

Best Evidence Topic Report 15

Titel:

Dient men groepen te beperken tot 5 personen om het risico op COVID-19 infectie te verlagen?

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Antwoord op klinische vraag:

Aangezien verspreiding van het coronavirus vooral gezien werd na nauw contact met besmette personen kan gesteld worden dat het individueel risico voornamelijk daalt door afstand te bewaren en met zo weinig mogelijk mensen in contact te komen. Het risico op besmetting in groep moet tegengegaan worden door voldoende afstand te bewaren zodat druppel overdracht en overdracht via oppervlakken niet kan plaatsvinden. Wetenschappelijk bewijs over het verlagen van het individueel risico op besmetting door het verkleinen van groepen werd niet gevonden.

In het verleden heeft men gezien dat influenza verspreiding vertraagd kan worden door groepen te verkleinen. Dit is wat men met de huidige maatregelen ook probeert te bereiken voor de verspreiding van het coronavirus, het zogenaamde 'flatten the curve'. Hoe meer social distancing, dus hoe minder mensen bewegen, hoe trager het coronavirus zal verspreiden.

Disclaimer:

Deze rapporten zijn ontwikkeld volgens de methode van de Best Evidence Topics, kortweg bestBETs. Een bestBET beoogt een antwoord te geven op een specifieke klinische vraag, geformuleerd op basis van het op dit ogenblik best beschikbare bewijs. Omwille van de beperkte beschikbaarheid van wetenschappelijk bewijs voor COVID-19 topics, worden ook studies van lagere kwaliteit gebruikt. BestBETs bevatten geen aanbevelingen. Studenten 3e Master geneeskunde van de KU Leuven werkten deze topics uit onder begeleiding van twee docenten, waarna ze volgens een vast stramien een eindrapport opstellen. Voor de validatie van deze rapporten, konden we beroep doen op de expertise van CEBAM, die de rapporten rigoreus toetste aan vooropgestelde kwaliteitscriteria.

Best Evidence Topic Report

Title	Transmissie en preventie van COVID-19: groepen beperken tot 5 personen verlaagt het risico op infectie fors meer dan in groepen van 10 personen. <i>Opmerking: originele onderzoeksvraag werd uitgebreid naar algemene informatie over transmissie en preventie om zo te trachten een antwoord te formuleren.</i>
Report by	Lone Philipsen, 3 ^e master geneeskunde Robin Packet, 3 ^e master geneeskunde
Search checked by	Prof. Dr. Birgitte Schoenmakers
Clinical scenario	COVID-19
Answerable question (PICO/PIRT/PEO/...)	P: general population I: Social interactions with a maximum of 5 people C: Social interactions with a maximum of 10 people O: Risk of covid-19 infection is lower in groups of 5 people compared to groups of 10 people
Search terms	“Covid-19” “Covid-19 AND social isolation” “Covid-19 social isolation” “Covid-19 AND prevention and control” “Covid-19 AND social distancing” “Coronavirus AND social distancing” “Social distancing” “Covid-19 prevention” “Covid-19 AND prevention” “Covid-19 AND transmission” “Covid-19 AND group transmission” “Influenza social distancing”
Search date	18-03-2020
Search outcome (number of hits)	1.107
Relevant papers (number of final inclusions)	18
Flow chart	<pre> graph TD A[Pubmed 481] --- B[Eerste selectie 30 artikels] C[Embase 499] --- B D[Web of science 52] --- B E[NJEM 21] --- B F[Annals of int med 1] --- B G[Lancet 53] --- B B -- "Tweede selectie op basis van volledige tekst" --> H[Tweede selectie 18 artikels] </pre> <p>Pubmed 481 Embase 499 Web of science 52</p> <p>NJEM 21 Annals of int med 1 Lancet 53</p> <p>↓ Eerste selectie op basis van titel en abstract</p> <p>Eerste selectie 30 artikels</p> <p>↓ Tweede selectie op basis van volledige tekst</p> <p>Tweede selectie 18 artikels</p>

