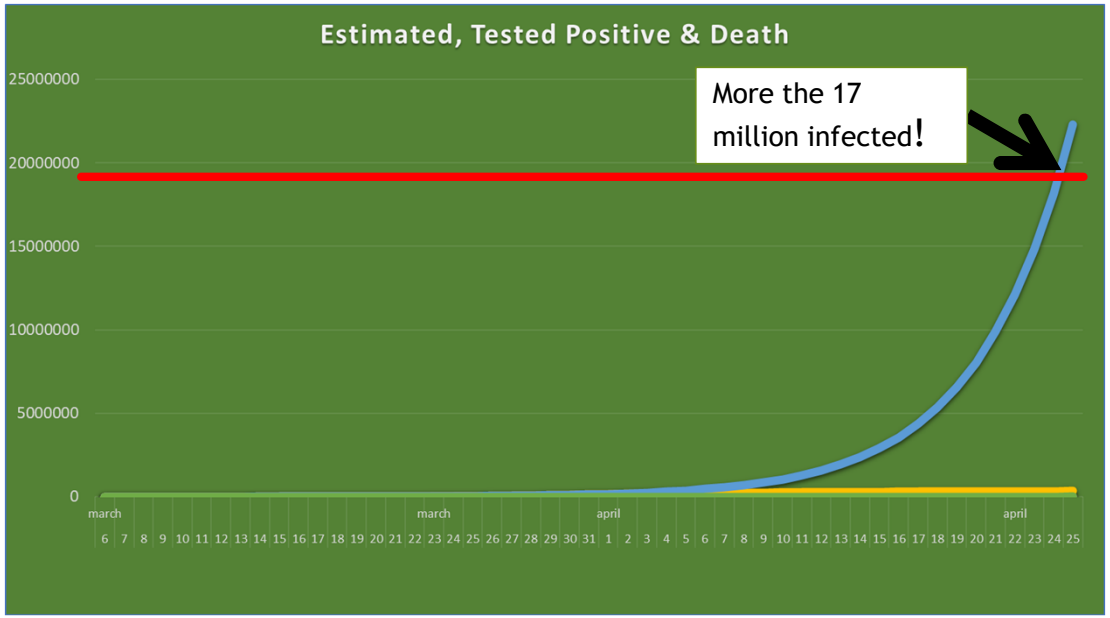
How does the R develop in the Netherlands?



The R is controlled but is it enough?
Not addressing that without the right exit strategy could lead to a disaster! (slide 8)

- By taking measures (social distancing) the Effective R can decrease
- When the R <1 the number of cases of infection decreases. But it it still there . To stop the virus a threshold of 60% is needed!
- For :Covid-19 this means R0 = 2.5 so threshold HIT : 1-1/2.5 = 60%

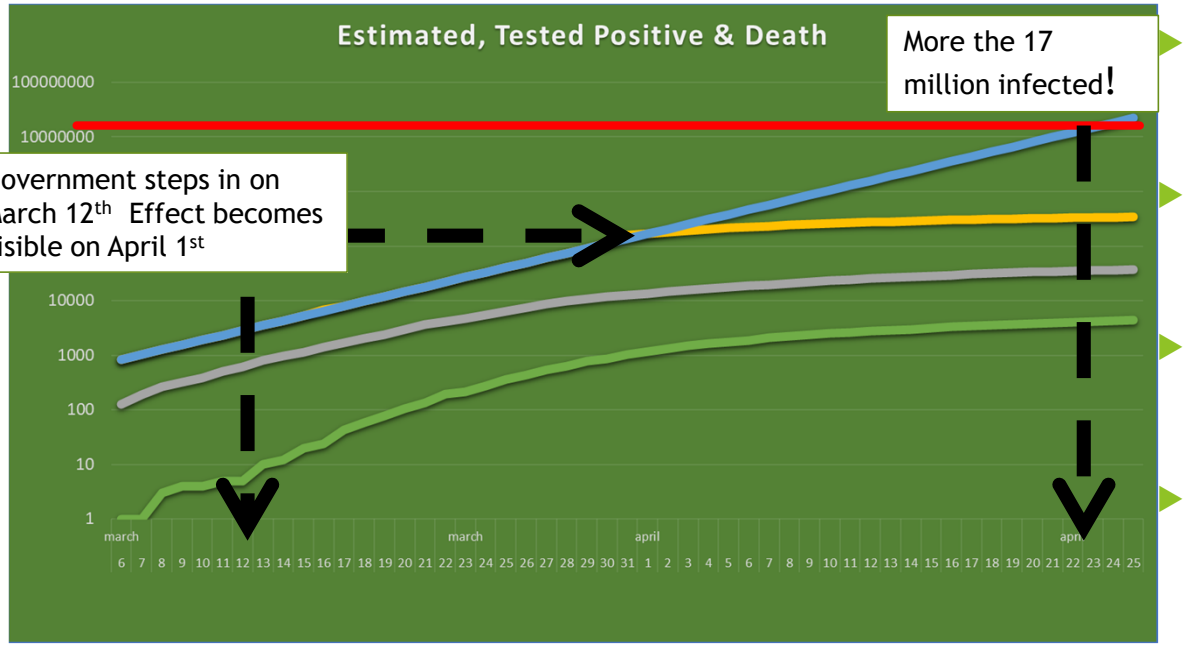
Analysing the data (did we do the right thing?)



