

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.youtube.com/watch?v=vrL9QKGQrWk>

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

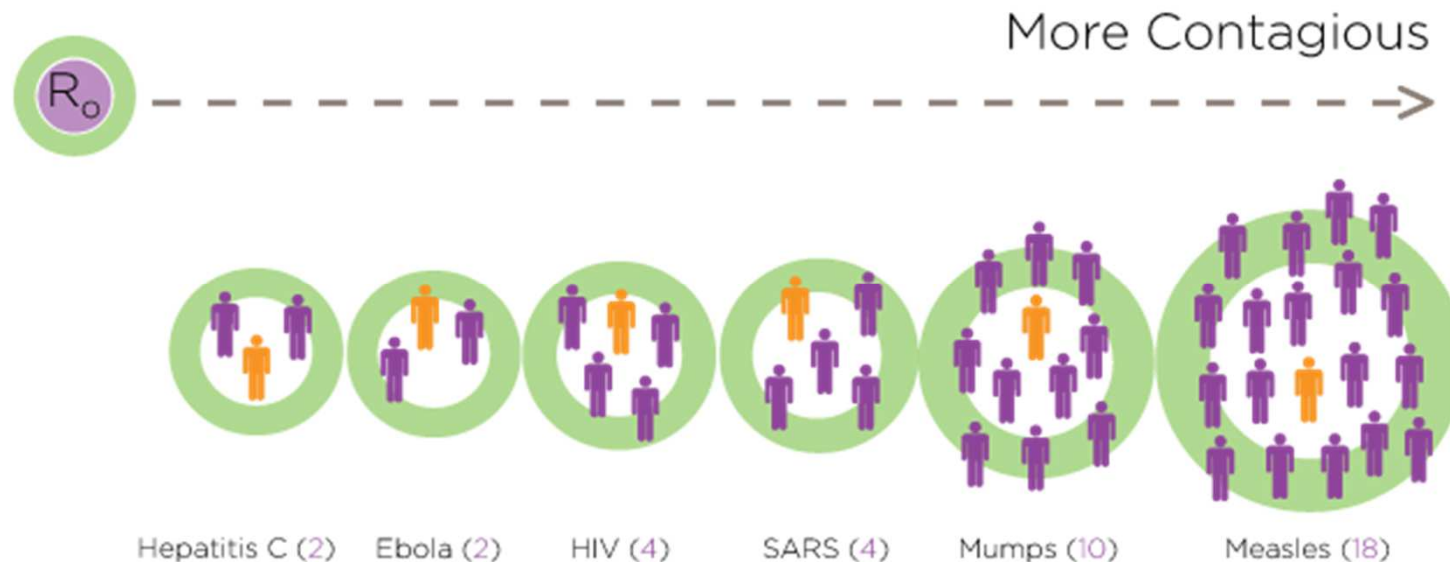
to note that \mathcal{R}_0 is a dimensionless number and not a rate, which would have units of time^{-1} . Some authors incorrectly call \mathcal{R}_0 the “basic reproductive rate.”