Inclusion and exclusion criteria	<ol style="list-style-type: none"> 1. Taal <ul style="list-style-type: none"> • Inclusie: Engels • Exclusie: andere taal 2. Jaartal <ul style="list-style-type: none"> • Inclusie: 2019-2020 • Exclusie: andere jaartallen 3. Soort artikel <ul style="list-style-type: none"> • Inclusie: systematic reviews, original research, case reports, ... • Exclusie: brieven, opinies, cover letters 4. Titel en abstract <ul style="list-style-type: none"> • Inclusie: artikels waarvan het abstract informatie blijkt te geven over transmissie, preventie, social distancing en/of reproductieve waarde van COVID-19. • Exclusie: artikels waarvan het abstract geen antwoord blijkt te geven op de onderzoeksvraag 5. Volledige tekst <ul style="list-style-type: none"> • Inclusie: artikels waarvan de volledige tekst informatie blijkt te geven over transmissie, preventie, social distancing en/of reproductieve waarde van COVID-19. • Exclusie: artikels waarvan de volledige tekst geen antwoord blijkt te geven op de onderzoeksvraag
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Evidence table

<i>Author, date and country</i>	<i>Study type</i>	<i>Main risks of bias</i>	<i>Patient characteristics</i>	<i>Intervention/index test/exposure</i>	<i>Comparator</i>	<i>Outcome and Key results</i>
Sohrabi, C. et al. 03/03/2020 UK	Narrative literature review	Review based on studies chosen by the writers, no search method included. It's a summary of the current state of knowledge.	90870 confirmed cases, 80304 of which are confined to China	COVID-19	/	Prevention: Avoiding travel to high-risk areas, contact with individuals who are symptomatic and consumption of meat from regions with known covid-19. Transmission: human-to-human during symptomatic and asymptomatic incubation period (estimated 2-10d)
Wang, Y. et al. 5/03/2020 China	Narrative literature review	Review based on studies chosen by the writers, no search method included.	82623 confirmed cases of COVID-19 and 2858 deaths globally	COVID-19	Comparison to its two predecessors (SARS-CoV and MERS-CoV)	Basic reproductive values (R0) of COVID-19 at the early stage were calculated between 2 and 3.5, which was higher than SARS and MERS. Human-to-human transmission through respiratory aspirates, droplets, contacts, feces and aerosol transmission is highly possible. Isolation is thought to be the most effective means of containing COVID-19 based on a model simulation study. Majority of infected individuals with no or mild symptoms can spread the virus to others.
Cheng, V. et al. 05/03/2020 China	Retrospective cohort	Small sample size	1275 patients, of which 42 patients with confirmed SARS-CoV-2	Laboratory diagnosis SARS-CoV-2	/	SARS- CoV-2 revealed in 1 (7.7%) of 13 environmental samples, but not in 8 air samples collected at a distance of 10 cm from patient's chin with or without wearing a surgical mask. Eleven (2.7%) of 413 HCWs caring these confirmed cases were found to have unprotected exposure requiring quarantine for 14 days. None of them was infected and nosocomial transmission of SARS-CoV-2 was not observed.