- Using R0: 2.5 and average infection time 4.5 days we can make a prediction on how the curve would go!
- With no action the whole country would be infected on 24th of April! The Blue line!
- That would result in dramatic situations!

- To understand the impact better we use a different X- as (logarithmic)
- This makes it easier to see how Government measures had it´s effect!

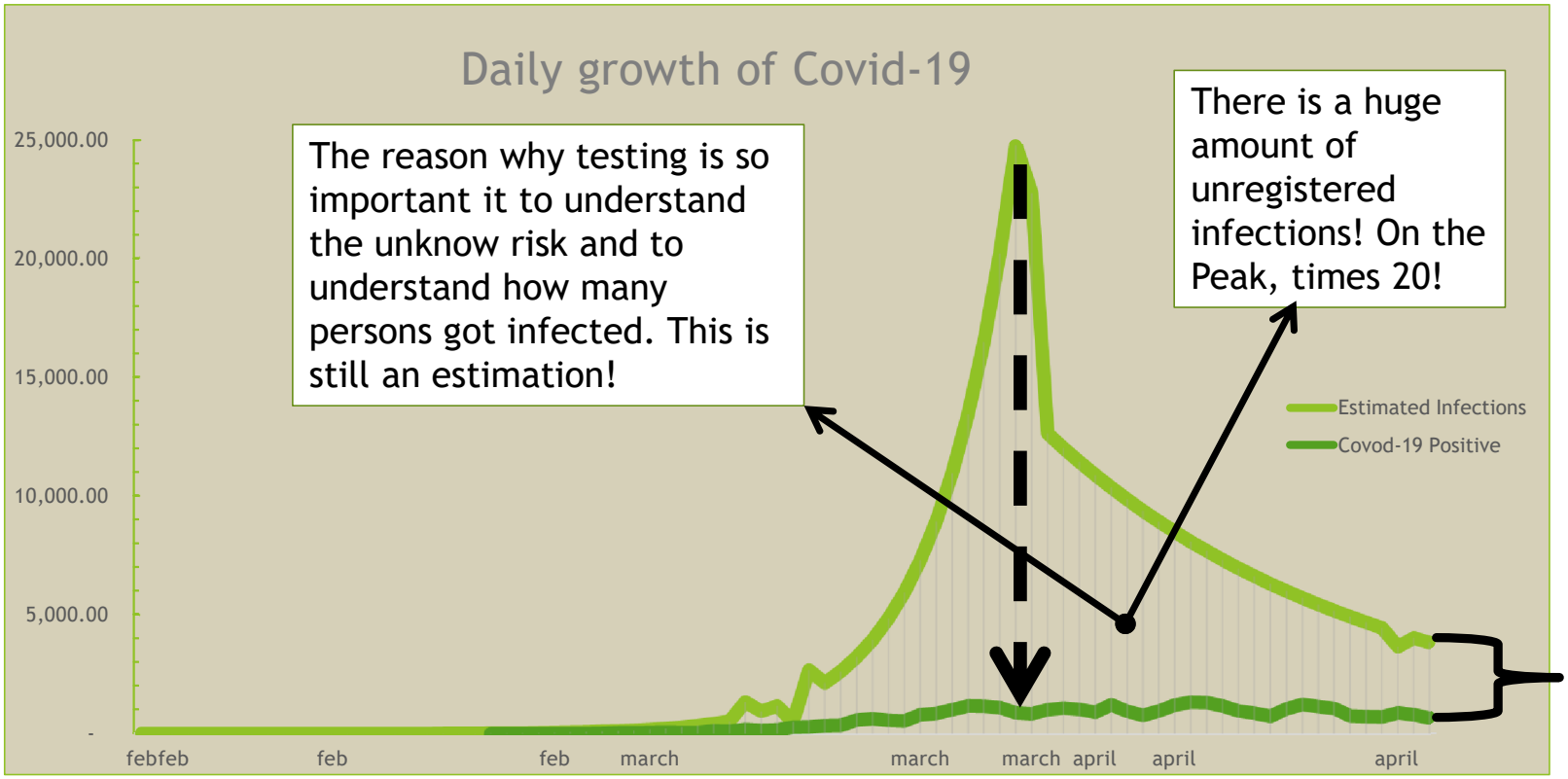
Analysing the data! (logarithmic scale)



- With no action the whole country would be infected on 24th of April! The Blue line!
- Using a few data point, 12, 16, 31 of March and 22, 29 April we calibrate a new curve!
- The date above where used for checking where the effective R was changing!
- On March 16th the effective R went to 1 but the the effect of the curve can be seen 2 weeks later (April 1st)

- With a different X- axis more becomes clear.
- The Yellow line shows that the measure the Government made where effective
- The Pink (the registered infected)and Green (the casualties)

Analysing the data! What is the underlying risk?

