

# Corona crisis NL



# What went wrong?

- Models -- effect vs. mechanism
- PCR testing -- viable vs. performance
- Antibody testing -- safe vs. real
- Treatment -- double blind vs. cross reference
- Measures – mitigation vs. containment
- Dogma's and how to avoid them

# What we knew in Feb 2020

- CFR ~1% at highest
- At least 30% asymptomatic
- Aerosols
- Loss of smell



<https://www.youtube.com/watch?v=gAk7aX5hksU&t=1565s>

# What we know now

- CDC → 0,26% IFR
- Chance per capita is lower
  - dying with COVID19 or from COVID19
  - No complete infection spread
- Fatality % = infection probability x mortality risk

<https://in.dental-tribune.com/news/new-estimate-by-the-cdc-brings-down-the-covid-19-death-rate-to-just-0-26-as-against-whos-3-4/?fbclid=IwAR02-kvwge-9M8J8bmqdY8ZYInGk34K5U0RZieQ8QGz6y7IBGnV1E1AJQZs> [https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck\\_et\\_al\\_Infection\\_fatality\\_rate\\_of\\_SARS\\_CoV\\_2\\_infection2.pdf/%24FILE/Streeck\\_et\\_al\\_Infection\\_fatality\\_rate\\_of\\_SARS\\_CoV\\_2\\_infection2.pdf](https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf/%24FILE/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf)<https://www.youtube.com/watch?v=vrL9QKGQrWk>

[https://www.youtube.com/watch?v=adj8MCsZKlq&feature=youtu.be&fbclid=IwAR2RSC311hTVw2fRiHFaqGh\\_su69B1a-X\\_gRMshB7CqpB3t5qQeVnDrca0Y](https://www.youtube.com/watch?v=adj8MCsZKlq&feature=youtu.be&fbclid=IwAR2RSC311hTVw2fRiHFaqGh_su69B1a-X_gRMshB7CqpB3t5qQeVnDrca0Y)

# Transmission of Corona

- Asymptomatic shedding of virus by breathing
- Rhino, Influenza & Corona are all airborne
- Corona less detectable in droplets and aerosols

<https://www.nature.com/articles/s41591-020-0843-2>

<https://www.youtube.com/watch?v=tQNuThIjGqg>

<https://www.inquirer.com/health/coronavirus/coronavirus-covid19-antiviral-cure-antibiotic-20200318.html>

**Models -- effect vs. mechanism**

# Model based on R0

- Based on effect observation

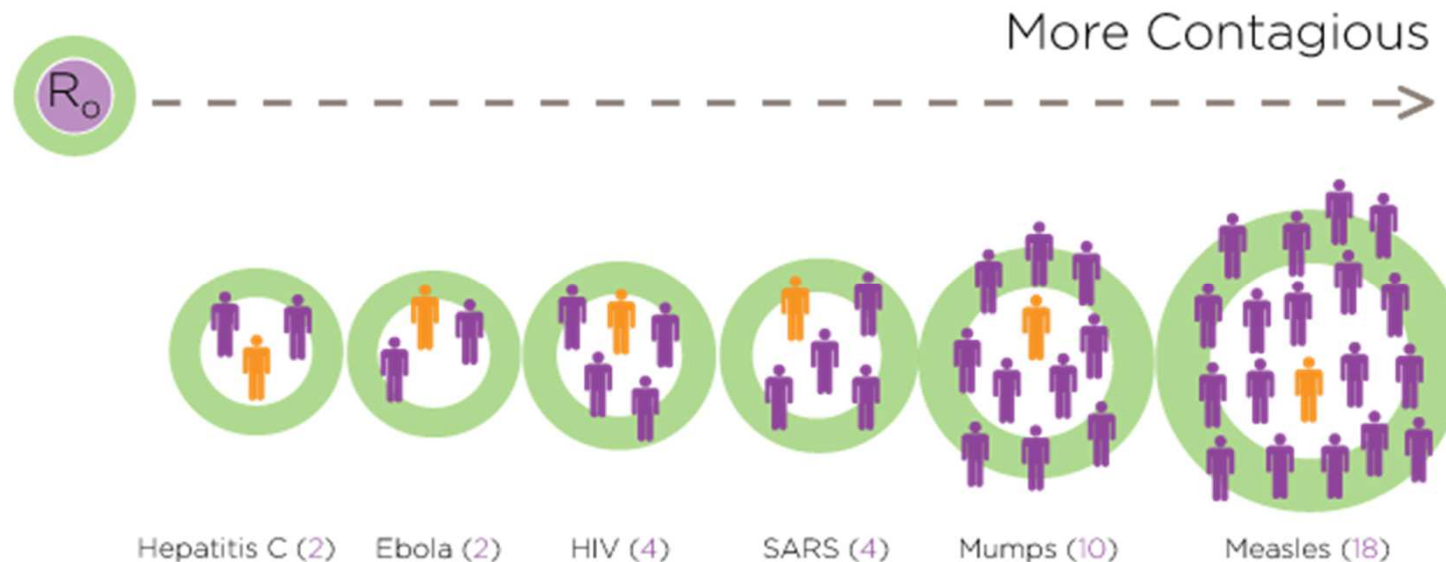
to note that  $\mathcal{R}_0$  is a dimensionless number and not a rate, which would have units of  $\text{time}^{-1}$ . Some authors incorrectly call  $\mathcal{R}_0$  the “basic reproductive rate.”

We can use the fact that  $\mathcal{R}_0$  is a dimensionless number to help us in calculating it.

$$\mathcal{R}_0 \propto \left( \frac{\text{infection}}{\text{contact}} \right) \cdot \left( \frac{\text{contact}}{\text{time}} \right) \cdot \left( \frac{\text{time}}{\text{infection}} \right)$$