Zhoa, S. et al. 30/01/2020 China	Statistical analysis	Changes in reporting likely occurred and should be taken into account in the estimation of R_0	/	Modelling of the epidemic curve of 2019-nCoV cases time series, in mainland China from January 10 to January 24, 2020, through the exponential growth. Estimation of R_0 by using the serial intervals (SI) of two other well-known coronavirus diseases, MERS and SARS, as approximations for the true unknown SI with the estimated intrinsic growth rate (γ).	Comparison to MERS and SARS	Estimates of the basic reproduction number, R_0 of 2019-nCoV in the early phase of the outbreak. The mean R_0 of 2019-nCoV ranging from 2.24 (95%CI: 1.96-2.55) to 3.58 (95%CI: 2.89-4.39)
Fong, M. et al. 06/02/2020 China	Systematic review	Review of 4 observational studies and 11 simulation studies, which makes the systematic review lower in quality.	Patients with confirmed influenza.	Influenza	/	Recommendations include voluntary isolation until 5-7 days after illness onset. Contact tracing was found to be effective in combination with isolation, quarantine and prophylactic treatment with antiviral drugs. The evidence base for home quarantine was weak, in general, the intervention is estimated to be effective. The overall transmission of influenza in the community is reduced when schools are closed. There was limited evidence about workplace measures or closures and avoiding crowding.
Pung, R. et al. 16/03/2020 Singapore	Retrospective study	Recall bias, small sample size	36 cases of COVID-19 were linked to the first three clusters of local transmission in Singapore, 425 close contacts were quarantined	COVID-19	/	There were three clusters showing local transmission of COVID-19 in Singapore. In one cluster all five patients visited the same church, they were all asymptomatic at that time. Direct or prolonged close contact was reported among affected individuals, although indirect transmission (eg, via fomites and shared food) could not be excluded. The mean incubation period was 4 days. Enhanced surveillance and contact tracing is essential to minimise the risk of widespread transmission in the community.
Kucharski, A. et al. 11/03/2020 China	Mathematical modeling study	Use of plausible biological parameters of SARS-CoV-2 based on current evidence, assumed latent period is equal to incubation period	/	Use of a stochastic transmission dynamic model to multiple publicly available datasets on cases in Wuhan	/	Estimates of early dynamics of transmission in Wuhan. The median daily reproduction number declined from 2,35 to 1,05 after travel restrictions were introduced. Once there are at least four independently introduced cases, there is more than 50% chance the infection will establish within that population
Chan, J. et al. 24/01/2020 China	Retrospective study	Small sample size	5 patients in a family cluster who presented with unexplained pneumonia after	COVID-19	/	The findings suggested that person-to-person transmission and intercity spread of 2019-nCoV by air travel are possible, supporting reports of infected Chinese travelers from

			returning to Shenzhen, after a visit to Wuhan. Plus an additional family member who didn't travel to Wuhan.			Wuhan being detected in other geographical regions.
Li, Q. et al. 29/01/2020 China	Retrospective study	Small sample size, only one region.	425 patients with confirmed novel coronavirus infected pneumonia (NCIP)	Laboratory confirmed NCIP	/	Evidence for human-to-human transmission among close contacts since the middle of December 2019. The doubling time was 7,4 days. The estimated R0 was 2,2. The mean incubation period was 5,5 days.
Imai, N. et al, 2020 Groot-Brittannië	Observational study	Small sample size, only patients from Wuhan.	40 patients with COVID-19	Mathematical prediction and possible influence of social distancing.	Comparison with SARS and MERS	Reports point to mildly symptomatic but infectious cases of 2019-nCoV, which were not a feature of SARS. Prompt detection and isolation of such cases will be extremely challenging, given the larger number of other diseases (e.g. influenza) which can cause such non-specific respiratory symptoms. The number of secondary cases caused by a case of 2019-nCoV is highly variable – with many cases causing no secondary infections, and a few causing many. Estimated case infected (R0) 2.6 (uncertainty range: 1.5-3.5) other people up to 18th January 2020. (R>1 to be self-sustainable)/ This implies that control measures need to block well over 60% of transmission to be effective in controlling the outbreak.
Remuzzi, A. et al. 2020 Italië	Observational study	Wuhan and Lombardia are 2 different regions with resp 19 million and 9 million inhabitants. More extreme measures were taken in Wuhan.	Patients who tested positive for SARS-cov-2.	Mathematical prediction and possible influence of social distancing.	Comparison between number of patients in Wuhan and Lombardia	Individuals infected with SARS-CoV-2 appear to shed the virus from their respiratory tract during the prodromal period, and viral shedding appears to occur in individuals who have minor clinical manifestations, contributing to the extensive community transmission that we are currently witnessing. Predictions about the number of infected people in Lombardia follows the same trend as Wuhan. Because of social isolation a flattening of the curve is expected like there was in Wuhan, this to prevent hospital beds from being totally occupied.
Wilder-Smith 2020 GB	Observational study	Focus on China and the more extreme measures they can take because of a different political environment.	Patients with who tested for SARS-cov-2	Social distancing	Comparison with SARS	The sheer magnitude of the new cases means that not all contacts can possibly be ascertained or monitored adequately. It means that many unidentified contacts are in the community. While SARS was mainly an outbreak that propagated itself within hospitals and confined communities, widespread community transmission is already evident for 2019-nCoV in Hubei Province. China has been preparing to contain future pandemics by applying lessons learnt from SARS ever since