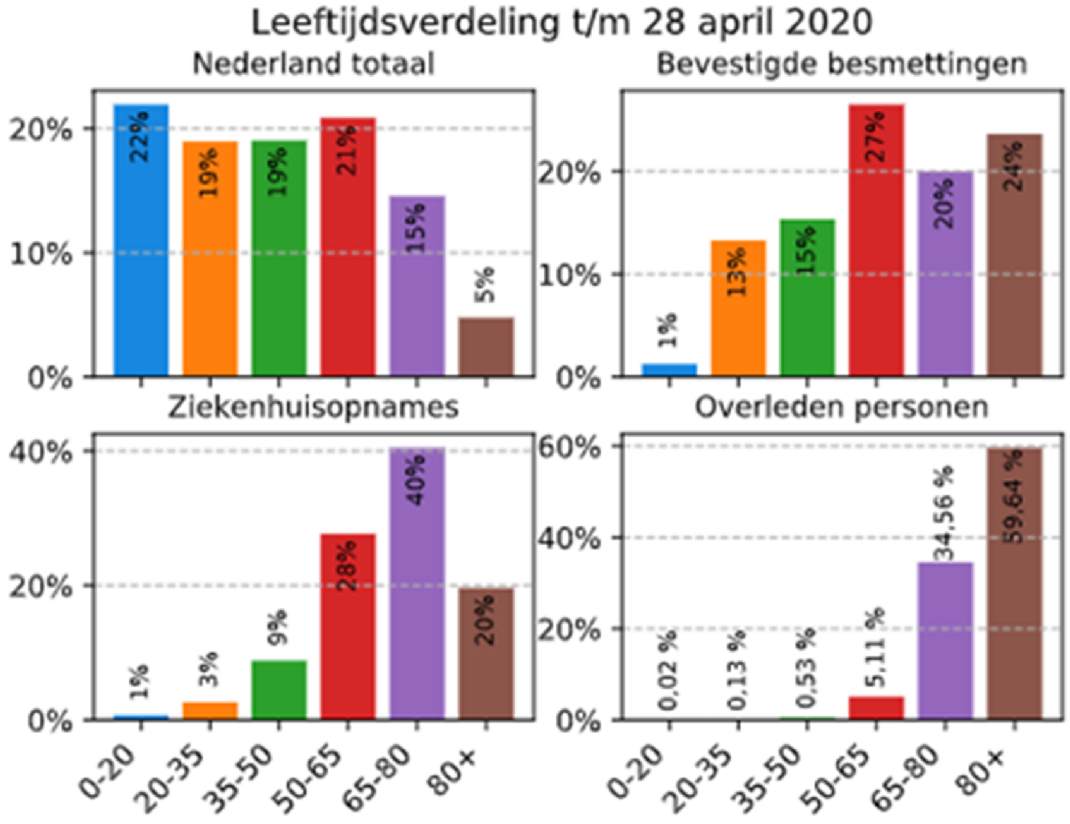


Choosing the wrong exit strategy could end up in a second wave. Basically everything starts again but now with more infections as a starting point leading to a quicker boost in infections!

Be aware of the Unknown Risk! Still every day infections!

- According to the model we reached the **peak of** the estimated infections on March the 30th with a total of 25 thousand a day! After that the curve dropped
- This is almost **2 weeks earlier than the peak on the registered cases which is expected** since more is happening under water!

Calculating the impact in society! Using the last statistics 28th April RIVM



Graph 1: How is the population divided
Graph 2: How are the positive cases divided per age
Graph 3: Which percentage per age went to the hospital (probably the 3% of the worldwide serious or critical condition)
Graph 4: The amount of fatalities per age