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

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

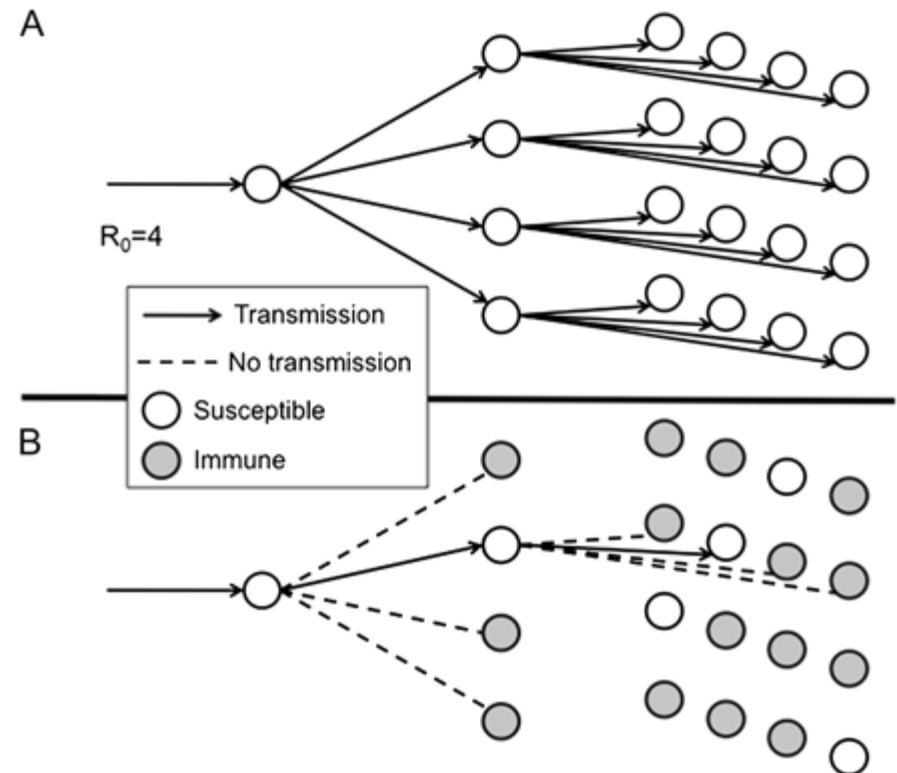
Assumptions for R_0

- 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

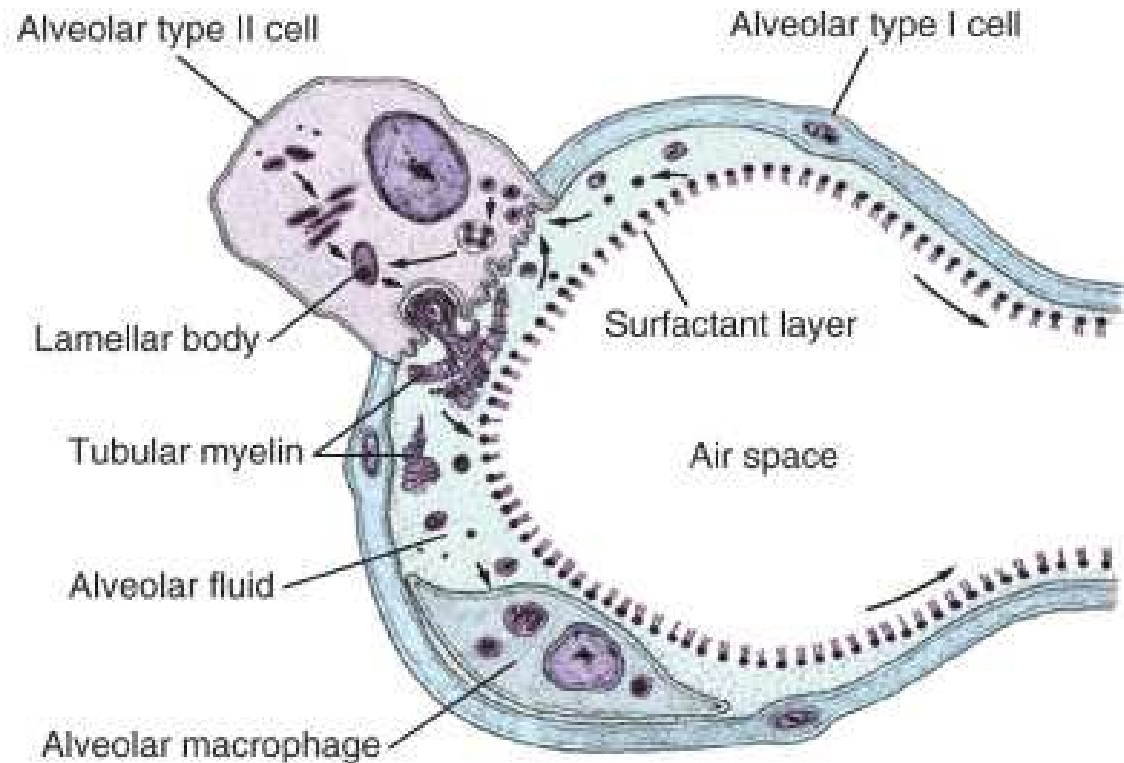
Based on multiple factors

- Aerosol factors
- Compartment factors
- Biological factors



Aerosols factors

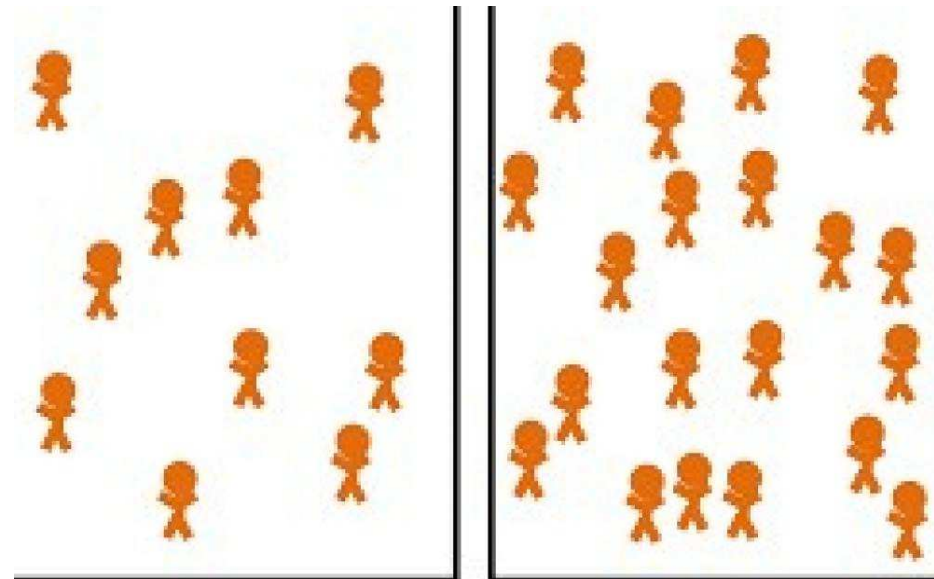
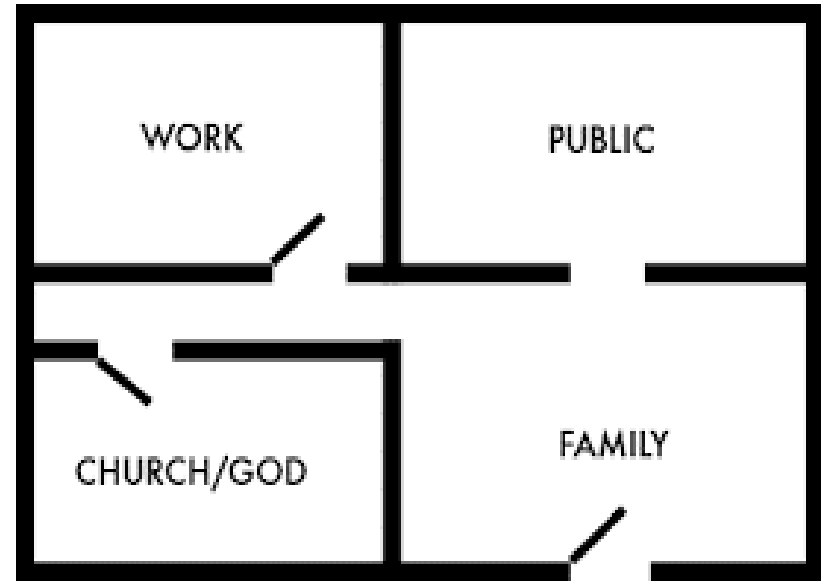
- Temperature
- Humidity
- Air pressure
- Vapor pressure (Surfactant)