						2003. We have to commend China for their swift and decisive response.
Hoang, V-T. et al 2018 Frankrijk	Narrative review	Different studies were evaluated with different number of people at events.	Infections, mostly viral at big events like the Olympics in London, festivals, Hadj, etc	Social distancing, vaccination, face mask, disposable handkerchief and hand hygiene.	Social distancing, vaccination, face mask, disposable handkerchief and hand hygiene.	Infectious diseases at MGs are dominated by respiratory tract and gastrointestinal infections. Inter-human transmission of airborne diseases is favored by the temporal and spatial concentration of people. Non-compliance with hygiene rules and inadequate sanitation are responsible for fecal-oral transmission of gastrointestinal infections. Because social distancing and contact avoidance are difficult measures to implement in the context of many MGs, individual preventive measures including vaccination, use of face mask, disposable handkerchief and hand hygiene may be recommended.
Ahmed, F. et al 2018 USA	Systematic review	Some studies based on theoretical models. Influenza.	The inclusion criteria included randomized controlled trials, epidemiological studies, and modeling studies reporting results of social distancing interventions in non-healthcare workplaces. The exclusion criteria included the following: review articles, commentaries, and editorials; studies in animals; studies conducted in health-care, school, or university settings; and studies on workplace closure.	social distancing in non-healthcare settings	Social distancing vs no social distancing	The included epidemiological and modeling studies indicate that social distancing in non-healthcare workplaces reduces the overall as well as the peak number of influenza cases. It also delays the influenza peak. The finding that reduction in influenza cases is more pronounced when workplace social distancing is combined with other nonpharmaceutical or pharmaceutical interventions highlights the importance of using a combination of measures to reduce the transmission of pandemic influenza. The effectiveness of social distancing and vaccination was estimated to decline with higher R_0 values, delayed triggering of workplace social distancing, or lower compliance. The lower effectiveness could be because social distancing may be less likely to reduce the effective reproduction number to below one if R_0 is higher.
Singh, M. et al 2019 USA	Model	Some studies based on theoretical models. Social distancing and vaccination where examined. Influenza.	A nationwide (USA) survey of 2168 respondents on influenza H1N1 in 2009.	social distancing and vaccination	Comparing epidemic scenarios wherein the social distancing and vaccination behaviors are uniform versus non-uniform across different demographic subpopulations.	We infer that a uniform compliance of social distancing and vaccination uptake among different demographic subpopulations underestimates the severity of the epidemic in comparison to differentiated compliance among different demographic subpopulations. This result holds for both urban and rural regions. The outcomes of the epidemic are significantly worse when demographics based behavior adaptation probabilities are used, as compared to the case when no demographic predictors are used to determine behaviors. The size of the epidemic is bigger, and the number of infections on the peak day are larger.