Assumptions needed for Exit strategy

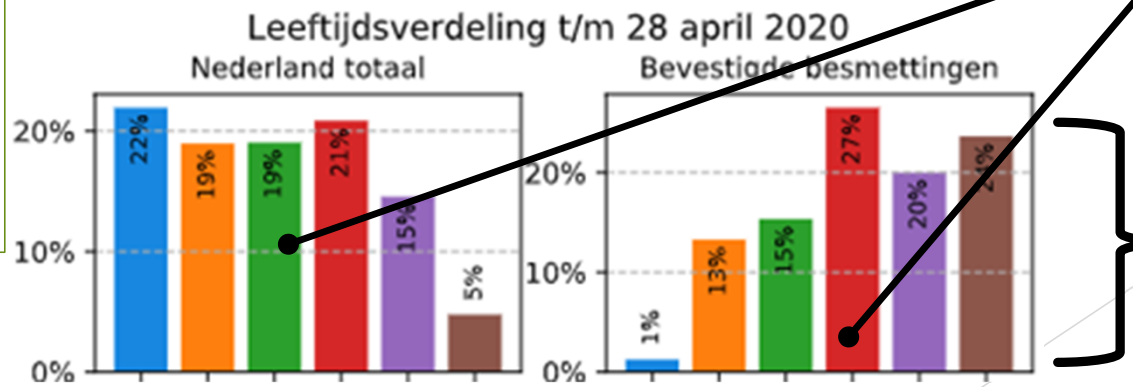
In the reports the amount of tested cases is used. (200 thousand).

- Roughly 40 thousand got tested positive and 4 thousand died from the virus.
- We know how the dead are divided by age but what we don´t know is:
  - How the rates are divided by age from the:
    - 160 thousand that where tested negative
    - From the unknow group that is not tested where we only have an estimation on how many there are.
- Is it possible the overall DFR will be higher than when separated per age?

In the picture below the problem is explained visually.

- The Dutch population as a whole is more is more weighted towards the 65 years and the test found positive more beyond the 65 years, which will have an effect on the exposure (the impact) on each age and there for the DFR overall!

Can we assume that the virus spread evenly over population or should it be according to the way the positive cases are found! Or does it not matter?



How many cases are undetected and are they equally divided over the population or more in the direction the second graphs ? The positive ones

200 thousand tests have been done and based on that **40 thousand** cases have been found positive. How is the rest (160 tested cases) divided over the age categories?

Assumptions needed for Exit strategy

To understand more about the DFR (mortality rate) on high level we will use 3 types of data sets.

- The estimated 360.000 cases based on slides 17 & 18
- The estimated ½ Million cases based on 3% Immunity
- An educated guess to understand the sensitivity of the results (1 million cases)

The amount of tests define the overall DFR (mortality rate)

Now we need to know how these rates are divided by age to calculate the exposure!

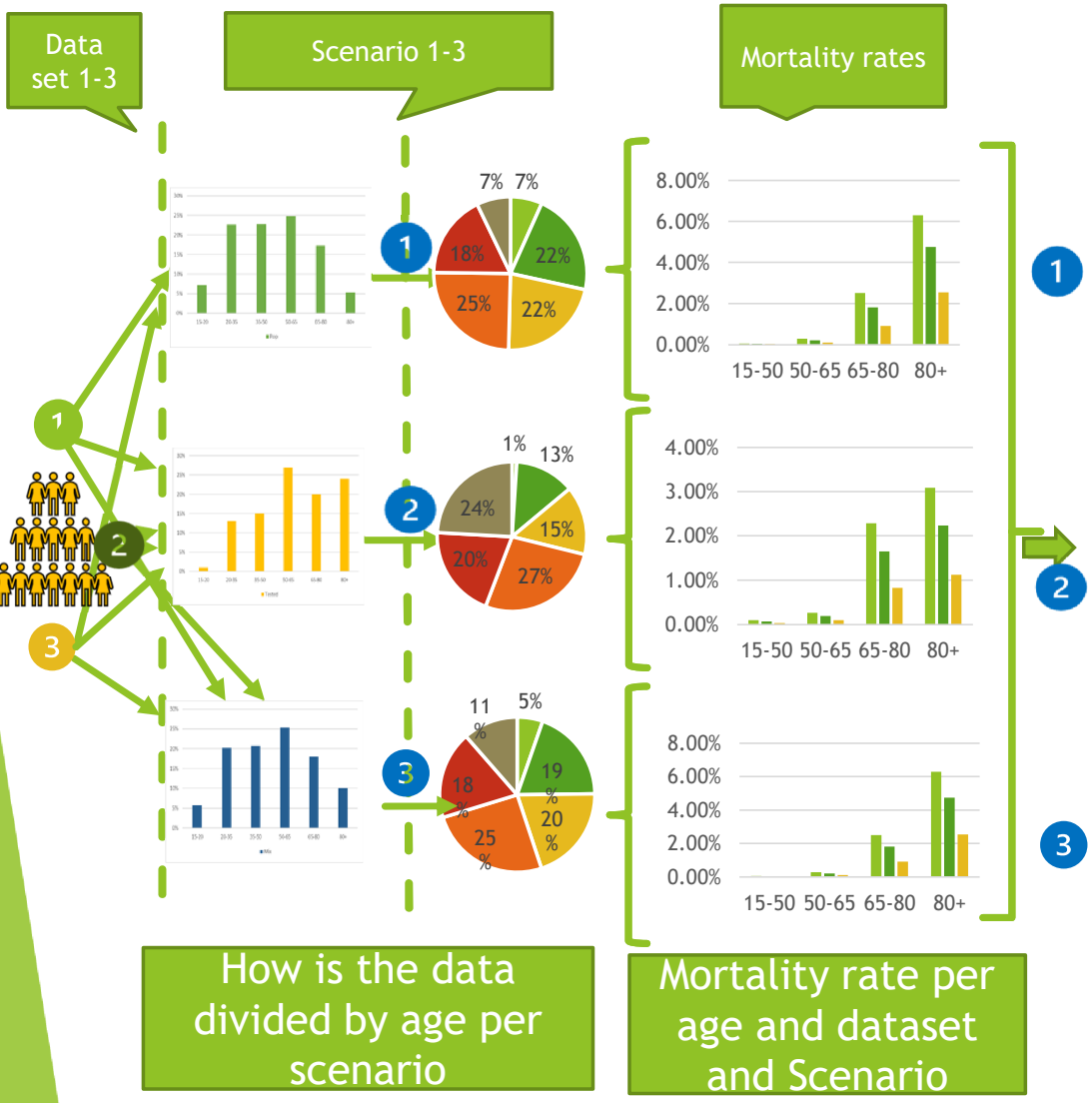
To do this we need to make assumptions! Therefore we define 3 scenarios.