# Assumptions for $R_0$

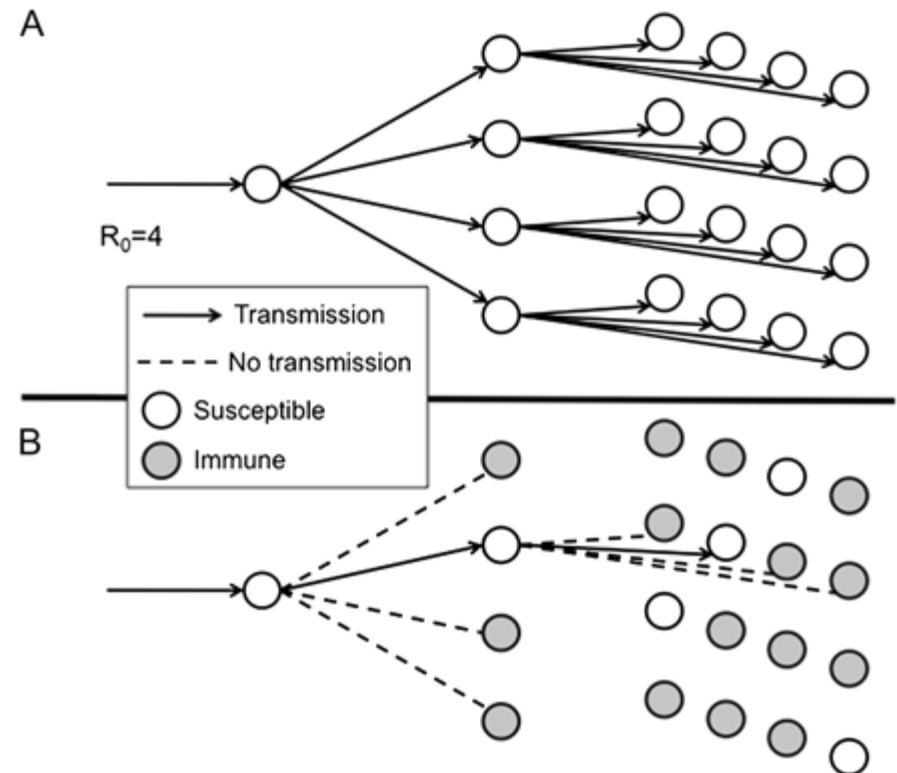
- no one has been vaccinated
- no one has had the disease before
- there's no way to control the spread of the disease





# Herd immunity

- Directly related to ( $R_0$ )
- Previous immunity
- Social interaction



# Problem with R0/Herd immunity

- Circular dependency  $R_0 \rightarrow \leftarrow$  Herd Immunity %
- $R_0$  is estimated on assumptions on population factors
- No actual “zero” state

# Mechanism model

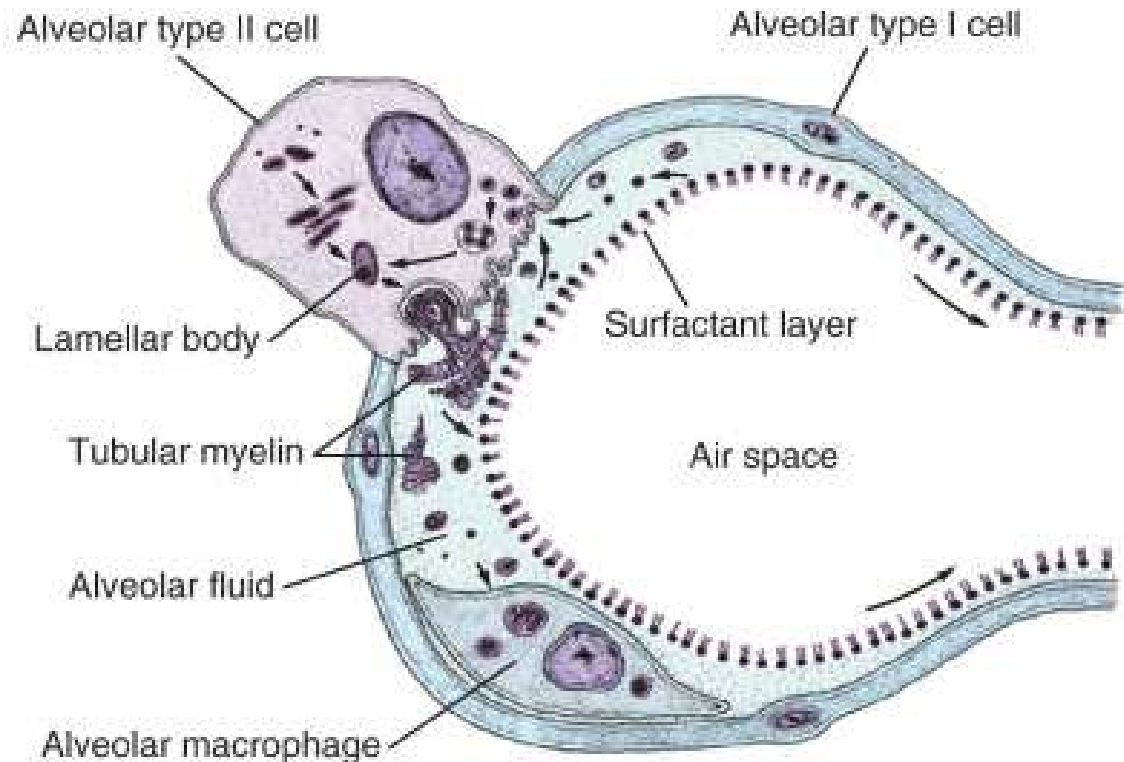
Based on multiple factors

- Aerosol factors
- Compartment factors
- Biological factors



# Aerosols factors

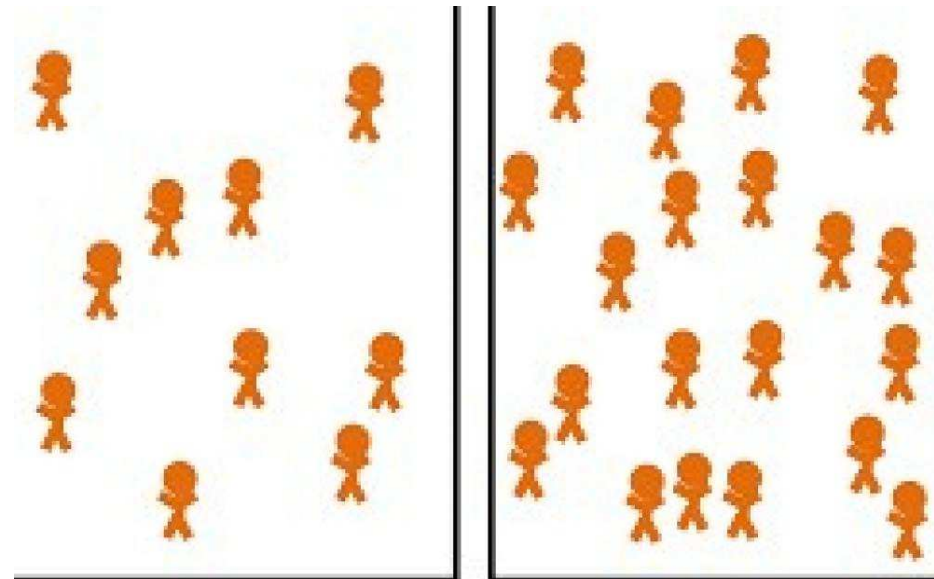
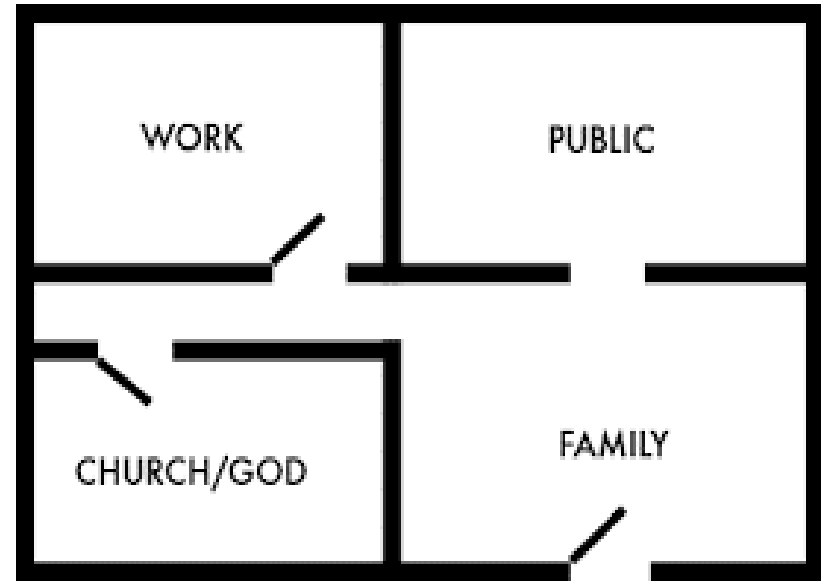
- Temperature
- Humidity
- Air pressure
- Vapor pressure (Surfactant)