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

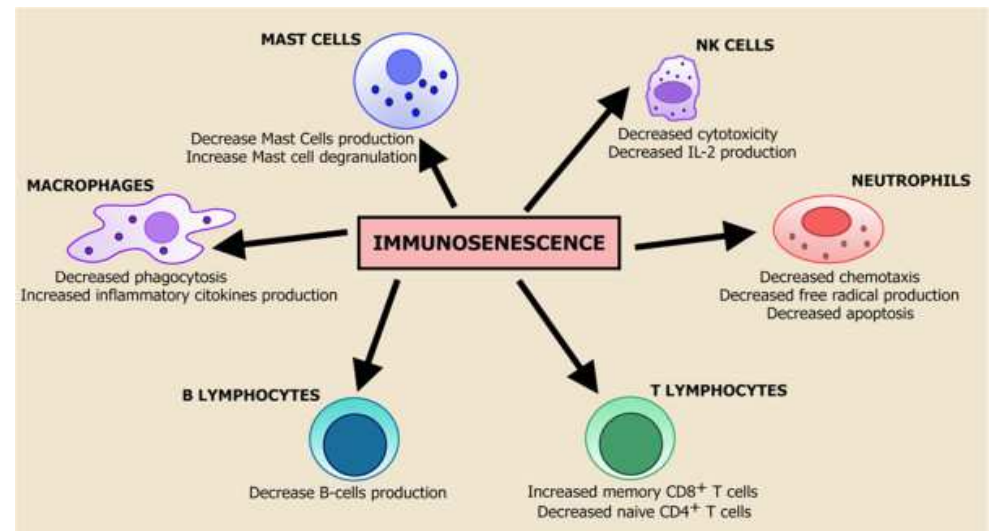
Compartments factors

- 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



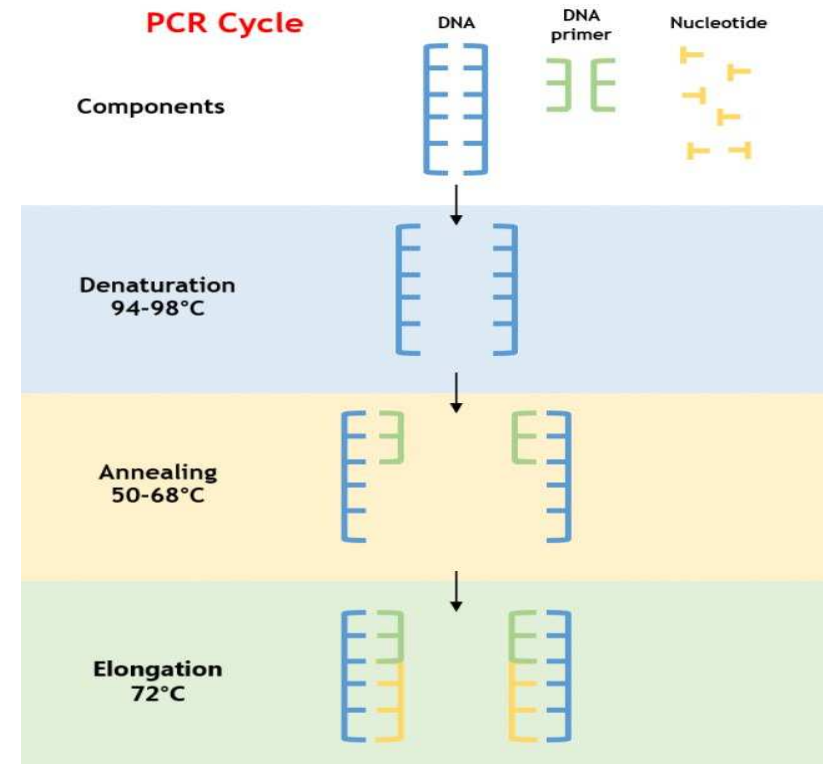
<https://academic.oup.com/cid/article/52/7/911/299077>

https://www.researchgate.net/figure/Immunosenescence-This-phenomenon-has-been-described-as-the-result-of-a-chronic_fig1_236051287

