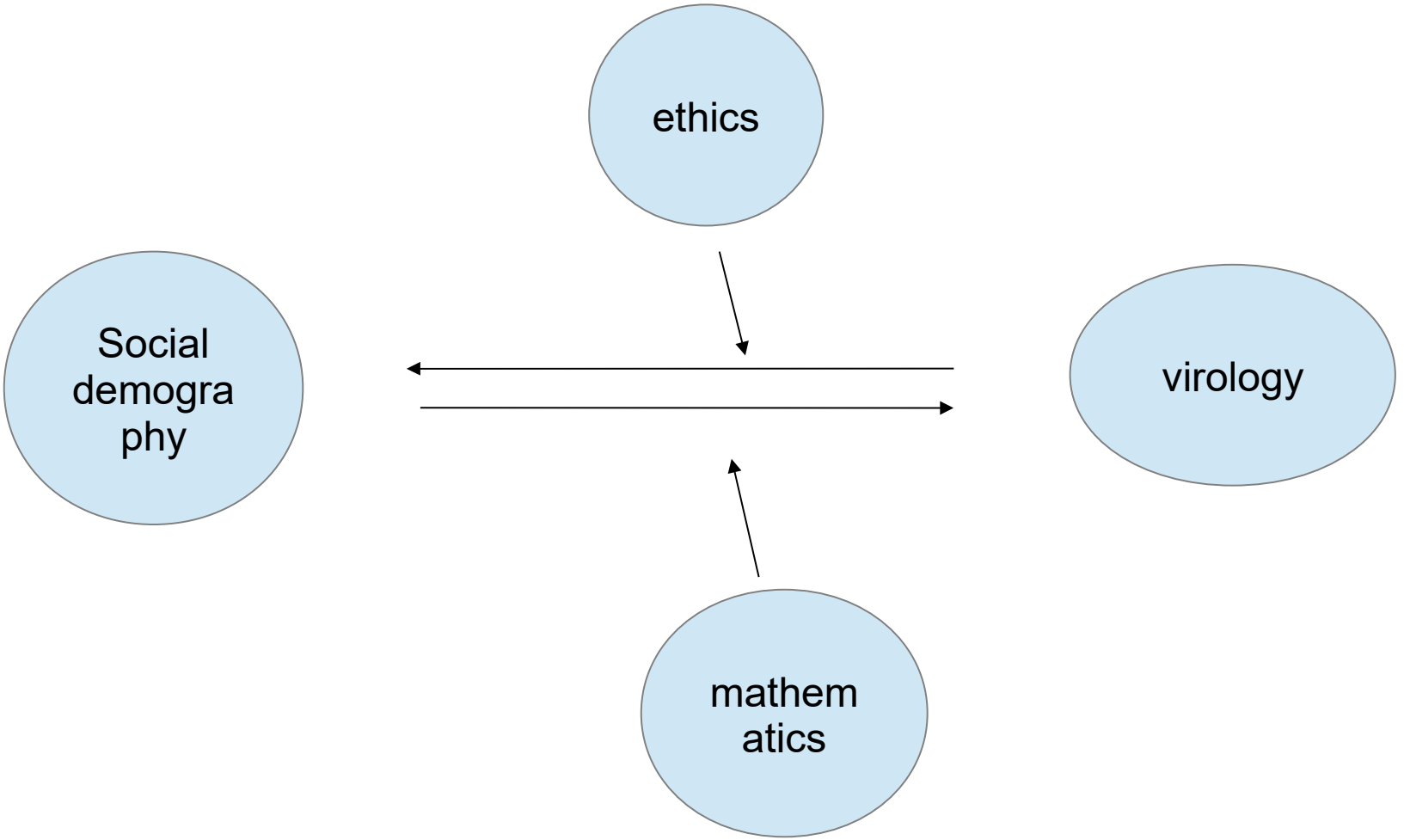
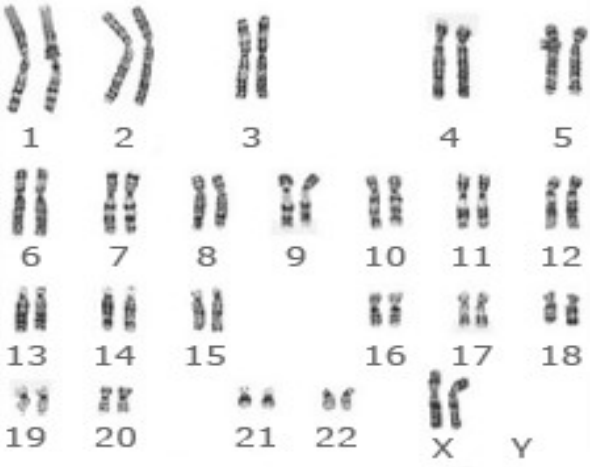
Cross refferencing



Dogmas

- Quote 1 *“Geleerden in die tijd dat de ziekte door de lucht verspreid zou worden. “*

- Quote 2 *“Door het dragen van het masker zouden de kwade luchten worden tegengehouden.”*



Karyotype of a woman.

https://wikikids.nl/Zwarte_Dood

Character of scientists

- Afraid to be wrong
- Know-it-all
- Territorial
- Rightous (overly ethic
- Tunnel vision

Viruses in airways

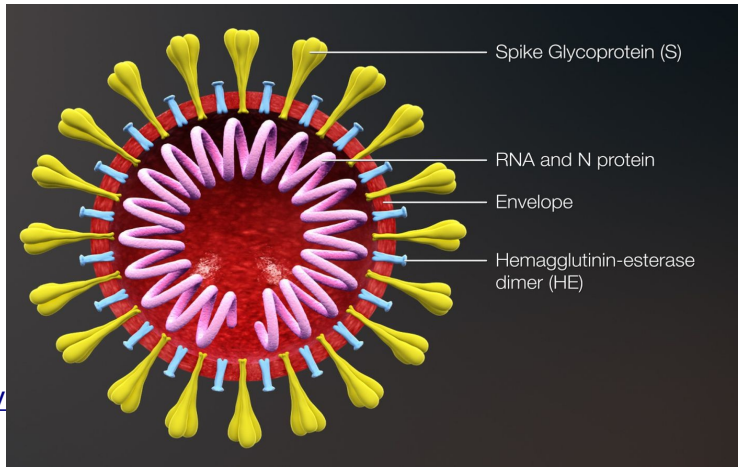
Virus that cause airways infections

- Influenza → the Flu
- Rhino → the Cold
- Corona → Flu & cold like symptoms
- Asymptomatic shedding of virus by breathing
- All of these are 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/coronav



Case Fatality Rate

- Gangelt → 0.36%

https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf/%24FILE/Streeck_et_al_

'https://www.youtube.com/watch?v=vrL9QKGQrWk

- CDC → 0.26%

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-9M8J8bm

- Chance per capita is lower
  - Not full infection spread
  - Based on cases, no innate-immune into account
  - With COVID19 or from COVID19

https://www.youtube.com/watch?v=adj8MCsZKlg&feature=youtu.be&fbclid=IwAR2RSC311hTVw2fRiHFaqGh_su69B1a-X_gRMshB7CqpB3t5qQeVnDrca0Y

- Chance for a healthy 40, <0,0026%

Knowledge feb 2020

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

  taste

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

Models old vs New

Calculation of 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."