<https://www.maurice.nl/2020/05/24/zo-werkt-airborne-besmetting-door-rebecca/>  
<http://flipper.diff.org/app/items/info/3790>

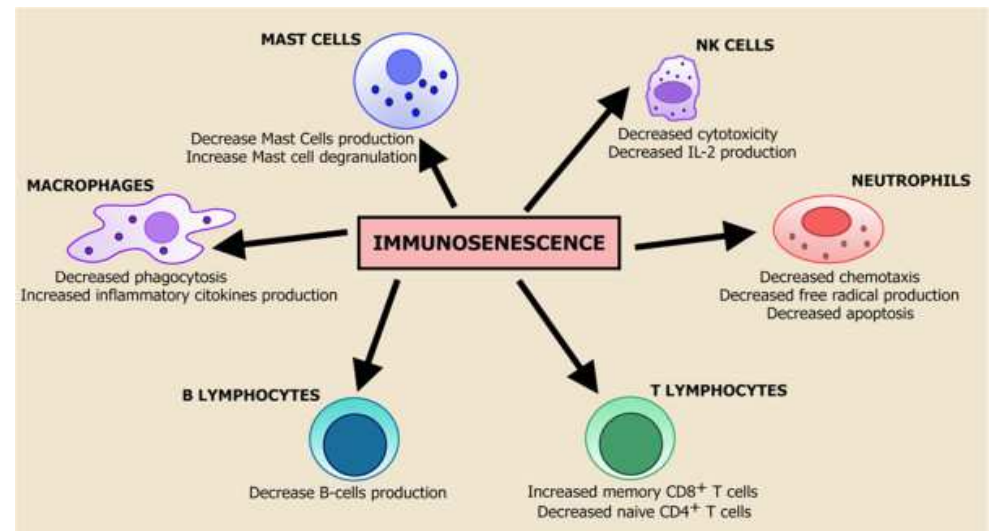
# Compartments factors

- Size of compartment
- Density
- Open compartments
- Duration



# Infection factors

- General immune system
- Previous immunity
  - Older strains of Corona
  - Previous Vaccination of other Virus
- General health
  - Cardio vasc. diseases
  - immuno scencence
  - Obese/Diabetic



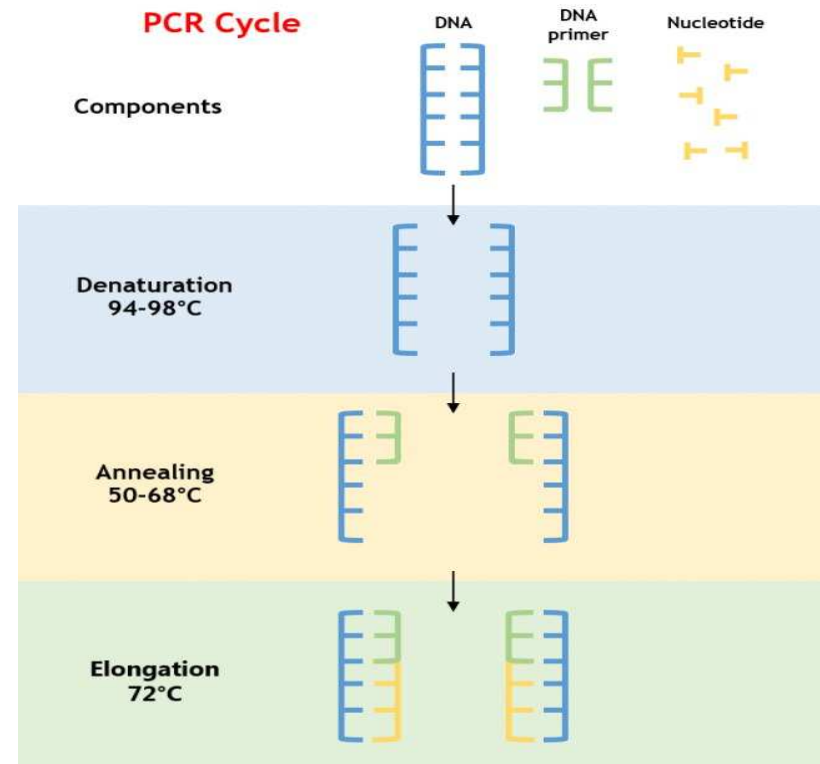
<https://academic.oup.com/cid/article/52/7/911/299077>

[https://www.researchgate.net/figure/Immunosenescence-This-phenomenon-has-been-described-as-the-result-of-a-chronic\\_fig1\\_236051287](https://www.researchgate.net/figure/Immunosenescence-This-phenomenon-has-been-described-as-the-result-of-a-chronic_fig1_236051287)

PCR testing -- viable vs.  
performance

# PCR false pos & false neg

- PCR picks up remnant of non viable virus
  - no second infections!
- Faringal swab →  
25% false negatives!
- Sheer size of operation



[https://www.ams.edu.sg/view-pdf.aspx?file=media%5C5556\\_fi\\_331.pdf&ofile=Period%20of%20Infectivity%20Position%20Statement%20\(final\)%202023-5-](https://www.ams.edu.sg/view-pdf.aspx?file=media%5C5556_fi_331.pdf&ofile=Period%20of%20Infectivity%20Position%20Statement%20(final)%202023-5-)

[https://www.youtube.com/watch?v=y6h8Tlxeg1g&fbclid=IwAR0Wxa\\_oKhAX5jW\\_2Y03WKgdVCN28G4YepTYTtVxpr62Zuh2sdpBNTaIOr0](https://www.youtube.com/watch?v=y6h8Tlxeg1g&fbclid=IwAR0Wxa_oKhAX5jW_2Y03WKgdVCN28G4YepTYTtVxpr62Zuh2sdpBNTaIOr0)



Antibody testing -- safe vs. real

# Antibody Studies

- Gangelt 14%

[https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck et al Infection fatality rate of SARS CoV 2 infection2.pdf/%24FILE/Streeck et al Infection fatality rate of SARS CoV 2 infection2.pdf](https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf/%24FILE/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf)