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

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>

- **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>

- **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
Innate (non-specific)	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
Adaptive (specific)	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 ←

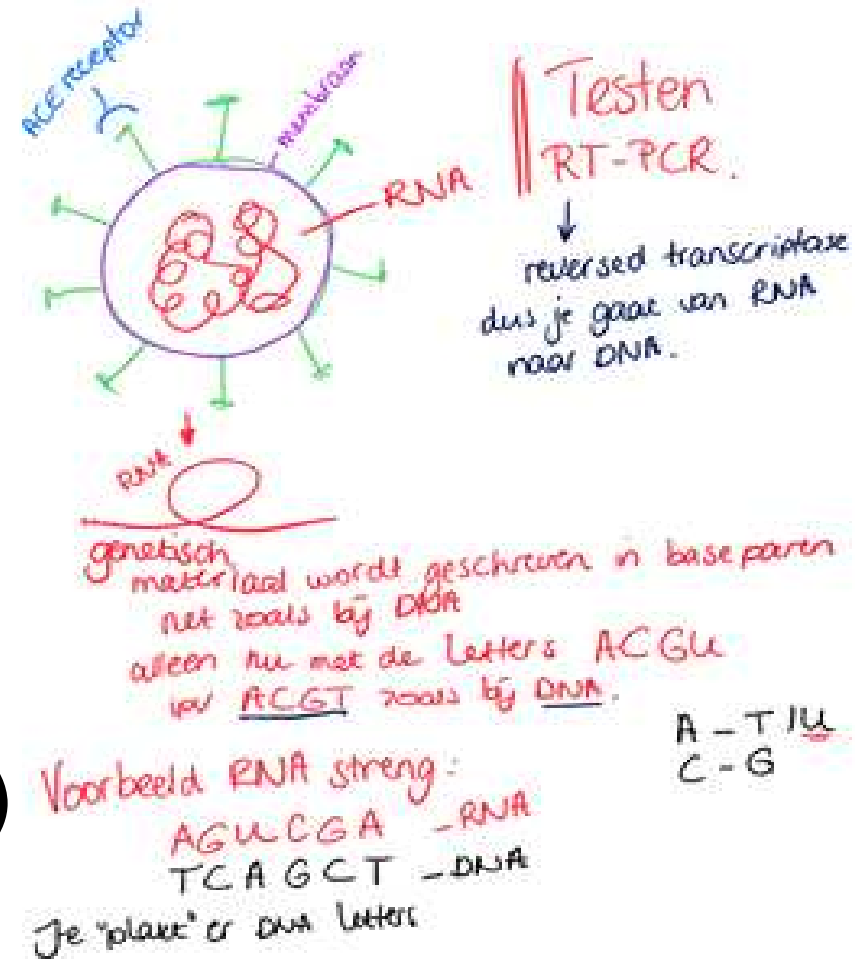
•The Lancet

- 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

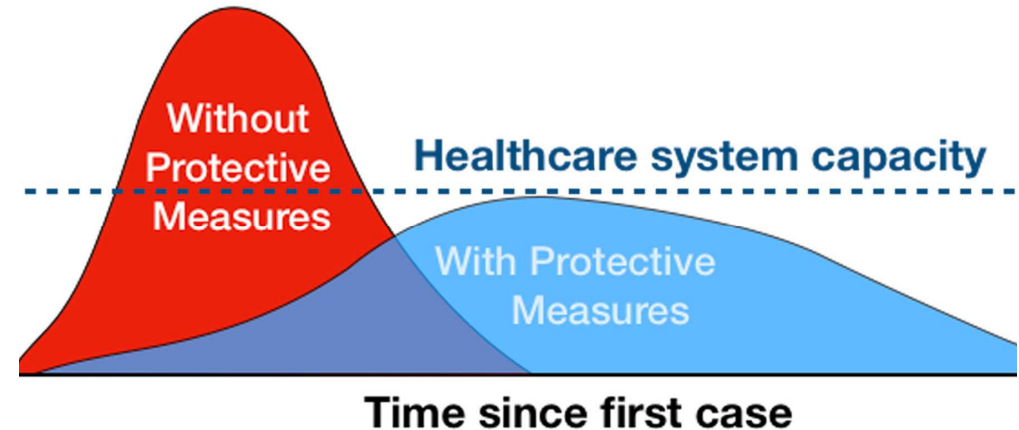
- HydroxyChloroquine
- Azitromycine
- Zinc
- Vit D
- Vit C
- Early stage (first symptoms)
- 4-5 days
- Contra-indication for cardio vascular diseases