Bults, M. et al 2015 GB	Systematic review	Only articles in English. Influenza.	Studies that focused on the general population and measured actual perceptions or behaviors during the pandemic (publication date of 2009 or later). Data had to be obtained with a quantitative study methodology, and only articles published in the English language were included. Studies were excluded when they targeted a specific group, like health care workers, parents, pregnant women, students, or patients at risk. 70 articles in total.	Hygienic practice and social distancing.	Different perceptions and behavioral responses during 2009 influenza (H1N1) outbreak.	Improved hygienic practice and social distancing were the most often reported preventive behaviors. During the early phase, the intention to improve hygienic practice, seek medical consultation at the onset of flu symptoms, and take antiviral medication was generally high. Furthermore, in Hong Kong most respondents reported that they would comply with quarantine measures and, if infected, would wear a facemask when going out. During the pandemic peak and post-pandemic phases, the intention to take preventive measures remained relatively high. This review showed that public perceptions and behaviors are not stable and can evolve over a short period of time. Public misconceptions were apparent regarding modes of transmission and preventive measures. To prevent misconceptions during future outbreaks, it is important that health authorities provide up-to-date information about the virus and possible preventive measures.
Rashid, H. et al 2015 Australië	Systematic review	Influenza	Terms representing all forms of influenza (both seasonal and pandemic influenza) such as 'Influenza, Human', 'Influenza A Virus, H1N1 Subtype' and 'Influenza A Virus, H5N1 Subtype' were combined with terms representing aspects of social distance and other mitigation measures. Searches were limited to 'Human' where this limit was available. No language or abstract restrictions were applied. 80 articles included.	Different forms of social distancing.	Social distancing vs no social distancing.	School closure, whether proactive or reactive, appears to be moderately effective and acceptable in reducing the transmission of influenza and in delaying the peak of an epidemic but is associated with very high secondary costs. Voluntary home isolation and quarantine are also effective and acceptable measures but there is an increased risk of intra-household transmission from index cases to contacts. Work place-related interventions like work closure and home working are also modestly effective and are acceptable, but likely to be economically disruptive. Internal mobility restriction is effective only if prohibitively high (50% of travel) restrictions are applied and mass gatherings occurring within 10 days before the epidemic peak are likely to increase the risk of transmission of influenza.
Hitoshi, O. et al 2006 Japan	Narrative review	Influenza. Different strategies next to social distancing are evaluated, no direct comparison.	Patients infected with influenza since 1918-1919.	Social distancing	Various strategies to mitigate the impact of an influenza pandemic. No direct comparison.	Various social distancing measures, such as the closure of schools and workplaces, home confinement, and cancellation of social gatherings were used to prevent the transmission of the virus during past pandemics. Some of these measures were implemented as official policy, but in many cases, they were implemented as voluntary behavior changes due to a fear of infection in crowded places. Similar behavioral changes were also seen during the SARS epidemic. There is little

						scientific evidence for the effectiveness of these interventions in reducing influenza transmission during periods of seasonal and pandemic influenza. Schools often play an important role in spreading the virus to the community. It was suggested that school closures were associated with a reduced incidence of influenza. Recent studies, using epidemiological models, have concluded that social distancing measures alone would have little impact on the overall number of cases, although they might have some effect in delaying the peak of an epidemic. Therefore, social distancing may only be effective in gaining time to produce sufficient vaccines or as a supplemental strategy in addition to pharmaceutical interventions.
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Add conclusions of overall body of evidence here:

- Main results

· Transmissie

Overdracht van mens op mens zou volgens meerdere studies plaatsvinden tijdens de symptomatische periode en de asymptomatische incubatieperiode, dit wil zeggen vanaf 2 dagen na besmetting tot genezing. De meerderheid van de besmette personen kunnen het virus dus ook verspreiden wanneer ze geen of slechts milde symptomen hebben. Transmissie vindt meestal plaats door nauw contact (Sohrabi et al, Wang Y et al, Chan J et al, Li Q et al, Pung et al, Remuzzi et al).

De transmissie gebeurt hoogstwaarschijnlijk via druppels, contacten (denk niezen, hoesten, maar ook via aanraken van oppervlakken) en stoelgang (Wang Y et al, Chan J et al). Over het al dan niet verspreiden van COVID-19 via de lucht werden tegenstrijdige resultaten teruggevonden. Zo werd in een studie geen SARS-CoV-2 teruggevonden in luchtstalen genomen in de omgeving van besmette patiënten (met en zonder chirurgisch masker) maar wel in de omgevingsstalen (Cheng et al). De gemiddelde incubatietijd was 4 tot 5,5 dagen (Pung et al, Li Q et al).