- Diamond Princess 19%

<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180>

[https://www.eurosurveillance.org/content/10.2807/1560-](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180)

- New York 13-21%

<https://www.cnn.com/2020/04/23/new-york-antibody-study-estimates-13point9percent-of-residents-have-had-the-coronavirus-cuomo-says.html>

[https://www.cnn.com/2020/04/23/new-york-antibody-study-estimates-13point9percent-of-](https://www.cnn.com/2020/04/23/new-york-antibody-study-estimates-13point9percent-of-residents-have-had-the-coronavirus-cuomo-says.html)

- NL

- PIENTER – not published

- Sanquin – 3 % (14% aspecific)

<https://www.researchsquare.com/article/rs-25862/v1>

# Innate & Acquired immunity

- Innate response → non specific
- Acquired response → specific
  - Current virus
  - Previous infections

While the innate immune response is immediate, the adaptive immune response is not. However, the effect of the adaptive immune response is long-lasting, highly specific, and is sustained long-term by memory T cells.

	Line of Defense	Timeline	Cells	Antigen Dependency	Examples
<b>Innate (non-specific)</b>	First	Immediate response (0-96 hours)	Natural killer cells, macrophages, neutrophils, dendritic cells, mast cells, basophils, eosinophils	Independent	Skin, hair, cough, mucous membranes, phagocytes, granulocytes
<b>Adaptive (specific)</b>	Second	Long term (>96 hours)	T and B lymphocytes	Dependent	Pus, swelling, redness, pain, T and B lymphocyte response

# Sanquin vs innate immunity

- Results

- Date 1-15 april
- Size 6000
- ~3% positive

- Claims

- Herd immunity not an option?

<https://erj.ersjournals.com/content/18/3/571>

<https://www.sciencedirect.com/science/article/abs/pii/S0022175998000891>

<https://www.researchsquare.com/article/rs-25862/v1>

- Uncertainties

- Sampled no sick
- Sensitivity
- Innate immune
- Previous acquired immune
- Assume 15% or higher?

# PIENTER-RIVM

- Date
  - March , still not published
  - Pico plus 8 june
  - Wrong sample size?
  - Why not publish now?



<https://www.rivm.nl/en/pienter-corona-study>

Treatment -- double blind vs. cross  
reference

# Different groups/treatments

- Innate Immune (& compatible ab) → not infectious
- Asymptomatic → infectious via aerosols
- Mild symptomatic → infectious
- Severe symptoms → infectious
  - Cardio Vascular diseases (underlying)
  - Diabetic/obese diseases (underlying)

<https://www.news-medical.net/news/20200416/Research-shows-speed-of-asymptomatic-SARS-CoV-2-transmission-in-Boston-homeless-shelter.aspx>

<https://www.nature.com/articles/s41591-020-0843-2>

# The case of HCQ

- The Lancet → NO
  - Efficacy no increase
  - Mortality increase
  - Double blind, randomized, peer reviewed ←
- Zelenko Protocol → YES
  - Efficacy high
  - Mortality decrease
  - Cross referenced ←



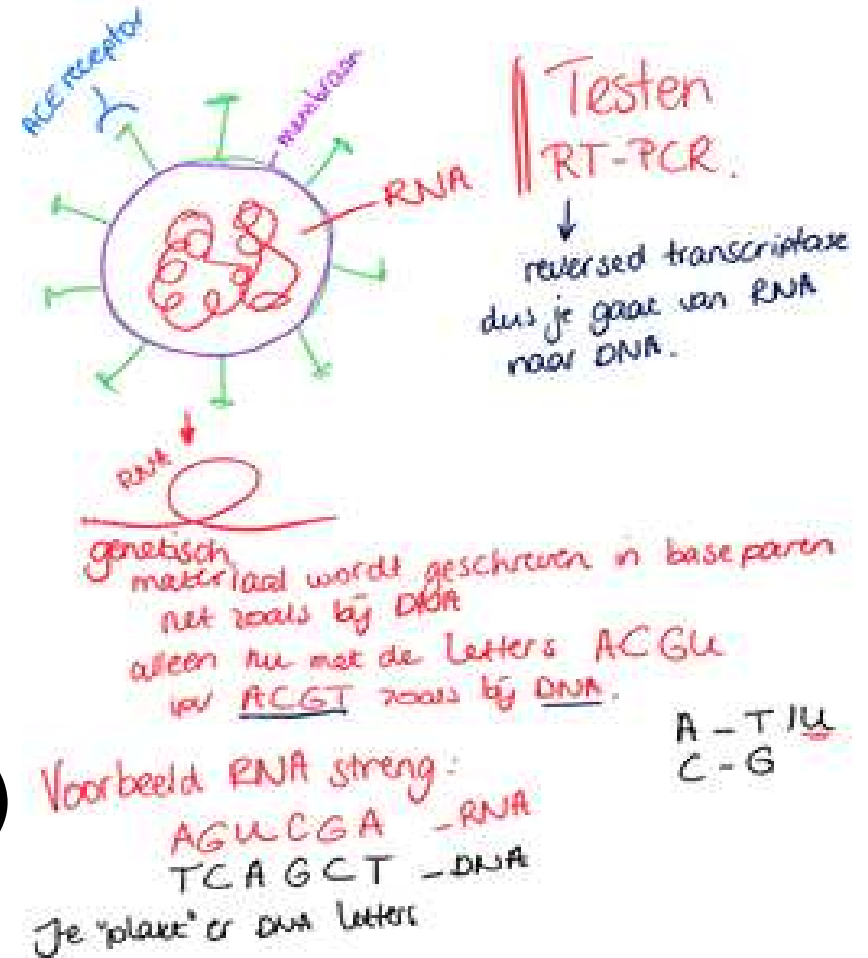
# •The Lancet

- No Zinc
- No supplements
- Late stage treatment
- Not a study! (review or collection of data)
- Increased mortality due to interaction of medicine
  - e. g. Digoxine and HCQ → interaction
  - Contra indications overlooked

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31180-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31180-6/fulltext)

# Zelenko Protocol

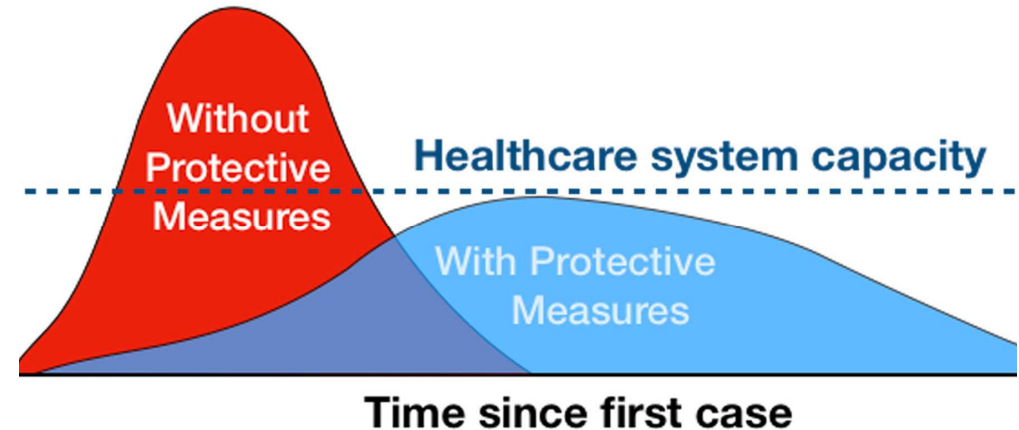
- HydroxyChloroquine
- Azitromycine
- Zinc
- Vit D
- Vit C
- Early stage (first symptoms)
- 4-5 days
- Contra-indication for cardio vascular diseases