Measures – mitigation vs. containment

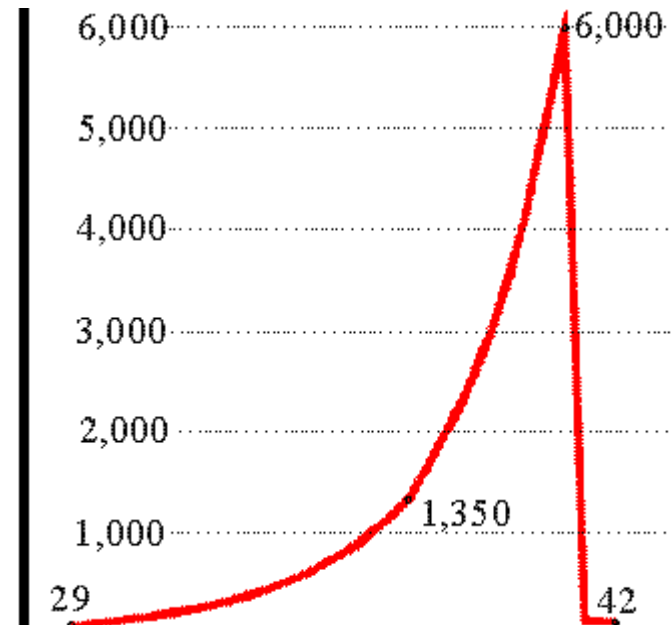
Mitigation vs Containment

- 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_Fm9gV7r2ZdlFdSSomTv3RIdMD0wRt-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

- 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>

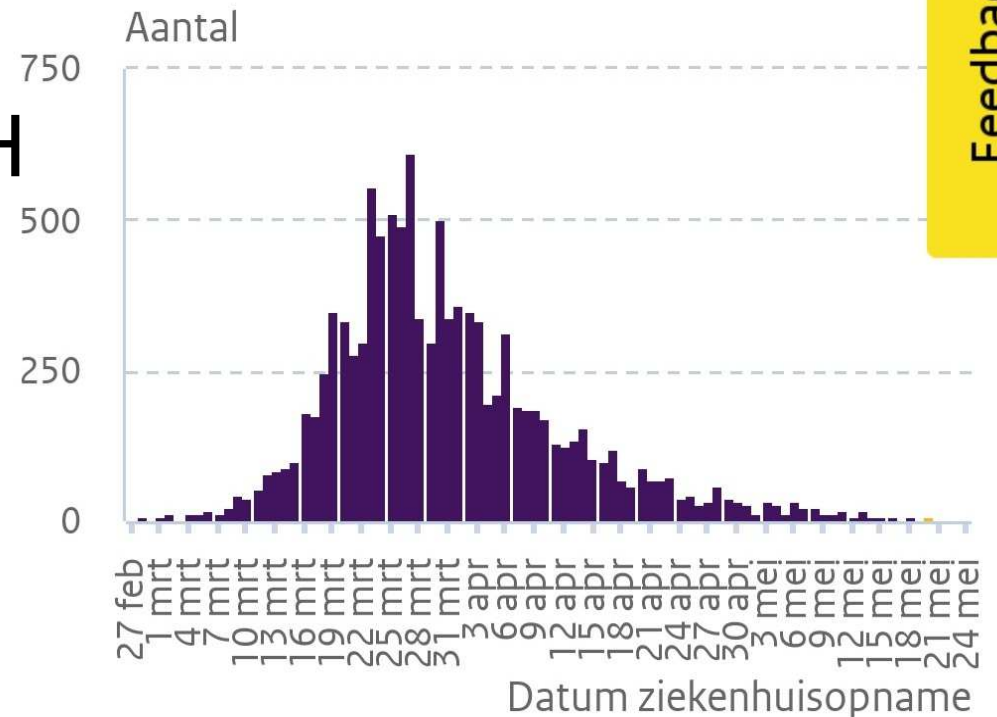
<https://lci.rivm.nl/richtlijnen/sars#profylaxe-behandeling>