- Scenario 1: Assume that the amount of cases are a reflection of the current population.(slide 23,Graph 1)
- Scenario 2: Assume that the amount of cases reflect the amount of positive cases so far. Input for this scenario is slide 23,Graph 2
- Scenario 3: A combination of the above scenarios. In this case we assume the weight is:75% the outcome of scenario 1 + 25% the outcome of scenario 2

Reasoning: In the beginning you test only the ones that show symptoms, then you test all the persons involved, So you testcases will be close to scenario 2

The more you test, the more you will also test you the more you will test the cases that reflect the current population (scenario 1) and therefor the weight will shift towards that direction.

Results



How is the data divided by age per scenario

Mortality rate per age and dataset and Scenario

What is the exposure per scenario, dataset and age

Scen 1	dataset 1	dataset 2	dataset 3
15-20	78	31	15
20-35	320	181	89
35-50	1,405	840	413
50-65	9,914	7,404	3,704
65-80	61,034	47,198	23,865
80+	36,144	58,804	33,704

Scen 2	dataset 1	dataset 2	dataset 3
15-20	296	212	106
20-35	426	305	152
35-50	1,729	1,239	617
50-65	9,557	6,854	3,418
65-80	57,444	41,434	20,813
80+	23,872	17,258	8,695

Scen 3	dataset 1	dataset 2	dataset 3
15-20	57	40	19
20-35	284	202	99
35-50	1,285	913	451
50-65	10,103	7,259	3,628
65-80	63,003	45,612	23,021
80+	48,650	36,711	19,606

Estimation of death over the population between (20-95)

In this group 50-55 gives a result of 1045 !

Scenario 3 and gives an estimated amount of 1150

Adding possibility of comorbidity see slide 25 will lower the results even more!

Based on ½ million cases for the age under 55 the exposure is still 50% less the tot total sum of casualties now!

Early R Calculations?

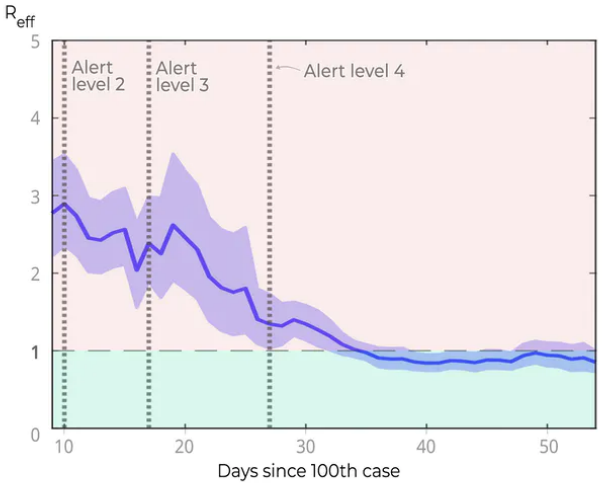
- As of March 10, 2020, Italy had reported 9172 COVID-19 cases with 463 deaths.
- We report the real-time reproductive numbers (R(t)) and case fatality rates for selected European countries (Italy, France, Germany, and Spain) by March 9, 2020.
- The R(t) was greater than 2 in the selected European countries, indicating that the outbreak will continue.
- As a global pandemic is inevitable, real-time monitoring of transmission is vital for containing the spread of COVID-19. The main objective of this study was to report the real-time effective reproduction numbers (R(t)) and case fatality rates (CFR) in Europe.
- Data for this study were obtained mainly from the World Health Organization website, up to March 9, 2020. R(t) were estimated by exponential growth rate (EG) and time-dependent (TD) methods. 'R0' package in R was employed to estimate R(t) by fitting the existing epidemic curve. Both the naïve CFR (nCFR) and adjusted CFR (aCFR) were estimated.
- With the EG method, R(t) was 3.27 (95% confidence interval (CI) 3.17–3.38) for Italy, 6.32 (95% CI 5.72–6.99) for France, 6.07 (95% CI 5.51–6.69) for Germany, and 5.08 (95% CI 4.51–5.74) for Spain. With the TD method, the R value for March 9 was 3.10 (95% CI 2.21–4.11) for Italy, 6.56 (95% CI 2.04–12.26) for France, 4.43 (95% CI 1.83–7.92) for Germany, and 3.95 (95% CI 0–10.19) for Spain.
- This study provides important findings on the early outbreak of COVID-19 in Europe. Due to the recent rapid increase in new cases of COVID-19, real-time monitoring of the transmissibility and mortality in Spain and France is a priority.
- **Source: International Journal of Infectious diseases**