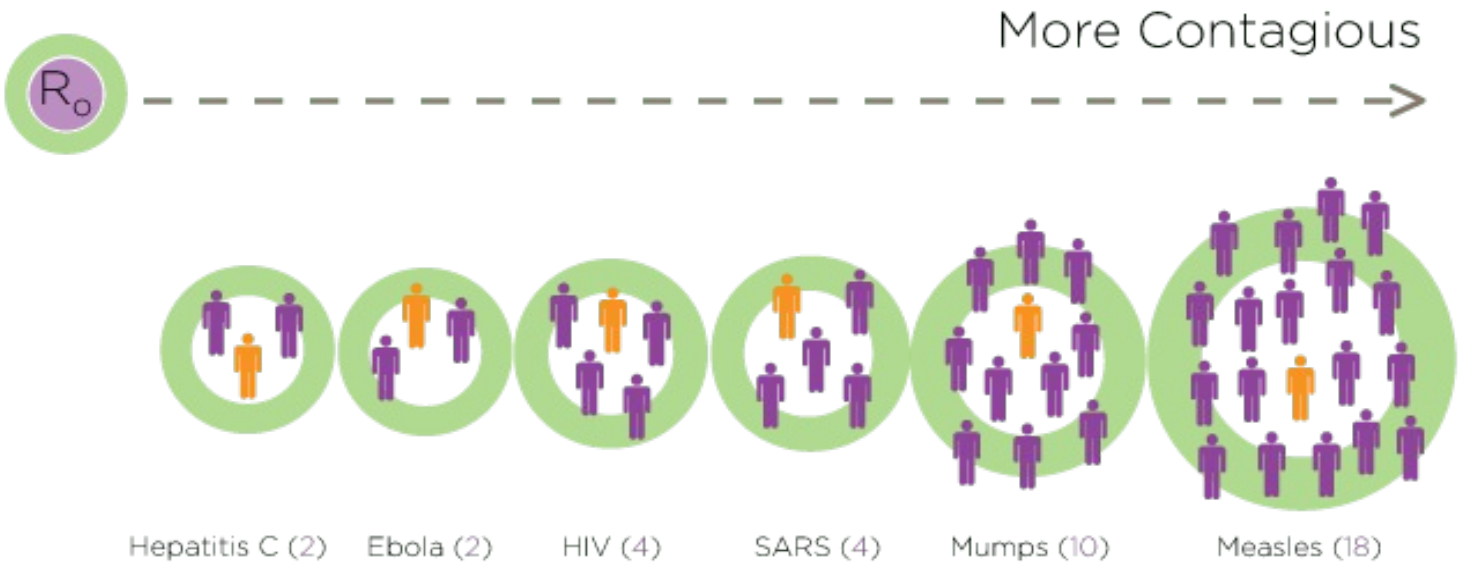
We can use the fact that $\mathcal{R}_0$ is a dimensionless number to help us in calculating it.

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

https://web.stanford.edu/~jhj1/teachingdocs/Jones-on-R0.pdf

Calculation R0

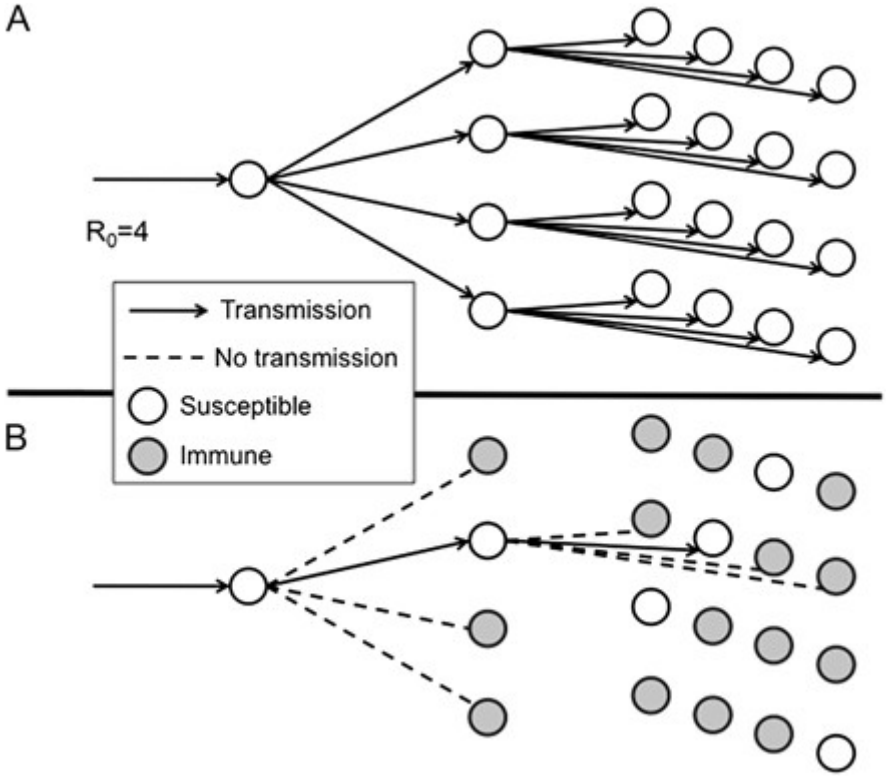
- no one has been vaccinated
- no one has had the disease before
- there's no way to control the spread of the disease



Herd immunity

Directly related to (R0)