# Measures – mitigation vs. containment

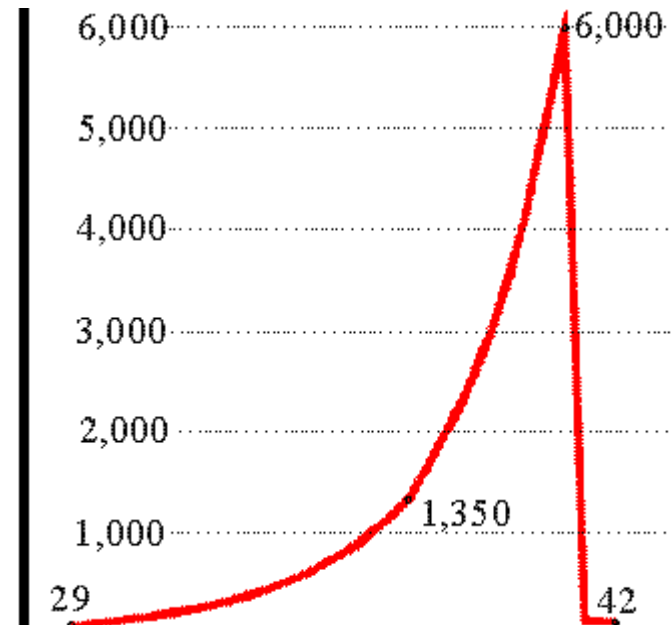
# Mitigation vs Containment

- Mitigation
  - Flatten the curve



*Adapted from CDC / The Economist*

- Containment
  - Crash the curve



# Current status – containment?

Group 1 → lockdown, is NOT suitable for mitigation! lockdown is for containment.

[https://www.forbes.com/sites/lisettevoytko/2020/05/06/majority-of-new-coronavirus-cases-in-new-york-are-from-people-staying-at-home-not-traveling-or-working/?fbclid=IwAR2fHUFKMPKqS1VOBhOSkI2\\_Fm9gV7r2ZdIFdSSomTv3RIdMD0wRt-ip5vY#613bfbf1655e](https://www.forbes.com/sites/lisettevoytko/2020/05/06/majority-of-new-coronavirus-cases-in-new-york-are-from-people-staying-at-home-not-traveling-or-working/?fbclid=IwAR2fHUFKMPKqS1VOBhOSkI2_Fm9gV7r2ZdIFdSSomTv3RIdMD0wRt-ip5vY#613bfbf1655e) [https://www.ams.edu.sg/view-pdf.aspx?file=media%5C5556\\_fi\\_331.pdf&ofile=Period%20of%20Infectivity%20Position%20Statement%20\(final\)%2023-5-20%20\(logos\).pdf&fbclid=IwAR0yKqmwC1DBr-9BqxRCoZ2uoXypoZKXrwAidb6UFf6ly5-](https://www.ams.edu.sg/view-pdf.aspx?file=media%5C5556_fi_331.pdf&ofile=Period%20of%20Infectivity%20Position%20Statement%20(final)%2023-5-20%20(logos).pdf&fbclid=IwAR0yKqmwC1DBr-9BqxRCoZ2uoXypoZKXrwAidb6UFf6ly5-) [https://nypost.com/2020/05/26/nobel-prize-winner-coronavirus-lockdowns-saved-no-lives/?utm\\_source=facebook\\_sitebuttons&utm\\_medium=site+buttons&utm\\_campaign=site+buttons](https://nypost.com/2020/05/26/nobel-prize-winner-coronavirus-lockdowns-saved-no-lives/?utm_source=facebook_sitebuttons&utm_medium=site+buttons&utm_campaign=site+buttons)

- Social distancing is not proven to be effective (0 articles)
- Social distancing is associated with Mental illness and Crowd control

# Group 2 – Mitigation

- Decrease travel (stop flying!)
- Profylaxe (vitamin D & C & Zinc)
- Testing and tracing, isolate
- Early treatment
- Isolate the risc groups
- Prepare the health and care facilities



<https://www.nature.com/articles/nature04795>

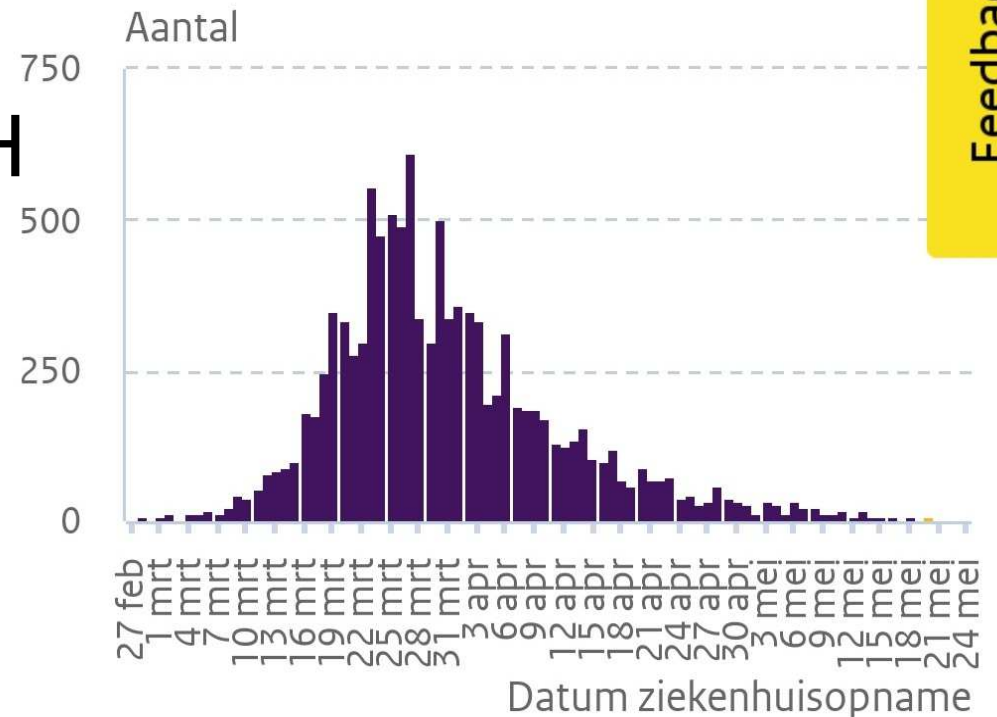
<https://lci.rivm.nl/richtlijnen/sars#profylaxe-behandeling>