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

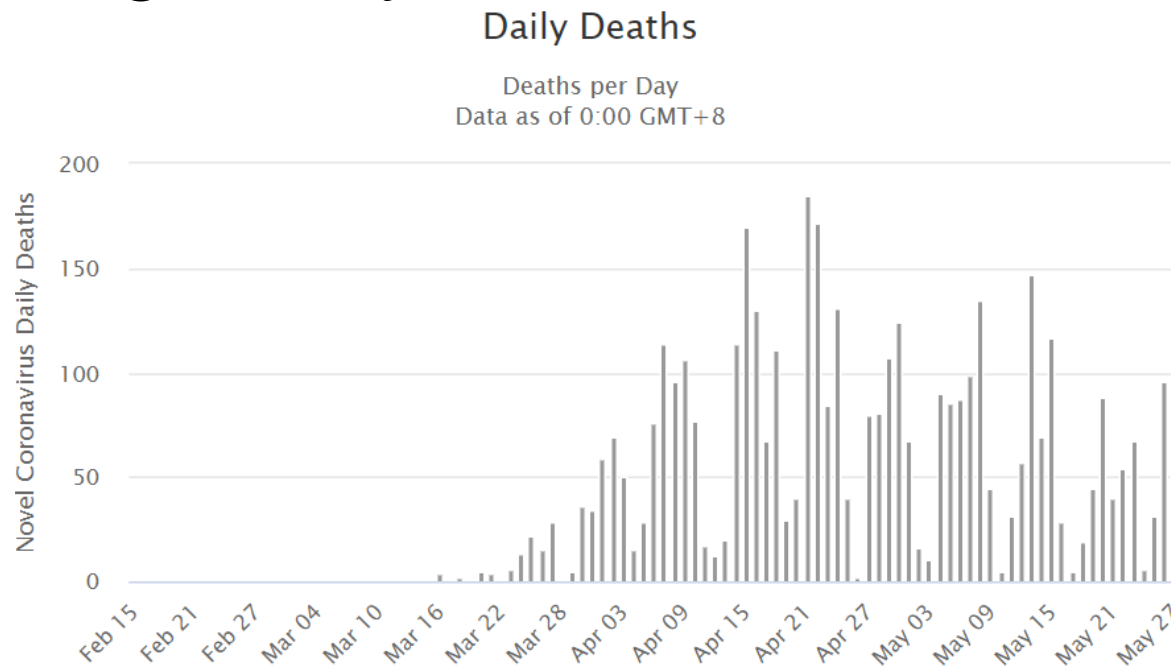
Bron: RIVM



Feedback

Sweden

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

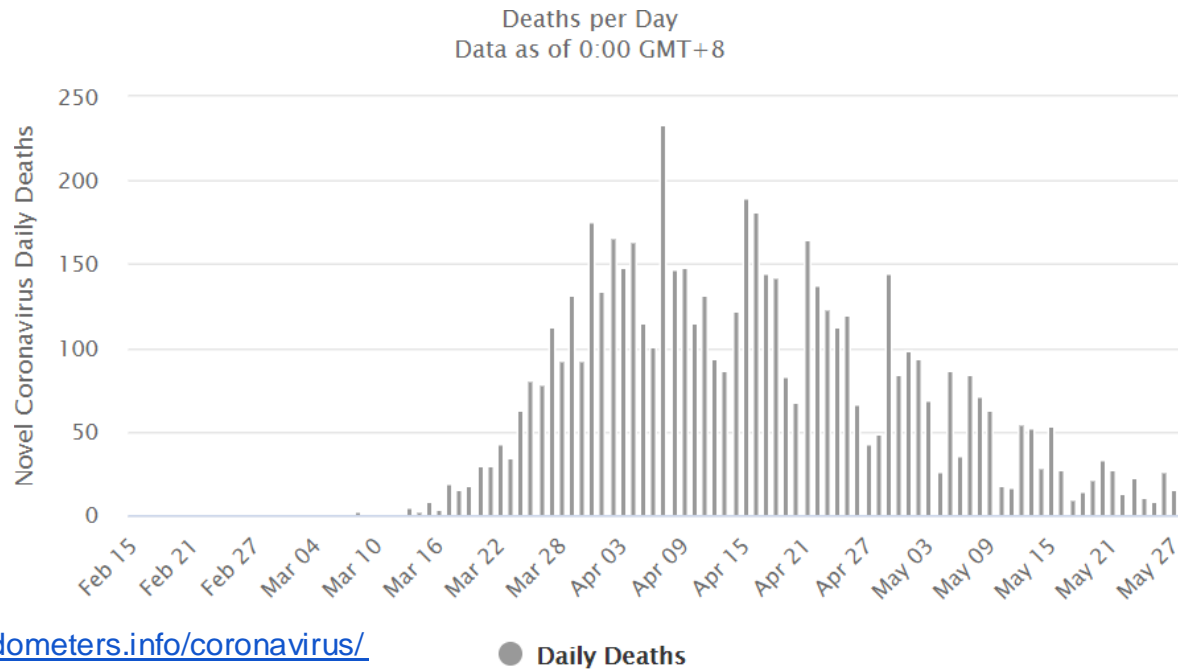


<https://www.worldometers.info/coronavirus/>

● Daily Deaths

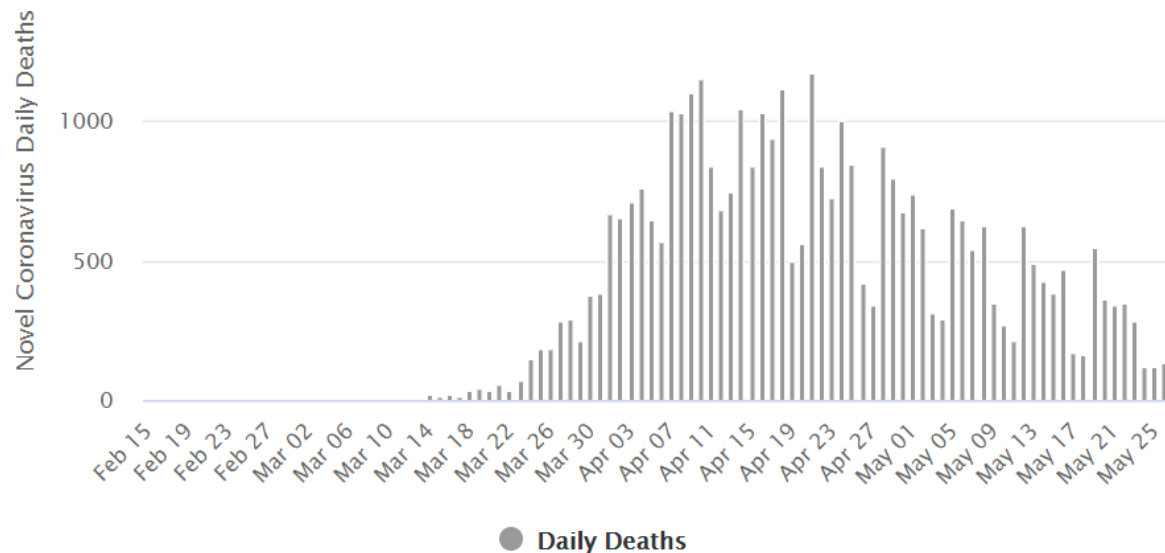
Netherlands

- 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 week¹³.

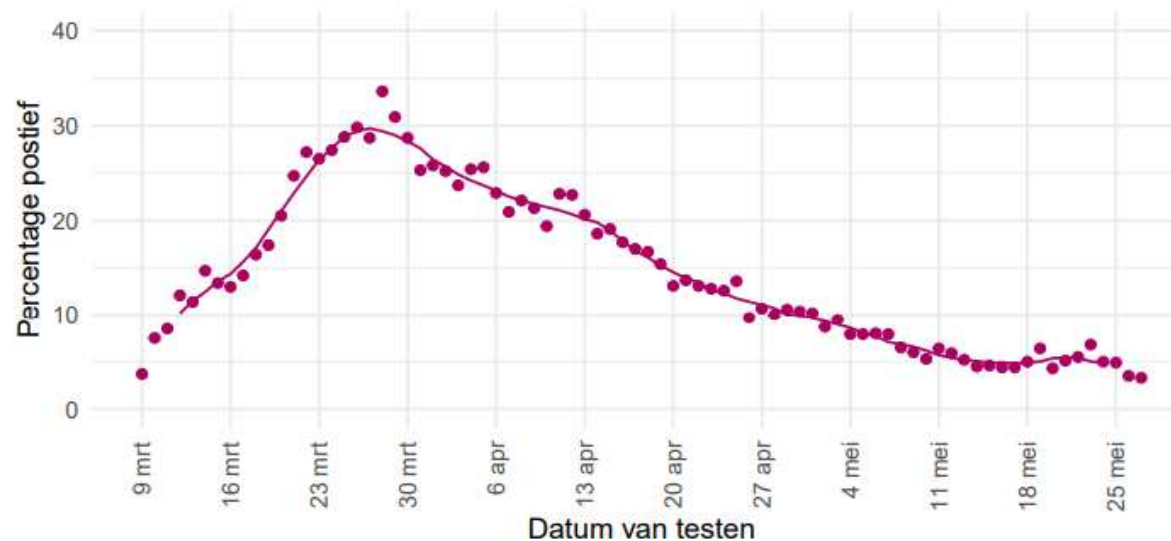
Datum van - tot	Labs	Geteste pers.	Pos. uitslag	% Pos.
2020-03-09 - 2020-03-15	30	17080	1529	9.0
2020-03-16 - 2020-03-22	35	21338	3953	18.5