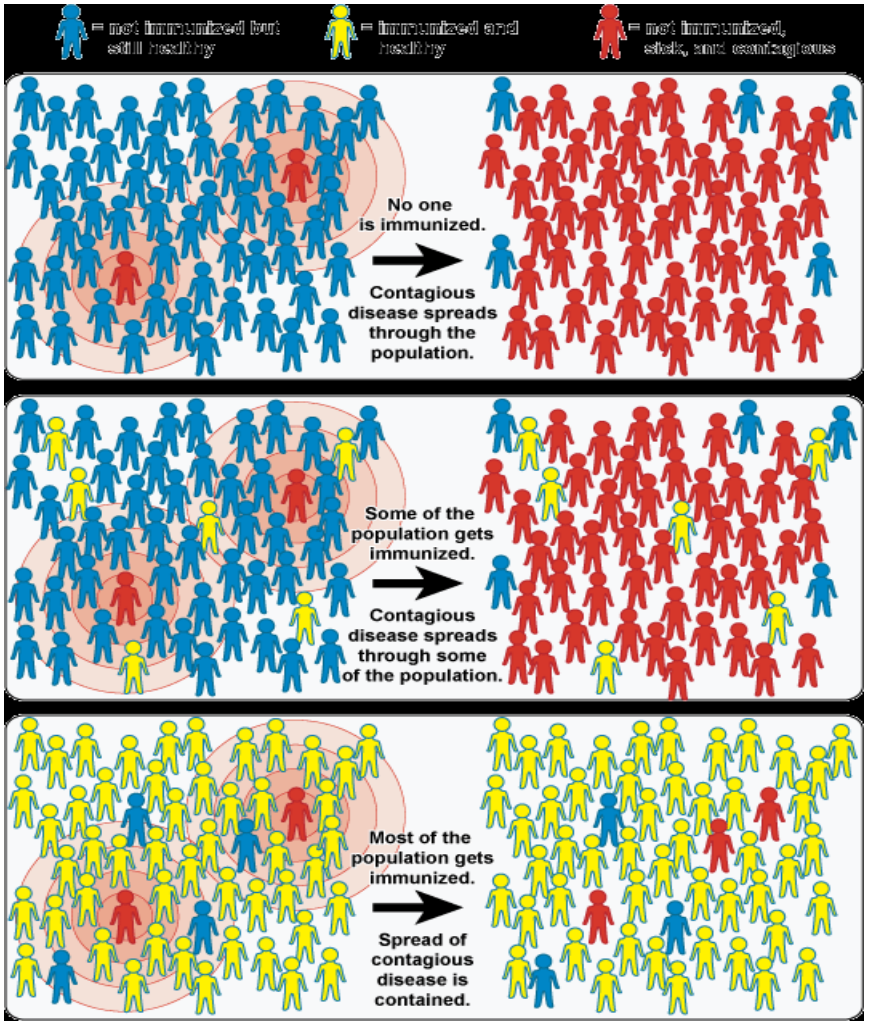
- Previous immunity
- Spacial factors
- Social interaction



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

Vaccines

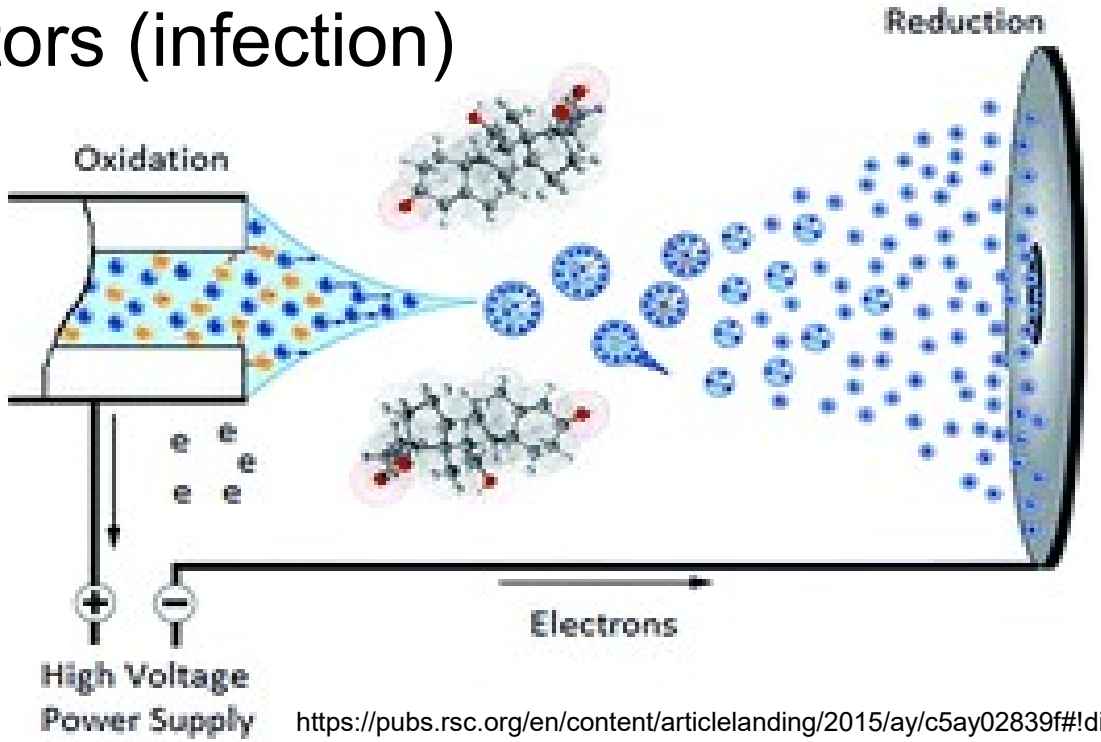
- Efficacy
- Effectiveness
- R0
- CFR
- Protection duration
- Mutation rate



https://thoughtscapism.com/2015/04/20/the-simple-math-of-herd-immunity/

The “New” model

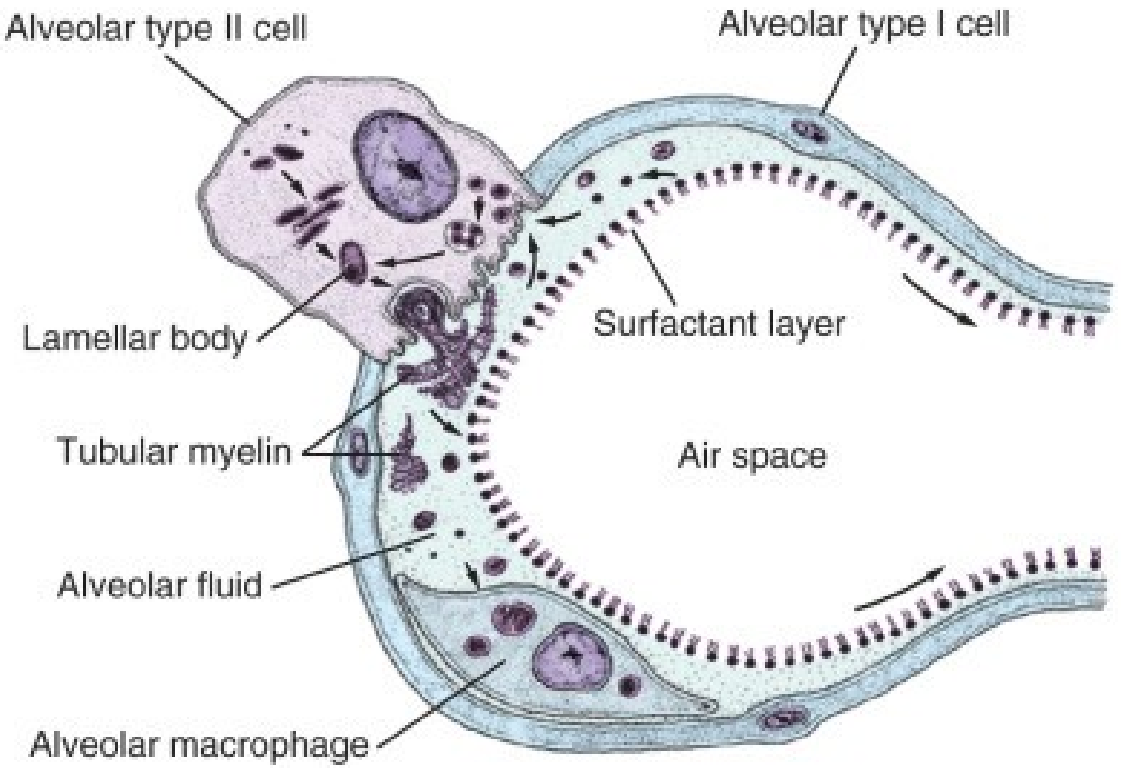
- Based on multiple factors
  - Atmospheric parameters
  - Compartment factors
  - Social behavior
  - Biological factors (infection)



https://pubs.rsc.org/en/content/articlelanding/2015/ay/c5ay02839f#!divAbstract

Airborne (aerosols)