· Preventie

Op basis van een simulatiestudie werd isolatie van besmette personen beschouwd als de meest effectieve manier is om het virus in bedwang te houden (Wang Y et al). Echter, isolatie van personen die verdacht zijn op besmetting is niet genoeg om de verspreiding van het virus tegen te gaan gezien er reeds overdracht is in de prodromale perioden. Bij studies over influenza zien we ook dat isolatie aanbevolen wordt op basis van de rationale maar niet op basis van wetenschappelijk onderzoek (Fong et al).

Daarnaast is er het probleem dat vele infecties (bv Influenza) eenzelfde beeld geven als COVID-19, wat zorgt dat er in de praktijk moeilijk voor iedereen isolatie kan volgen die symptomen vertoont (Natsuko et al). In tegenstelling tot bijvoorbeeld SARS waarbij patiënten vrijwel steeds ernstige symptomen vertoonden is dit niet het geval bij COVID-19, heel wat personen zijn niet tot licht symptomatisch.

China heeft snel gereageerd op het opkomende coronavirus met zeer extreme maatregelen wat social distancing betreft. De verspreiding is hierdoor op dit moment teruggevallen met een afbuigen van de curve. China had reeds in het verleden ervaring met SARS en MERS waardoor zij goed voorbereid waren (Wilder-Smith et al).

Contact tracing is essentieel om het risico op verspreiding te verminderen, zowel bij COVID-19 als bij vroegere pandemieën met influenza (Pung et al, Fong et al).

· Reproductieve R0 waarde

De basis reproductieve waarden in de vroege fase van COVID-19 werden berekend op 2 tot 3,5, wat wil zeggen dat iedere besmette persoon gemiddeld 2 à 3 andere personen besmet. Deze getallen liggen hoger dan bij vorige pandemieën met SARS en MERS. De bedoeling van de maatregelen, zoals social distancing, is deze onder de 1 te krijgen (Wang Y et al, Zhou et al, Li Qn et al, Natsuko et al). Er werd een daling gezien van de reproductieve waarde, van 2,35 naar 1,05, nadat reis restricties werden ingesteld in Wuhan, China (Kucharski et al).

· Resultaten uit studies over influenza

Transmissie van influenza in de samenleving werd verminderd wanneer scholen gesloten werden. Er was weinig bewijs over de effectiviteit van maatregelen op het werk of het vermijden van grote groepen. (Fong et al, Oshitani et al.)

Social distancing heeft weinig invloed op het totale aantal mensen dat besmet raakt met Influenza maar geeft tijd om vaccins en antivirale middelen te ontwikkelen en het aantal bedden in de gezondheidszorg uit te bouwen (Oshitani et al.) Het effect van social distancing neemt af bij een hogere besmettelijkheid, vertraging van maatregelen en minder goede opvolging door de populatie. Bij een hogere besmettelijkheid is het moeilijker de reproductieve waarde onder 1 te krijgen. Bij influenza wordt gezien dat social distancing zorgen voor een lagere en latere piek (Ahmed et al, Singh et al, Rashid et al.).

Wanneer een populatie reeds een epidemie meemaakte, heeft dit gevolgen voor de toekomst. Mensen zullen sneller en vaker uit zichzelf hygiënische maatregelen en social distancing toepassen (Bults et al.).

- **Risks of bias**

Meerdere studies hadden een geringe omvang van de steekproef. Er werden geen RCT's gevonden maar voornamelijk reviews die de huidige kennis samenvatten en retrospectieve studies waar men heeft gekeken naar de situatie in Wuhan. Omdat er nog niet heel veel geweten is over COVID-19 hebben werden ook studies toegevoegd over het influenzavirus.