2020-03-23 - 2020-03-29	37	24745	7232	29.2
2020-03-30 - 2020-04-05	40	29098	7424	25.5
2020-04-06 - 2020-04-12	41	38960	8391	21.5
2020-04-13 - 2020-04-19	42	40102	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

¹³Labs = 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 16th → resurge until peak on March 28th

Figuur 18. Percentage van personen dat getest is op SARS-CoV-2, met een positieve testuitslag, gemeld door de virologische laboratoria^{14,15}.



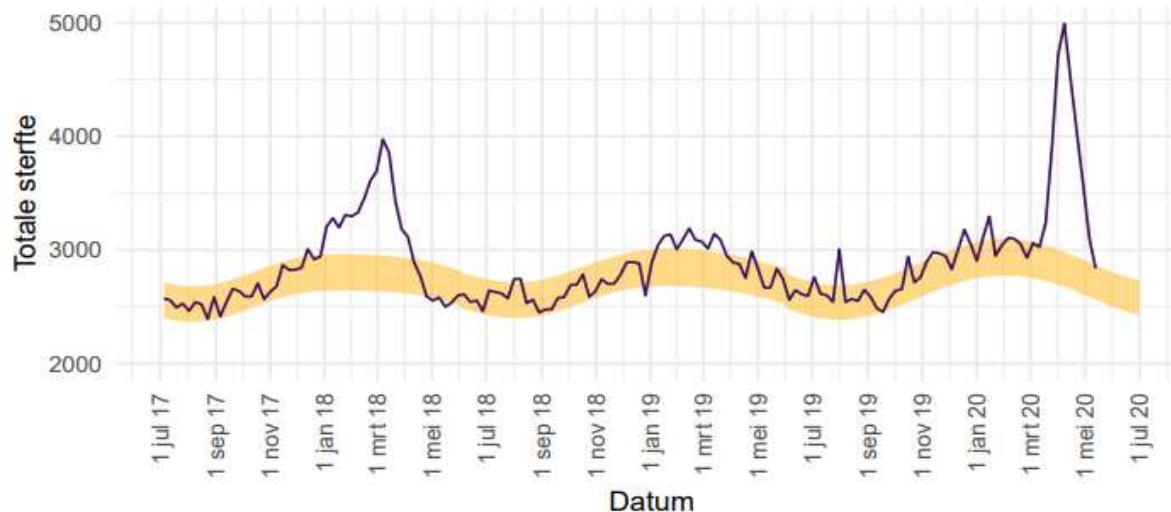
Deze gegevens worden iedere maandag t/m vrijdag bijgewerkt, behalve op feestdagen.