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

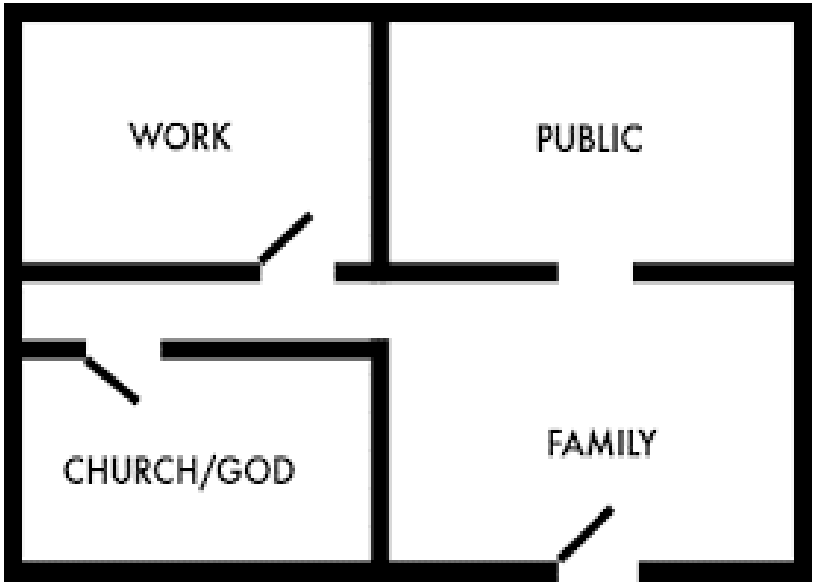


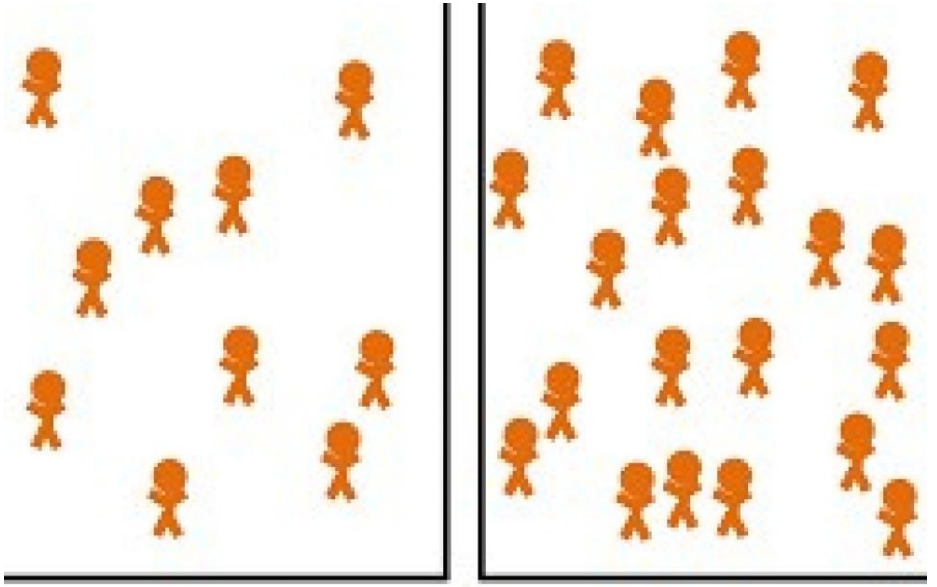
https://www.maurice.nl/2020/05/24/zo-werkt-airborne-besmetting-door-rebecca/

http://flipper.diff.org/app/items/info/3790

Compartments factors

- Size of compartment
- Density
- Open compartments
- Duration





https://www.maurice.nl/

Social behavior

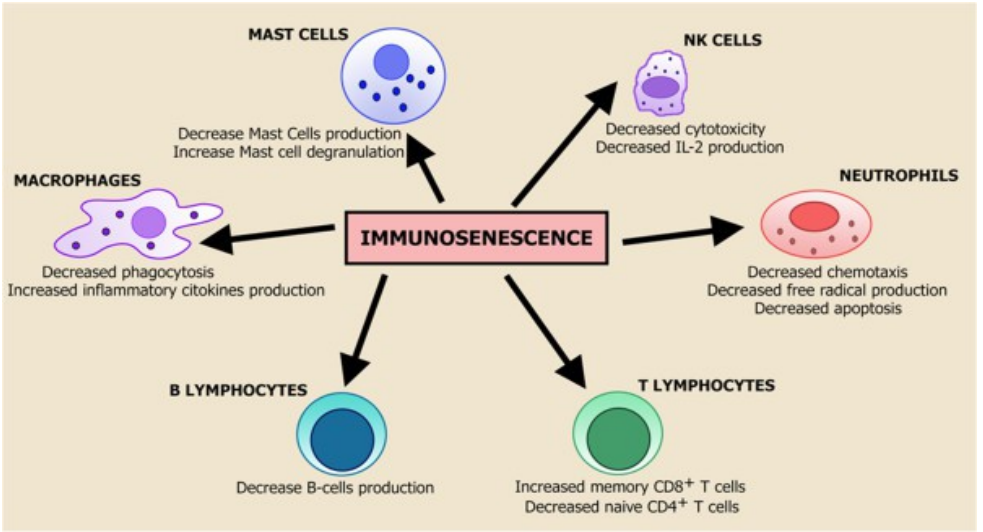
- Personal space
- Indoors vs outdoors
- Large houshold

vs small households

- Community activities (sports, singing etc)

Infection factors

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



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

https://www.researchgate.net/figure/Immunosenescence-This-phenomenon-has-been-describe

immunology-serology

Immunology

- Innate response → non specific
- Acquired respons → 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

https://www.healio.com/hematology-oncology/learn-immuno-oncology/the-immune-system/the-inna

Serologic Research

- Time stamp → date
- Representative sample size
- False positives (innate immune, or aspecific)
- False negatives (Sensitivity)

https://www.nvmm.nl/media/3519/20200519_status-en-resultaten-validatie-elisa-en-auto-ar

Studies antibody

- Gangelt 14%
  https://www.ukbonn.de/C12582D3002FD21D/vwLookupDownloads/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf/%24FILE/Streeck_et_al_I
- Diamond Princess 19%
  https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180
- New York 13-21%
  https://www.cnbc.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

Sanquin vs innate immunity

- Results
  - Date
  - Size
  - Selection
- Claims
  - Herd immunity not an option?