Presentation made by R.J. Smit during lockdown

What is the R in other countries?

- The R started different in each country?
- What was the impact of the measurements really?

At the time of modelling, **Italy** was at the equivalent of **alert level 4**, which it entered 27 days after the 100th case.



Source: Te Punaha Matatini, University of Auckland

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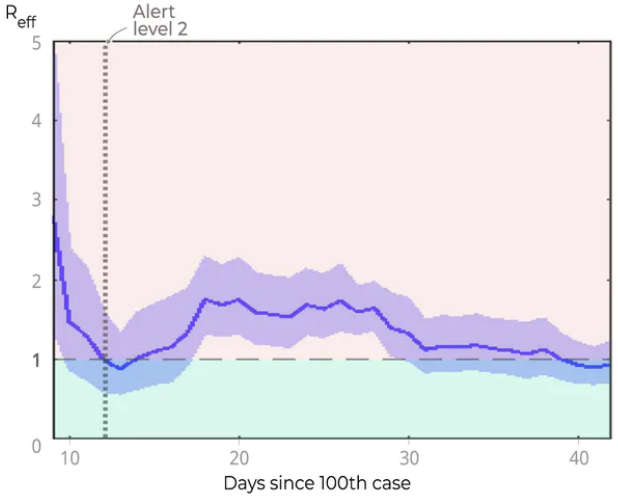
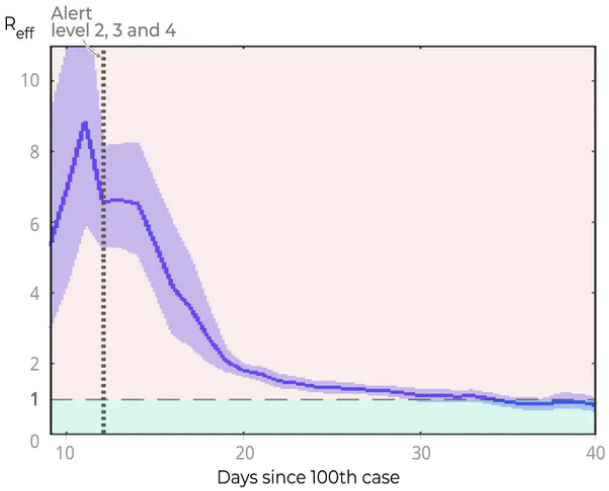
At the time of modelling, **Sweden** was at the equivalent of **alert level 2**, which it entered 12 days after the 100th case.



Source: Te Punaha Matatini, University of Auckland

At the time of modelling, **New York** was at the equivalent of **alert level 4**, which it entered 12 days after the 100th case.



Source: Te Punaha Matatini, University of Auckland

The R in other countries

Location	Reff: before and after	Cumulative cases	Cumulative deaths	Alert level
New South Wales, Australia	3 → 0.5	2,926	26	4 (13 days)
Austria	3.6 → 0.5	14,595	431	4 (32 days)
Norway	2.9 → 0.7	6,937	161	4 (24 days)
Germany	2.9 → 0.7	141,397	4,352	4 (26 days)
Denmark	1.5 → 0.8	7,073	336	4 (29 days)

A value of Reff > 1 means an outbreak is likely (the larger the value, the faster the increase in the number of infections). A sustained value of Reff < 1 means the virus will be eliminated from the community.

The alert levels correspond to interventions equivalent to (but not perfectly aligned with) New Zealand's alert levels 1 to 4. The levels are: level 1 – prepare, level 2 – reduce, level 3 – restrict, and level 4 – eliminate.