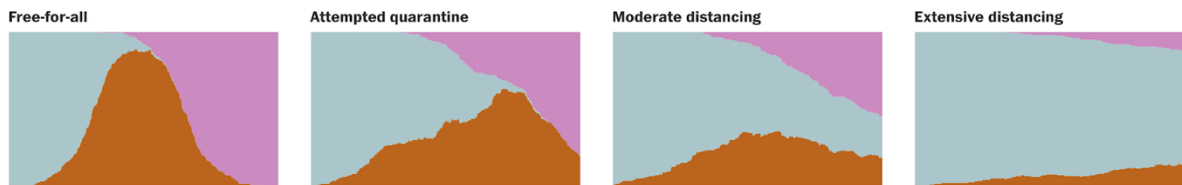
- **Heterogeneity**

Meerdere studies hebben een verschillende outcome. Omdat er niet meteen studies gevonden werden over het individuele risico op besmetting werden ook studies geïnccludeerd met uitkomsten over transmissie, preventie en R0 om zo een beter zicht te krijgen op de manier waarop dit virus overgedragen wordt en hoe dit te voorkomen.

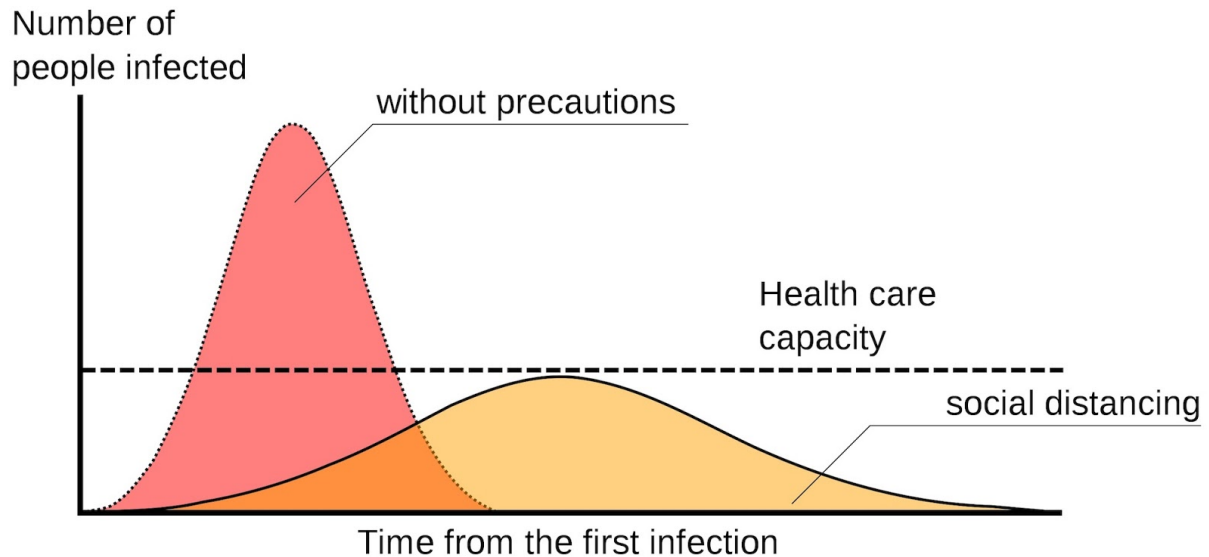
Add clinical bottom line here:

Aangezien verspreiding van het coronavirus vooral gezien werd na nauw contact met besmette personen kan gesteld worden dat het individueel risico voornamelijk daalt door afstand te bewaren en met zo weinig mogelijk mensen in contact te komen. Het risico op besmetting in groep moet tegengegaan worden door voldoende afstand te bewaren zodat druppel overdracht en overdracht via oppervlakken niet kan plaatsvinden. Wetenschappelijk bewijs over het verlagen van het individueel risico op besmetting door het verkleinen van groepen werd niet gevonden.

In het verleden heeft men gezien dat influenza verspreiding vertraagd kan worden door groepen te verkleinen. Dit is wat men met de huidige maatregelen ook probeert te bekomen voor de verspreiding van het coronavirus, het zogenaamde 'flatten the curve'. Hoe meer social distancing, dus hoe minder mensen bewegen, hoe trager het coronavirus zal verspreiden. Dit is mooi te zien in de simulaties van Washington post.