- Uncertainties
  - Samples (no sick)
  - Period
  - Sensitivity
  - Specificity

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

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

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

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

Sickness-treatment

Different groups/treatments

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

https://www.news-medical.net/news/20200416/Research-shows-speed-of-asymp
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 ←

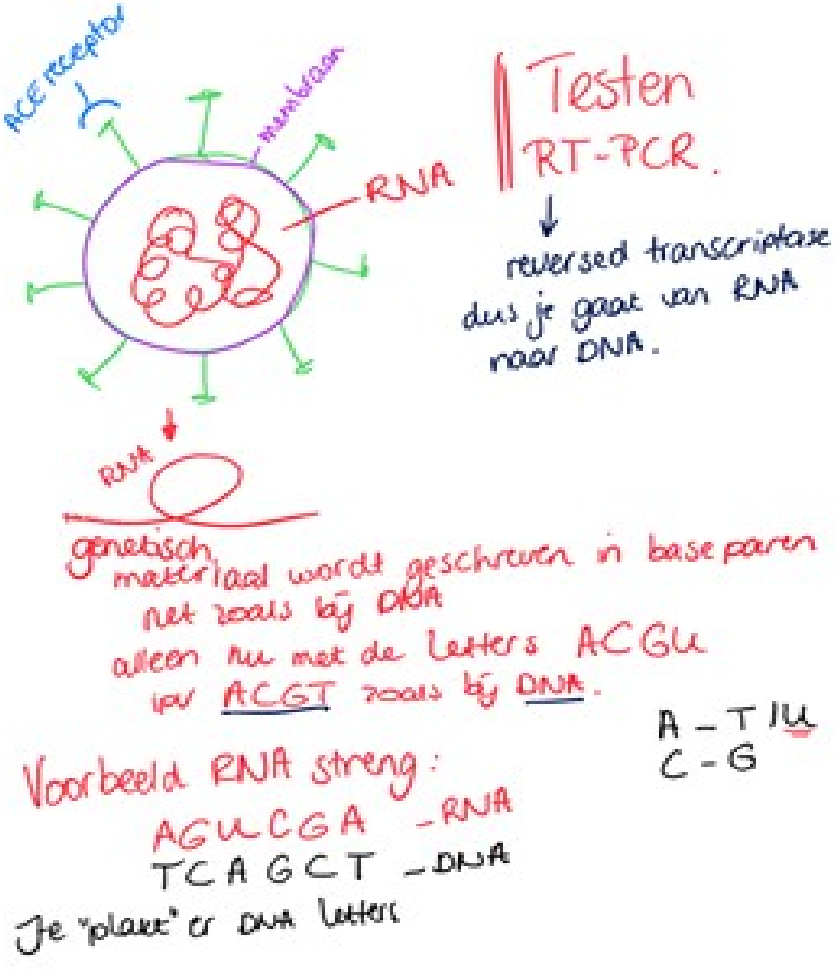
•The Lancet

- No Zinc
- No supplements
- Late stage treatment
- Not a study
- 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

Zelenko Protocol

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



https://internetprotocol.co/hype-news/2020/04/14/a-detailed-coronavirus-treatment-dr-zelenko/

Complications

- 2 groups

- CardioVascular Diseases
  - Blood cloths → Aspirine (bloodthinner)

https://www.youtube.com/watch?v=y6h8TIxeg1g&fbclid=IwAR0Wxa_oKhAX5jW_2Y03WKgdVCN28G4YepTYTtVxpr62Zuh2sdpBNTaIOr0

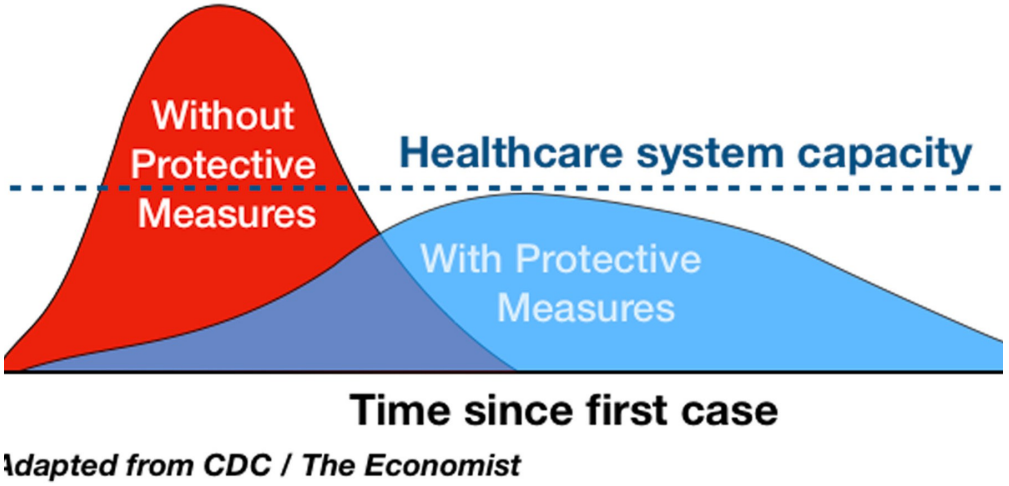
- Obese/Diabetic disease
  - Citokines storm → immuno suppresor

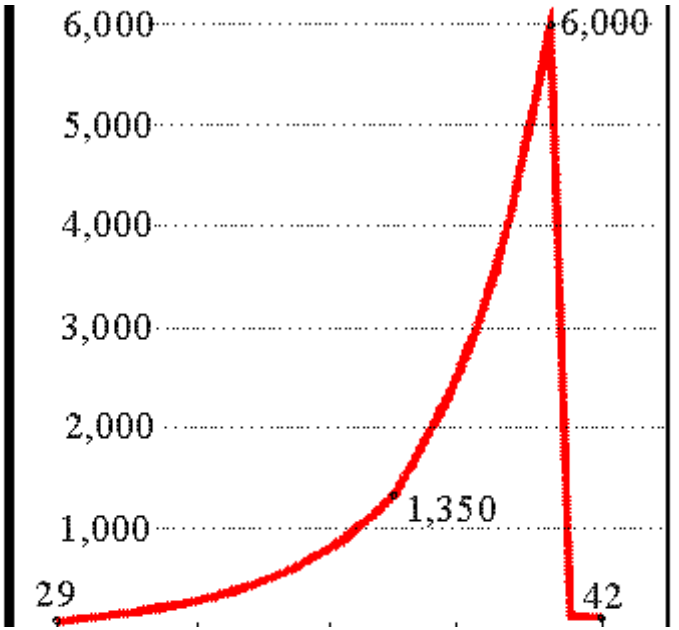
https://l.facebook.com/l.php?u=https%3A%2F%2Fcdn.fbsbx.com%2Fv%2Ft59.2708-21%2F99013