Table: The Conversation • Source: Te Pūnaha Matatini, University of Auckland

Location	Reff: before and after	Cumulative cases	Cumulative deaths	Alert level
New York, USA	5.4 → 0.8	230,597	14,832	4 (28 days)
Italy	2.8 → 0.9	172,434	22,745	4 (27 days)
United Kingdom	3.3 → 0.9	108,692	14,576	4 (25 days)
France	2.7 → 1	147,969	18,681	4 (31 days)
Spain	4.7 → 1	190,839	20,002	4 (33 days)

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Location	Reff: before and after	Cumulative cases	Cumulative deaths	Alert level
Switzerland	3.1 → 0.6	27,078	1,327	3 (32 days)
South Korea	3 → 0.7	10,635	230	3 (54 days)
Iran	4.3 → 0.9	79,494	4,958	3 (18 days)
Netherlands	2.3 → 0.9	30,449	3,459	3 (33 days)
Belgium	2.8 → 0.9	36,138	5,163	3 (31 days)

A value of Reff > 1 means an outbreak is likely (the larger the value, the faster the increase in the number of infections). A sustained value of Reff < 1 means the virus will be eliminated from the community.

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Location	Reff: before and after	Cumulative cases	Cumulative deaths	Alert level
Turkey	4 → 1	78,546	1,769	3 (20 days)
Quebec, Canada	5.4 → 1.1	16,798	688	3 (27 days)
Sweden	2.8 → 0.9	13,216	1,400	2 (30 days)
Japan	2.2 → 1.3	9,787	190	1 (46 days)
Brazil	2.9 → 1.3	33,682	2,141	1 (29 days)

A value of Reff > 1 means an outbreak is likely (the larger the value, the faster the increase in the number of infections). A sustained value of Reff < 1 means the virus will be eliminated from the community.

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Table: The Conversation • Source: Te Pūnaha Matatini, University of Auckland

Are Government actions overrated

- Social Distancing has an impact
- To what extend does it has an impact on the R?
- Closing down like New York did had an effect. The spread was however to high to stop it form having issues in the healthcare system.
- Sweden is not using 1.5 m distance as a rule. Is the R so much different?
- Denmark changed from 2 to 1 meter. Why?
- Portugal is using 2 m, but not on the beach. Why?
- Every country is using some kind of distance but what is the scientifical prove of this!
- School were closed in Norway under 20 years old. The found out it had no impact on the R
- Portugal is opening up more and more. It looks that is has no impact on the R
- Why? Shouldn´t we experiment more to find out what exit strategy we can use?

Next steps: Let´s put the data in perspective!

- The results for the **Age < 35** shows choosing the most likely scenario overall **100-350 possible death!**
- Figure 4 shows the age distribution of the road deaths in 2018. Most road deaths (21%) involved people who were 80 years old or older, followed by the group aged between 70 and 80 years (19%). Proportionately, measured by population size, the number of road deaths among the elderly is also high (70+; not in figure). The number of road deaths among children and youngsters under 20 years was lowest (8%).
- The amount of death while being on the road in 2018 : **678** ! For the age < 35 in 2018: between 142 – 202!
- The numbers have been quite stable for the past 10 years. Between 570-720.

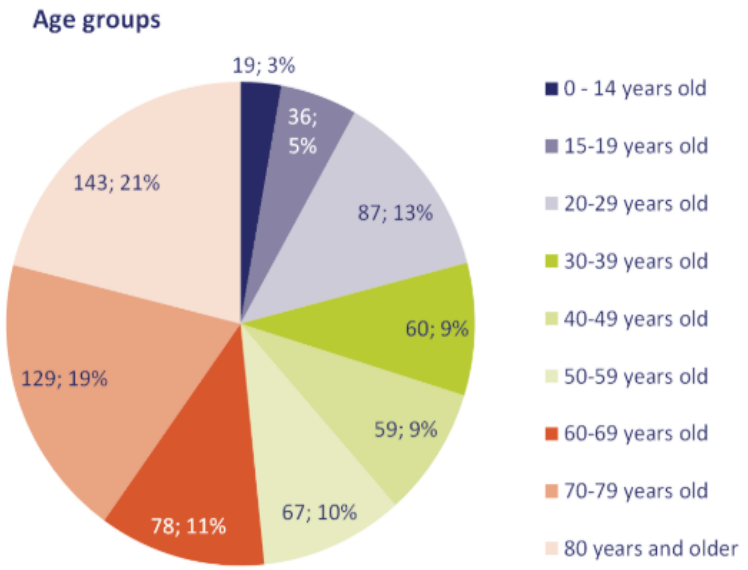

Figure 4. Road deaths in the Netherlands in 2018, by age group. Source: Statistics Netherlands.