¹⁴Gegevens van de huidige week zijn nog incompleet.

¹⁵De 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

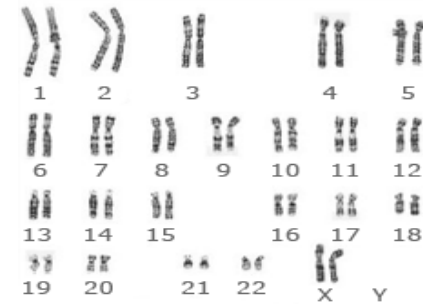


Dogma's and how to avoid them

Dogmas

- During the Bubonic plague (14th 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

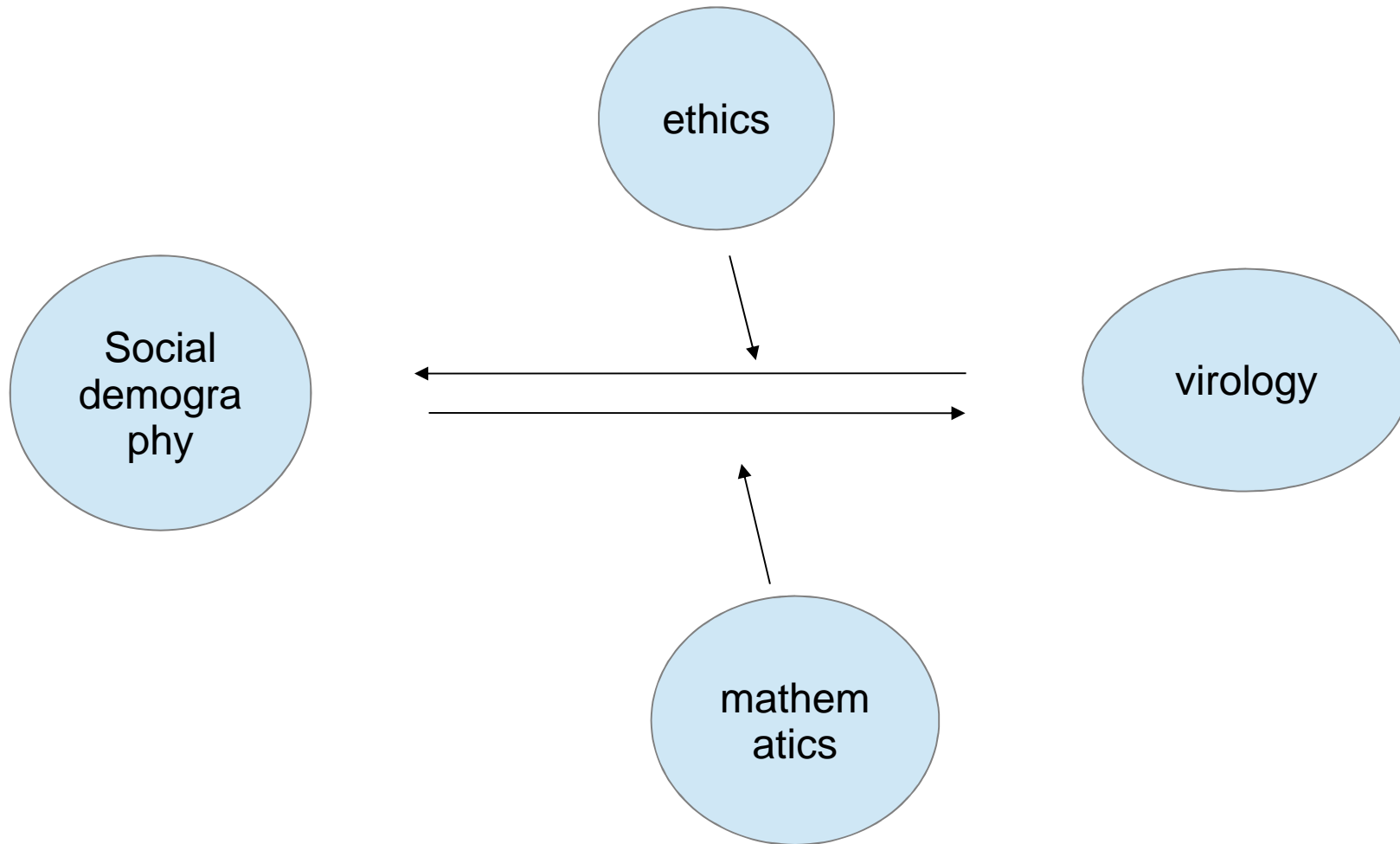
Uses
tools to
solve
problems

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