Strategy

Mitigation vs Containment

- Containment
  - Crash the curve
- Mitigation
  - Flatten the curve
- 2 groups of measures
  - The ones taken
  - The ones not taken

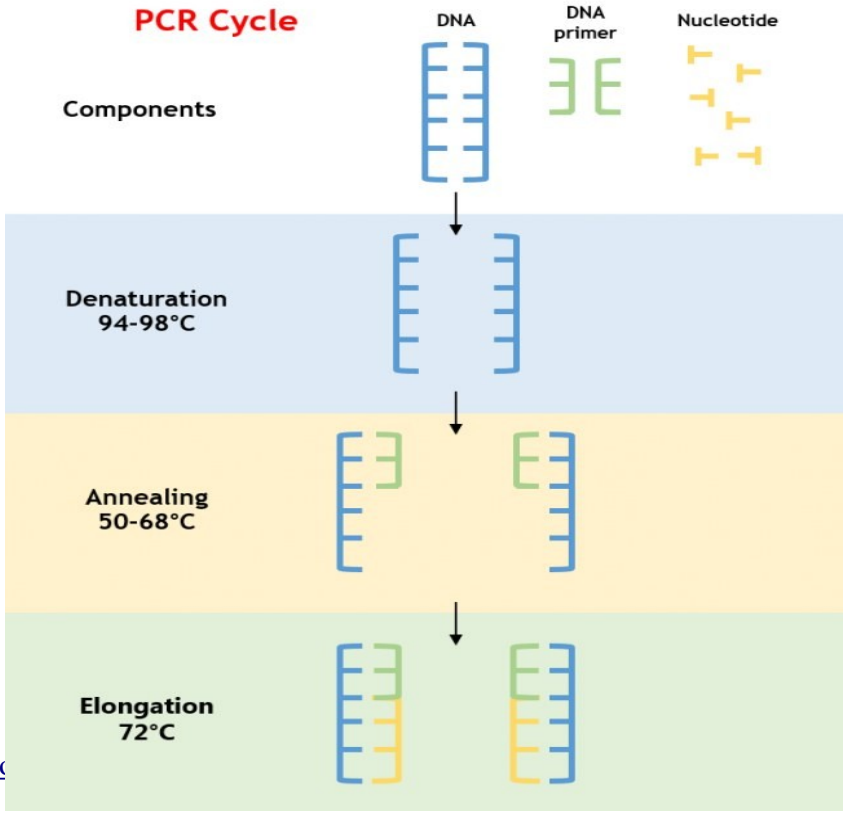




Problems with PCR testing

- PCR picks up remnant of 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&c
%20Infectivity%20Position%20Statement%20(final)%2023-5-

https://www.youtube.com/watch?v=y6h8TIxeg1g&fbclid=IwAR0Wxa_oKhAX5jW_2Y03WKgdVCN28G4YepTYTtVxpr62Zuh2sdpBNTaIOr0

Current status

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=IwA

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&

https://nypost.com/2020/05/26/nobel-prize-winner-coronavirus-lockdowns-saved-no-lives/?utm_source=facebook_sitebuttons&utm_medium=site+buttons&utm_campaign=s

- Social distancing is not proven to be effective (0 articles)

- Social distancing is associated with Mental illness and Crowd control

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

Mitigation

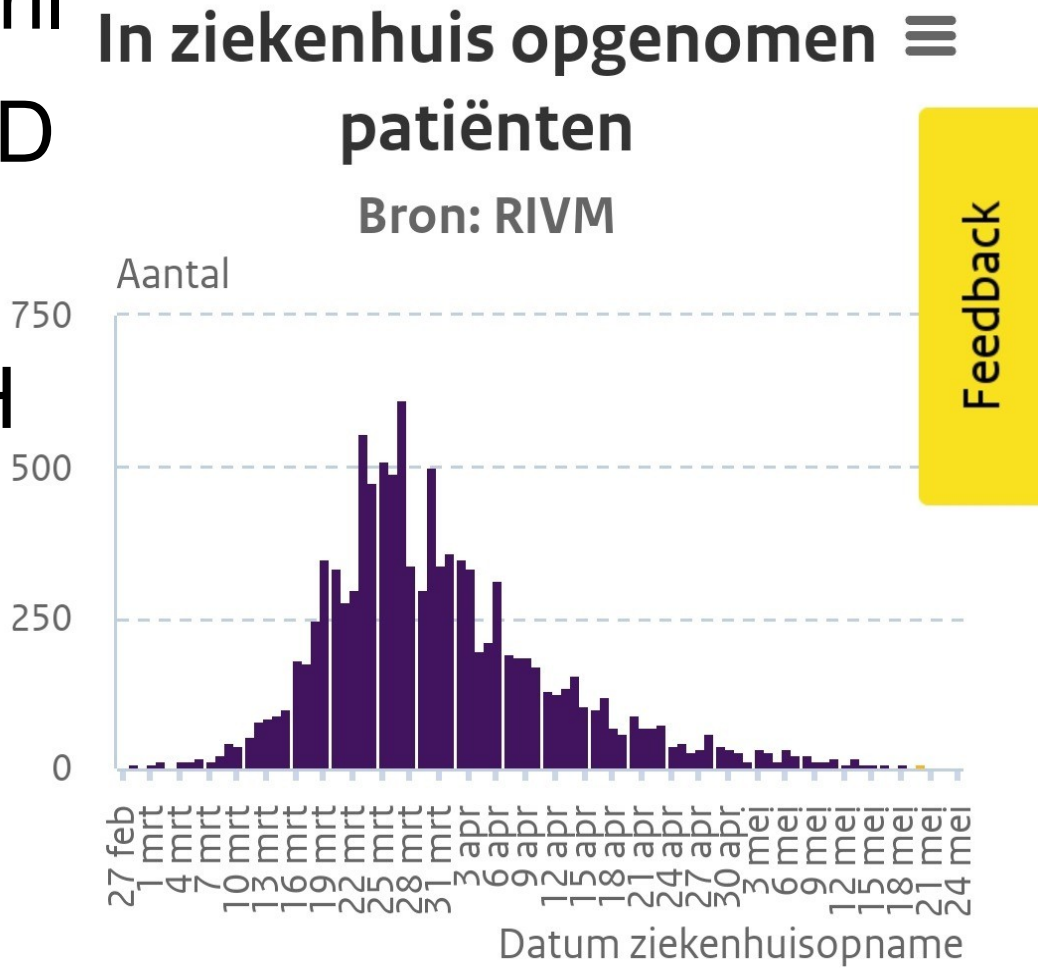
- Decrease travel (stop flying!)
- Profylaxe (vitamin D & C & Zinc)
- Testing and tracing, isolate
- Early treatment
- Isolate the risc groups
- Prepare the health and care facilities