Are we taking all the drivers license of our younger generation because of this?

Next steps: Let´s put the data in perspective!

- **Age 35-50! Possible impact 400-1300 casualties!**
- The table on the right side shows the amount of death of Corona with a pre-existing conditions based on data from New York! April 14th)
- For 18-44 years and 45-64 years the underlying illnesses : Diabetes, Lung Disease, Cancer, Immunodeficiency, Heart Disease, Hypertension, Asthma, Kidney Disease, and GI/Liver Disease. Play a crucial part in the cause of death!
- The numbers might be even overrated due to an overrun of the healthcare system at that time!

AGE	Number of Deaths	Share of deaths	With underlying conditions	Without underlying conditions	Unknown if with underlying cond.	Share of deaths of unknown + w/o cond.
0 - 17 years old	3	**0.04%**	3	0	0	0%
18 - 44 years old	309	**4.50%**	244	25	40	1.00%
45 - 64 years old	1,581	**23.10%**	1,343	59	179	3.50%
65 - 74 years old	1,683	**24.60%**	1,272	26	385	6.00%
75+ years old	3,263	**47.70%**	2,289	27	947	14.20%
TOTAL	**6,839**	100%	5,151	137	1,551	24.68%
			75%	2%	23%	

From 18-65: (25+40+59+179)/(244+1343): 143/1587 <10% Died without having an underlying condition! (so presumably healthy)

Should we not know these numbers for the Netherlands & all the other countries in the world?
If these are similar, this means that the impact on healthy people for the age 35-50 less then 150!
Are we shutting a whole country down for this?

Next steps: Are underlying conditions related to obesity?

- Age 50-65 shows on the 3rd most likely scenario on all datasets 3500-10000 possible death
- Taking into account the pre-existing condition, graph slide 14, this could lower to 3.5%*max(10000)< 350!
- How many people die in this age every year?
- How many with underlying condition as mentioned in slide 14?

If we know these numbers for the Netherlands and they are similar, this means that the impact on healthy people for the age 50-65 less then 350!
Are we shutting a whole country down for this?

Create Split Herd Immunity (Is it possible?)

Start with the area that is less infected and where the R is low. (The northern provinces)

Overall the demographic situation is:

- 95% of deaths is over 65, and of the other 5% younger people where 90% had an underlying issue:
  - The DFR based on death vs estimated infections of ½ M = 0.93%
  - If you take into account how the population is divided the DFR get to 0.63%
  - Focus on the 65- group will lead to a DFR of 8413/11.2M ~0,075%
- DFR for Healthy people: 0.0075%
- Splitting the two groups FRAGILE (65+ and fragile, say 23%) vs STRONG (younger and healthy, 77%)
  - FRAGILE group social distancing stop transmission there, while having the STRONG apply 'social approaching' and reaching a very high degree of infected and then immunized
  - **Assume 90% get´s infected in a short time (2 to 4 weeks). That would make 70% of population immune.**
- Putting the groups back together and asking them to stick to hygiene measures and no large gatherings, the epidemic will stop there.

The R must go up to create the spread

By social approaching the R will go up again. This is the only way to get the group it´s immunity

- Start all the activities. Sports, Events, Social activities to increase the R!
- Positive effect is that it will improve the immune system and start the younger generation moving
- Another group might be needed to participate, use the next group to do this!

- **What if Herd Immunity doesn´t work.**
  - Then the group 50-65 & 65+ needs special attention! But….
- **The key is to control the pressure on the hospitals, not the Herd Immunity!**
  - As long as there is no issue there we can continue socializing!
- **Be aware: It is possible that we get the whole society going without reaching Herd Immunity!**
- **Open points:** We used the info from New York for the underlying condition. That needs to be updated for the Netherlands. It may influence the results. Also the % used per age hospitalised could be lower (now we only look at the healthy group!)
- Is it needed to understand within the group who the healthy ones are. It will be difficult to put a norm and also to deny the ones with underlying condition no to take part. Even if it is for their own benefit. This could increase the pressure on hospital beds

Conclusion

- Governments stepped in. It worked!
  - Social Distancing works to lower the R
  - The moment when it is done is important to handle the healthcare
- We are not measuring the R to see if we do the right thing. Is this measurable?
- The Impact on the R of specific measurements are not clear. It there prove that 1.5 meter works? Everywhere the started different. Why?

We need an exit strategy and therefor experimental data.

That can only be done by opening up the country in increasing the R

- Investigate if split Herd Immunity could work. If we focus on the healthy group under 65 and start in the area that is less infected we can measure the effects
- We need more specific information on persons with an pre existing condition
  - Person that died
  - Persons treated in the IC
  - Persons that came into the hospitals or were registered as positive
- In Germany universities are involved in analysing all the area. Not just based on expert wrt virology but also economical, socials etc...