# Graphs explained

- Hospital peak on 26 march
- Mortality peak on 7 april
- 12 days between H & D
- 5-6 days incubation
- 10 days between I & H
- 3 weeks I & D

In ziekenhuis opgenomen   
patiënten

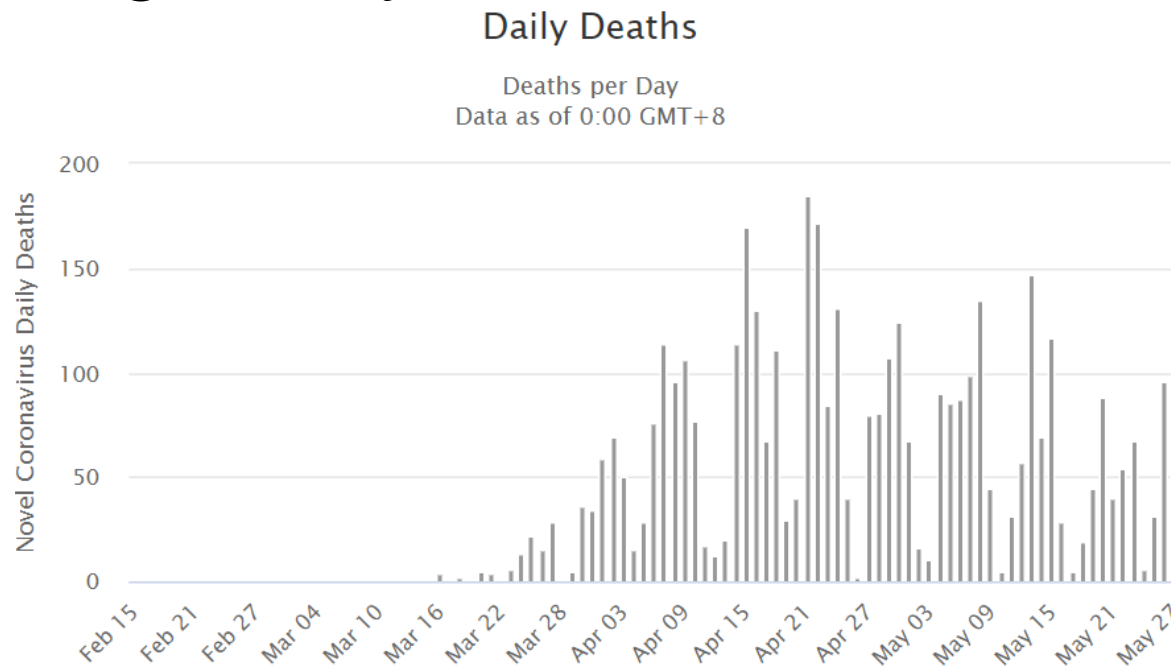
Bron: RIVM



Feedback

# Sweden

- Start 16 march, Peak 21 april, Crash ~ 1 August
- Measures asked, not forced
- Declining slowly



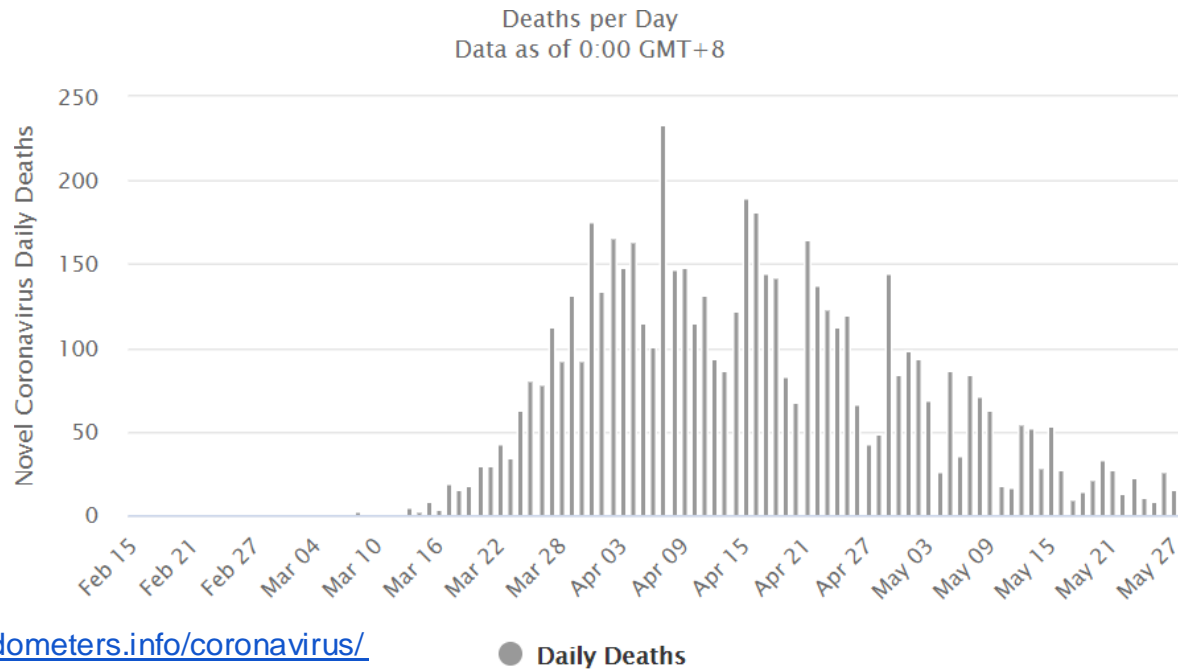
<https://www.worldometers.info/coronavirus/>