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

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

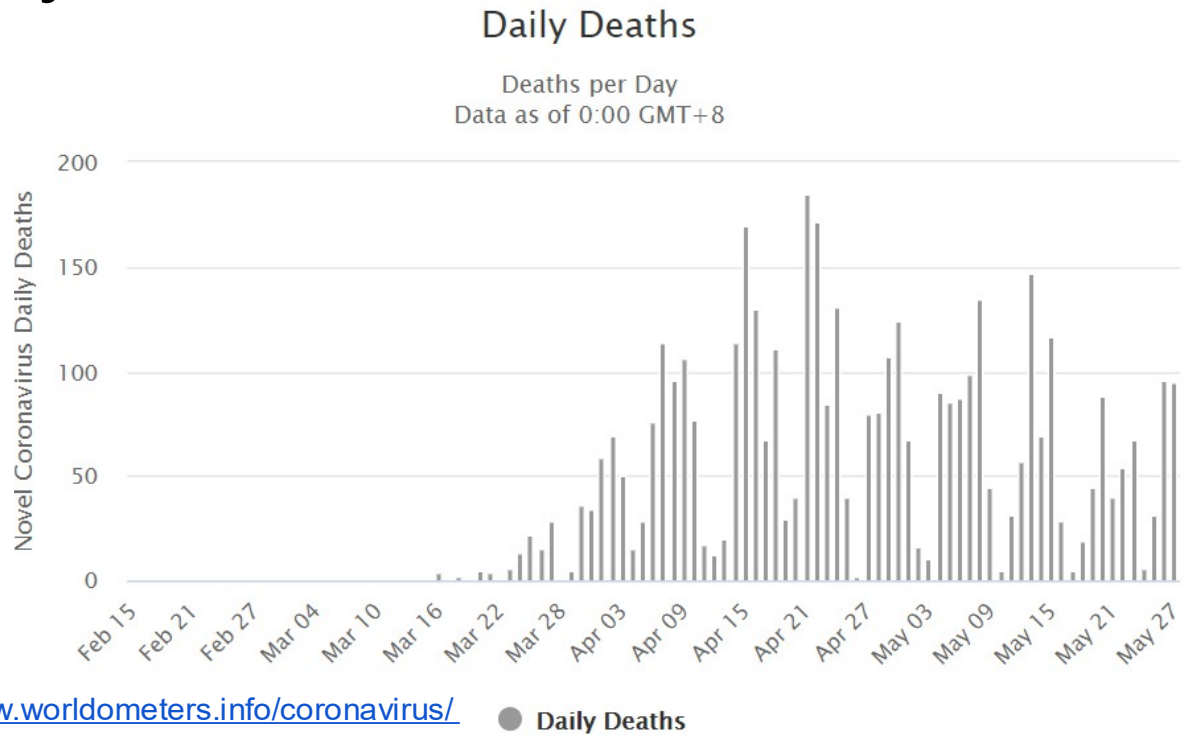
Graphs explained

- 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



Sweden

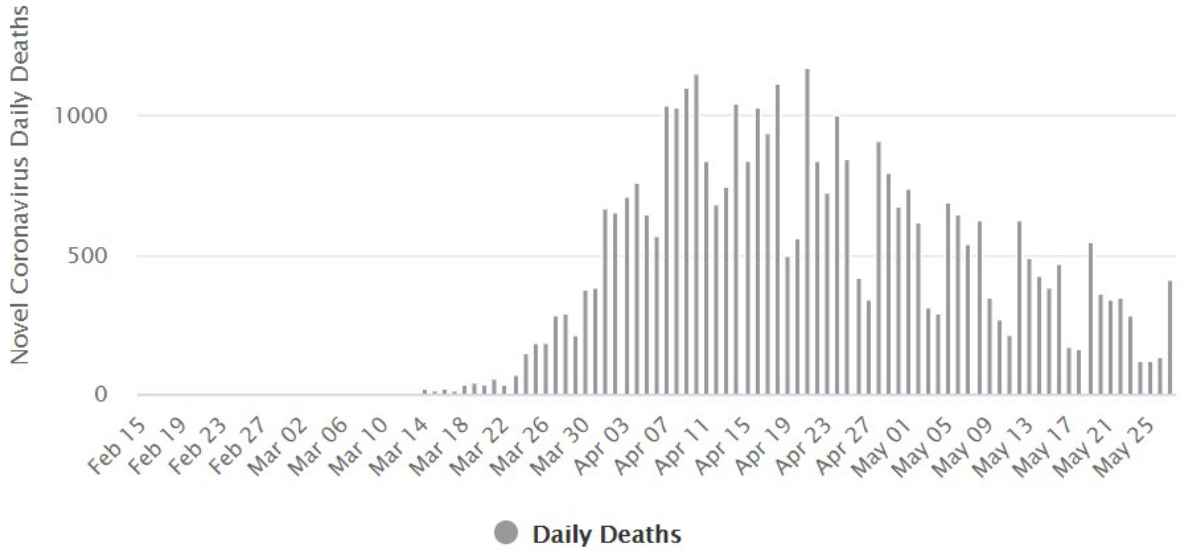
- Start 16 march, Peak 21 april, Crash ~ 1 August
- Measures asked, not forced
- Steady state or decline



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

UK

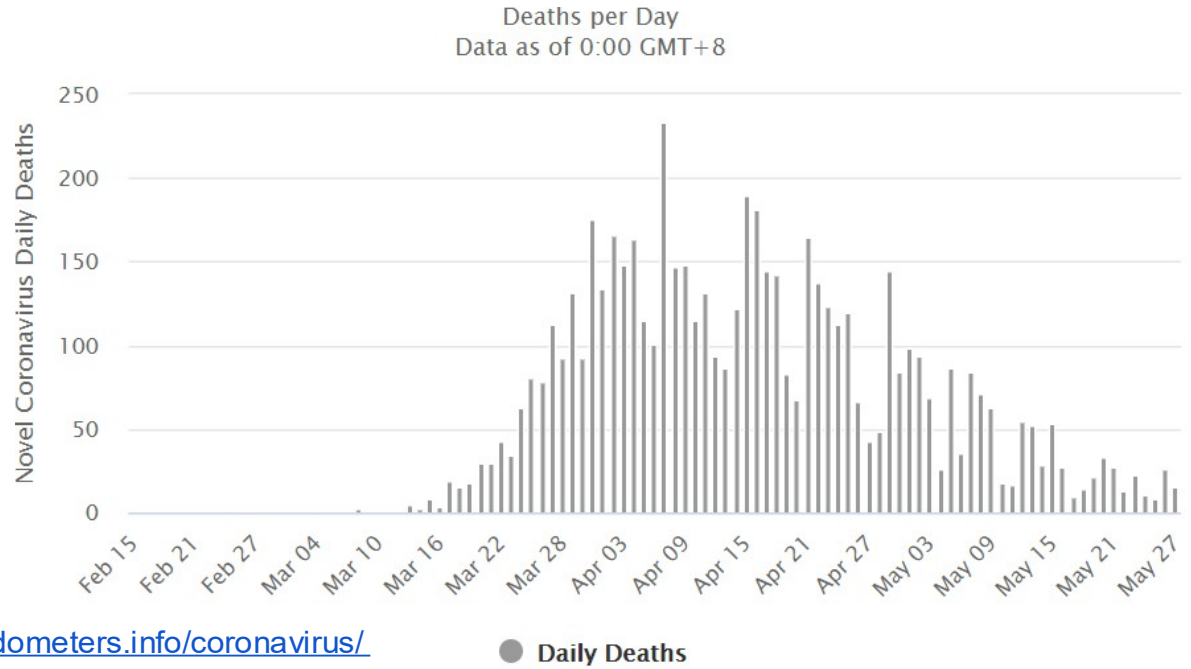
- Start 16 march, Peak 10 april, Crash ~ half june
- Lockdown was after the peak of infections
- The peak of infections is the same date as NL
- Shape is similar to Sweden