<https://www.washingtonpost.com/graphics/2020/world/corona-simulator/>



<https://www.livescience.com/coronavirus-flatten-the-curve.html>

Bronnen

Ahmed F, Zviedrite N, Uzicanin A. Effectiveness of workplace social distancing measures in reducing influenza transmission: a systematic review. *BMC Public Health*. 2018;18(1):518.

Bults M, Beaujean DJ, Richardus JH, et al. Perceptions and behavioral responses of the general public during the 2009 influenza A (H1N1) pandemic: a systematic review. *Disaster Med Public Health Prep*. 2015;9(2):207-19.

Chan J. F.-W., Yuan, S., Kok, H.-K., To, K.K.-W., Chu, H., Yang, J., et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster, *The Lancet*, Volume 395, Issue 10223, 514 - 523.

Cheng, V., Wong, S., Chen, J., Yip, C., Chuang, V., Tsang, O., et al. Escalating infection control response to the rapidly evolving epidemiology of the Coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in Hong Kong. *Infection Control & Hospital Epidemiology*, 1-24. doi:10.1017/ice.2020.58

Fong, M.W., Gao, H., Wong, J.Y., Xiao, J., Shiu, E.Y.C., Ryu, S., et al. Nonpharmaceutical measures for pandemic influenza in nonhealthcare settings—social distancing measures. *Emerg Infect Dis*. 2020 May [date cited]. doi: <https://doi.org/10.3201/eid2605.190995>

Hoang VT, Gautret P. Infectious Diseases and Mass Gatherings. *Curr Infect Dis Rep*. 2018;20(11):44.

Kucharski, A., Russell, T.W., Diamond, C., Liu, Y., Edmunds, J., Funk, S., et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study, *The Lancet Infectious Diseases*, 2020. doi: [https://doi.org/10.1016/S1473-3099\(20\)30144-4](https://doi.org/10.1016/S1473-3099(20)30144-4)

Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia, *N Eng J Med.*, 2020. doi: 10.1056/NEJMoa2001316

Natsuko Imai, Anne Cori, Ilaria Dorigatti et al. Report 3: Transmissibility of 2019-nCoV. Imperial College London COVID-19 Response Team. 2020. DOI: <https://doi.org/10.25561/77148>.

Oshitani H. Potential benefits and limitations of various strategies to mitigate the impact of an influenza pandemic. *J Infect Chemother.* 2006;12(4):167-71.

Pung, R., Chiew, C.J., Young, B.E., Chin, S., Chen, M.I-C., Clapham, H.E., et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures, *The Lancet*, 2020. doi: [https://doi.org/10.1016/S0140-6736\(20\)30528-6](https://doi.org/10.1016/S0140-6736(20)30528-6).

Rashid H, Ridda I, King C, Evidence compendium and advice on social distancing and other related measures for response to an influenza pandemic. *Paediatr Respir Rev.* 2015;16(2):119-26.

Remuzzi A, Remuzzi G .COVID-19 and Italy: what next? *Lancet.* 2020.. pii: S0140-6736(20)30627-9. doi: 10.1016/S0140-6736(20)30627-9.

Singh M, Sarkhel P, Kang GJ, et al. Impact of demographic disparities in social distancing and vaccination on influenza epidemics in urban and rural regions of the United States. *BMC Infect Dis.* 2019;19(1):221.

Sohrabi, C., Alisafi, Z., O'Neill, N., Khan, M. , Kerwan, A., Al-Jabir, A., et al. World health organization declares global emergency: a review of the 2019 novel Coronavirus (COVID-19), *Int. J. Surg.*, 76 (2020), 71-76.

Wang, Y., Wang, Y., Chen, Y., Qin, Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol*, 2020. Accepted Author Manuscript. doi:[10.1002/jmv.25748](https://doi.org/10.1002/jmv.25748)

Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. *J Travel Med.* 2020;27(2).

Zhao, S., Lin, Q., Ran, J., Yang, L., He, D., Wang, M.H., et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak, *Int J Infect Dis.*, 92 (2020), 214 - 217.