● Daily Deaths



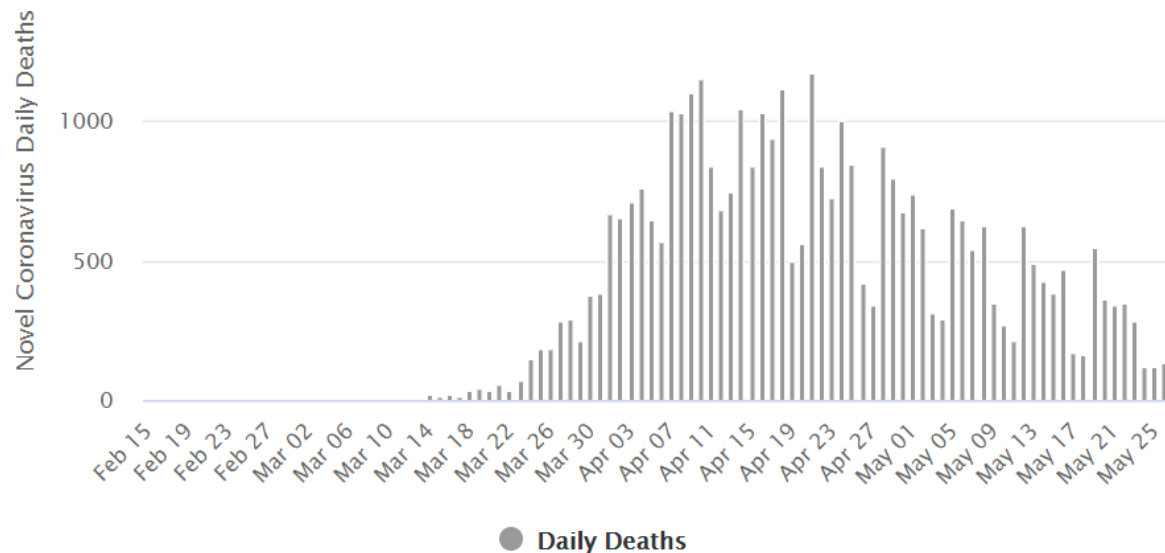
# Netherlands

- Start 16 march , Peak 10 april , Crash ~ 1 june
- Lockdown just before the maximum spreading
- No overflow of health care, even at the peak



# UK

- Start 16 march, Peak 10 april, Crash ~ half june
- Lockdown was *AFTER* the peak of infections
- The peak of infections is the same date as NL
- Shape is in between Sweden and NL



# Lockdown and surge (NL)

- lockdown has caused the surge

Tabel 6. Virologische dagstaat. Meldingen t/m 24 mei zijn samengevoegd per week<sup>13</sup>.

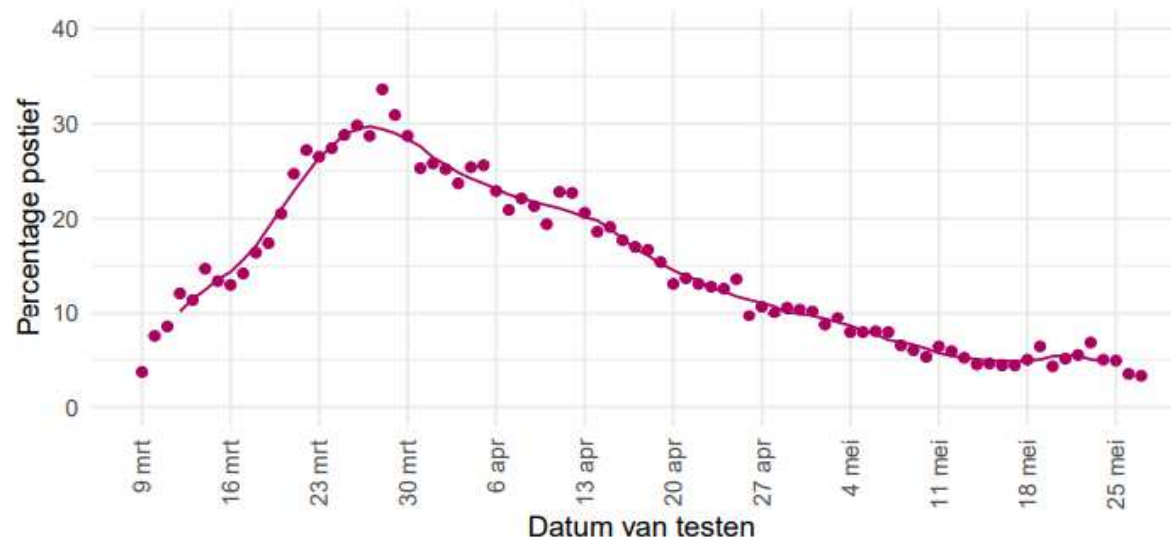
Datum van - tot	Labs	Geteste pers.	Pos. uitslag	% Pos.
2020-03-09 - 2020-03-15	30	17080	1529	9.0
2020-03-16 - 2020-03-22	35	21338	3953	18.5
2020-03-23 - 2020-03-29	37	24745	7232	29.2
2020-03-30 - 2020-04-05	40	29098	7424	25.5
2020-04-06 - 2020-04-12	41	38960	8391	21.5
2020-04-13 - 2020-04-19	42	40102	7140	17.8
2020-04-20 - 2020-04-26	43	38395	4947	12.9
2020-04-27 - 2020-05-03	43	28814	2900	10.1
2020-05-04 - 2020-05-10	45	28854	2067	7.2
2020-05-11 - 2020-05-17	47	32592	1677	5.1
2020-05-18 - 2020-05-24	49	27929	1532	5.5
2020-05-25	44	4003	195	4.9
2020-05-26	41	5466	190	3.5
2020-05-27	39	5305	173	3.3

<sup>13</sup>Labs = Aantal rapporterende laboratoria, Geteste pers. = Aantal geteste personen, Pos. uitslag = Aantal personen met een positieve laboratoriumuitslag, Percentage pos. = Percentage positieve uitslagen.

# Curvature shows surge (NL)

- Curvature → on March 16<sup>th</sup> → resurge until peak on March 28<sup>th</sup>

Figuur 18. Percentage van personen dat getest is op SARS-CoV-2, met een positieve testuitslag, gemeld door de virologische laboratoria<sup>14,15</sup>.



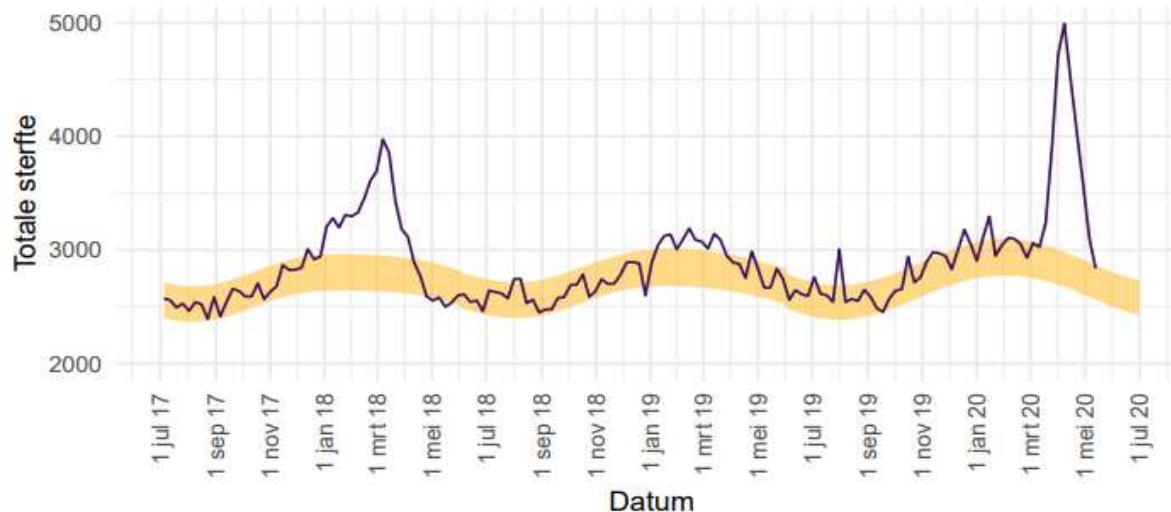
Deze gegevens worden iedere maandag t/m vrijdag bijgewerkt, behalve op feestdagen.