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

Netherlands

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



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

Lockdown and surge

- lockdown has caused the surge

Tabel 6. Virologische dagstaat. Meldingen t/m 24 mei zijn samengevoegd per week[13].

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

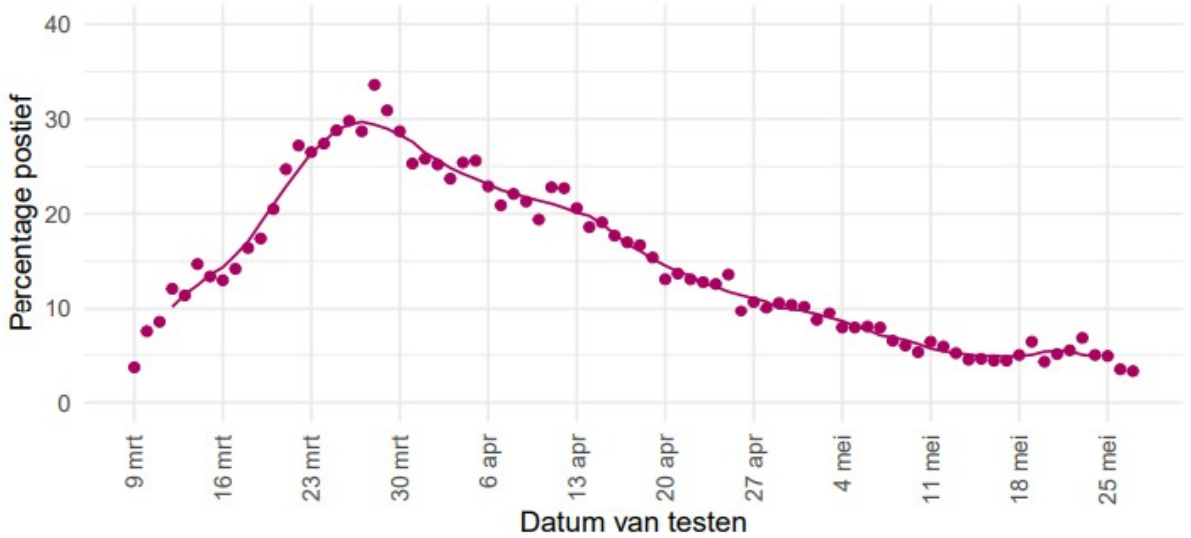
[13]Labs = Aantal rapporterende laboratoria, Geteste pers. = Aantal geteste personen, Pos. uitslag = Aantal personen met een positieve laboratoriumuitslag, Percentage pos. = Percentage positieve uitslagen.

https://www.rivm.nl/documenten/epidemiologische-situatie-covid-19-in-nederland-28-mei-2020

Curvature shows surge

- 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].



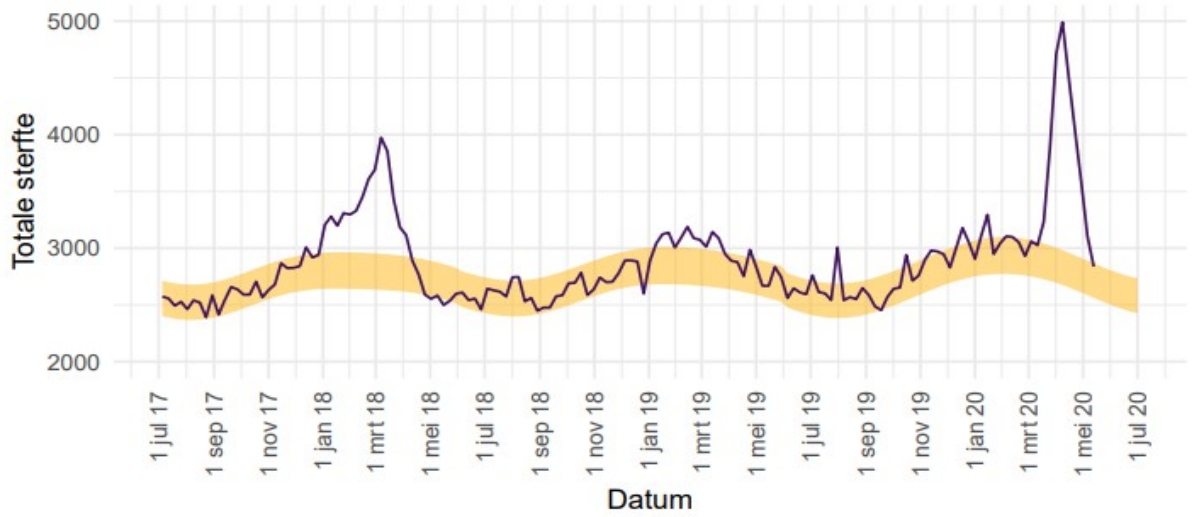
Deze gegevens worden iedere maandag t/m vrijdag bijgewerkt, behalve op feestdagen.

[14]Gegevens van de huidige week zijn nog incompleet.
[15]De bolletjes geven het percentage per dag aan; de lijn een 7-daags lopend gemiddelde per dag.

https://www.rivm.nl/documenten/epidemiologische-situatie-covid-19-in-nederland-28-mei-2020

Area under the curve

- 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 Sterftecijfers en CBS. Zie EuroMOMO voor een Europees overzicht.

- Lockdown → surge of infections & surge IC's

https://www.rivm.nl/documenten/epidemiologische-situatie-covid-19-in-nederland-28-mei-2020

summary

- Sweden flattened → mitigation
- UK & NL did not → no mitigation & no 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 caused to overwhelm the hospitals

https://www.spectator.co.uk/article/norway-health-chief-lockdown-was-not-needed-to-tame-covid?fbclid=IwAR1HYCMI4AHFcgveilVTAdlapY072QocwV1IrSweR0pWZ6GeIg6qxrSRFjo

Exit strategy

- Mitigation → chance of success : large
  - Sweden as example
  - Limited measures

- Containment → chance of success : small
  - Surrounding countries
  - Testing volume challenge
  - Collateral damage

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