<sup>14</sup>Gegevens van de huidige week zijn nog incompleet.

<sup>15</sup>De bolletjes geven het percentage per dag aan; de lijn een 7-daags lopend gemiddelde per dag.

# Area under the curve (NL)

- Almost the same area
- 2020 a steeper peak
- Highest # infections after lockdown



Deze grafiek wordt iedere vrijdag in deze rapportage bijgewerkt. Voor gedetailleerde informatie zie: [RIVM - Monitoring Sterftcijfers](#) en [CBS](#). Zie [EuroMOMO](#) voor een Europees overzicht.

- Lockdown → surge of infections & surge IC's

# Summary

- Sweden flattened → mitigation
- UK & NL did not → no mitigation, containment ?
- Deaths per capita ~ equal
- Sweden decreases → herd immunity
- The lockdown did not have a significant effect on the mitigation
  - It has caused a sharp increase and nearly overwhelmed the hospitals

# Exit strategy

- Mitigation → chance of success : large
  - Sweden as example
  - Limited measures
- Containment → chance of success : small
  - Surrounding countries
  - Testing volume challenge
  - Collateral damage



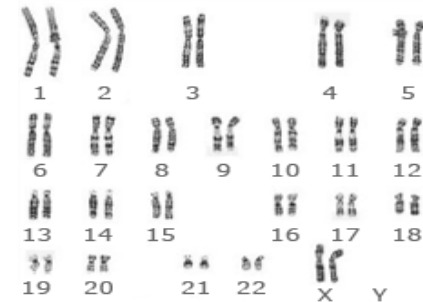
Dogma's and how to avoid them



# Dogmas

- During the Bubonic plague (14<sup>th</sup> century)
  - Quote 1 “*The illness spread through the air*”
  - Quote 2 “*Wearing a mask prevents vapors*”
  - In reality it was transmitted by flees..

- 48 chromosomes counted in 1923
  - not corrected until 1956



Karyotype of a woman.

- Spinache has 0,81 mg iron
  - Brussels sprouts have 1,2 mg iron



# stressed

- Afraid to be wrong
- Know-it-all
- Territorial
- Overly ethical
- Tunnel vision

# unstressed

**A Scientist**  
is someone who...

Observes  
and  
wonders

Shares  
their ideas  
and  
discoveries

Listens to  
the ideas  
of others

Explores  
the world  
around  
them

Asks  
questions

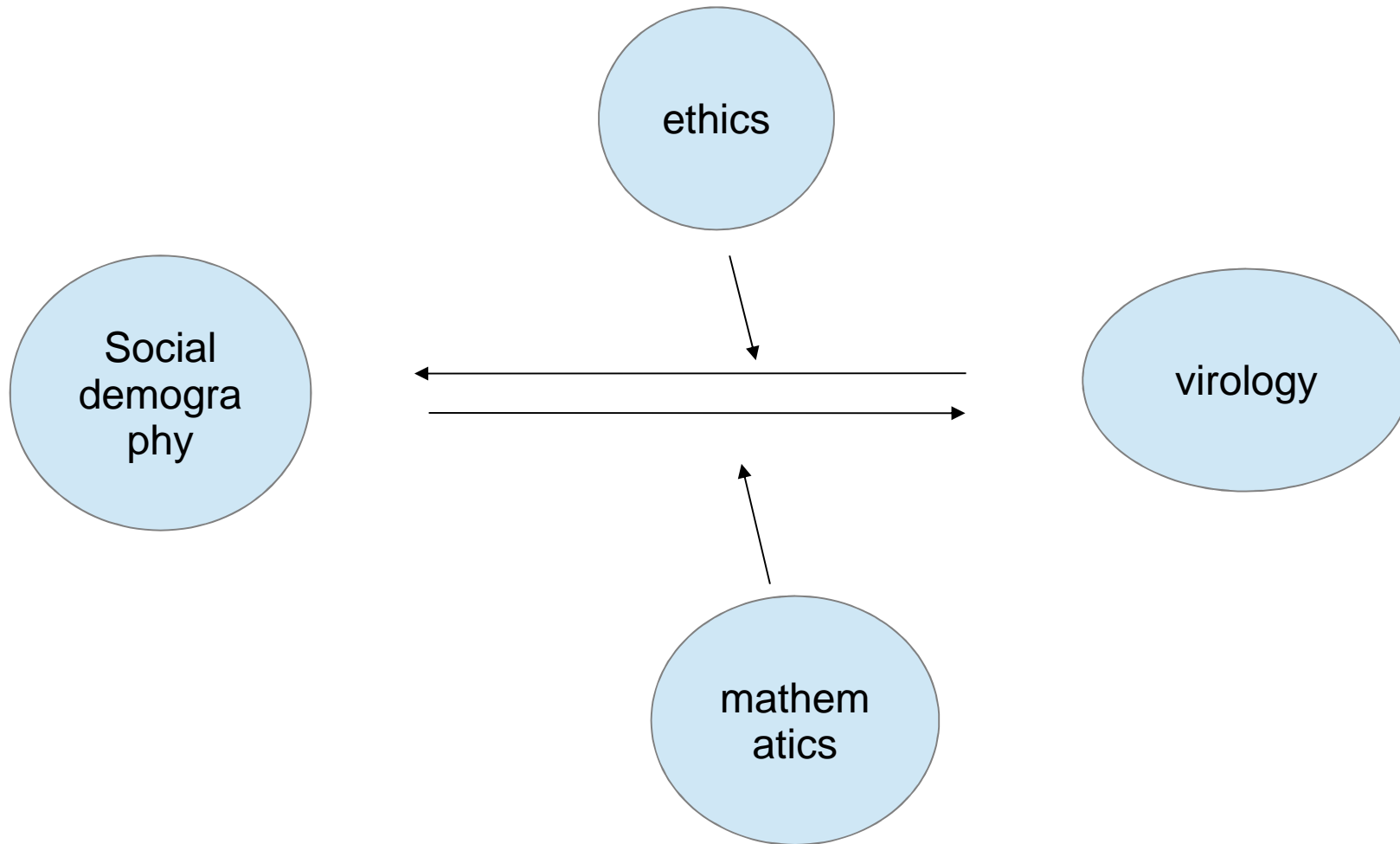
Uses  
tools to  
solve  
problems

Conducts  
experiments



**A Scientist**  
is someone like you!

# Cross refferencing



# Conclusion

- Very likely close to herd immunity
- Low CFR
- Likely only ~25% of population can be infected
- Most spreading is via Aerosols
- Virus shedder might be surfactant dependant
- Old models failed
- Cross referencing as crisis model for science
- Lockdown caused surge on IC
- Mitigation is the only real option