Conclusie van **antwoord en uitlating producties in kort geding** inzake:

DE STAAT SURINAME, m.n. het Ministerie van Volksgezondheid, gedaagde,
gemachtigden Mr. C.B. Lachman en Mr. Mohnie Babulall, advocaten

contra

DONK, KAREL, eiser, procederende in persoon,

Gedaagde concludeert als volgt:

1. Gedaagde ontkent alle stellingen van eiser in het inleidend verzoekschrift en daarmee overeenstemmende conclusie van eis, voor zover hij deze hieronder niet gaaf en onvoorwaardelijk erkent. Gedaagde wil niet geacht worden enig feit of enige omstandigheid stilzwijgend te hebben erkend.

2. Eiser heeft eerder een proces, bekend onder A.R. No. 210733, in kort geding tegen gedaagde waarin hetzelfde werd gevorderd, namelijk het opschorten van de maatregelen voortvloeiende uit de Wet Uitvoering Burgerlijke Uitzonderingstoestand (WUBU). Op 24 maart 2021 heeft de kantonrechter in voormeld proces vonnis gewezen, waarbij het door eiser gevorderde hem werd ontzegd. Vide het hierbij in fotokopie overgelegd vonnis d.d. 24 maart 2021, A.R. No. 210733 **(productie 1)**.

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3. Gedaagde moet thans ervaren dat eiser voor de tweede maal hetzelfde vordert in dit proces. Gedaagde doet dan ook een beroep op het ne bis in idem beginsel, aangezien eiser niet voor de tweede maal voor dezelfde vordering de rechter in kort geding kan adiëren. Door zo te handelen maakt eiser namelijk misbruik van het procesrecht. Eiser dient daarom niet-ontvankelijk te worden verklaard in zijn vordering, althans dient de vordering hem te worden ontzegd.

4. Indien U E.A. van oordeel bent dat eiser wel ontvankelijk is, dan voert gedaagde het volgende aan. Vanwege de covid-pandemie is gedaagde ingevolge artikel 23 juncto 72 van de Grondwet (GW), ertoe overgegaan tot het maken en afkondigen van de WUBU. Ter uitvoering van deze wet (WUBU) bestaat er een Presidentieel Besluit van 31 mei 2021, inhoudende wijziging van

het Presidentieel Besluit van 2 januari 2021 (P.B. no. 11/2021). Ingevolge artikel 2 van genoemd Besluit van 31 mei 2021 is het een ieder verboden om zich in de periode van 31 mei 2021 tot en met 18 juni 2021 in heel Suriname op de openbare weg te begeven of te bevinden. Er is sprake van een uitzonderingstoestand, omdat er een pandemie heerst die de volksgezondheid ernstig in gevaar brengt. De door gedaagde toegepaste Lockdown maatregel is gestoeld op de WUBU met het daaraan voortvloeiende Presidentieel Besluit. Deze maatregel heeft een wettelijke grondslag.

4. Al de stellingen van eiser in het inleidend rekest komen in het kort erop neer dat de door gedaagde toegepaste maatregelen c.q. Lockdown maatregelen niet nodig, althans niet efficiënt is of zijn. Dus zou volgens eiser deze maatregel(en) moeten worden opgeschort.

5. Gedaagde betwist al deze stellingen van eiser met klem en wel op grond van het hierna volgende. Gedaagde erkent de Lockdown maatregel, alsmede de mohana-maatregelen te hebben toegepast, aangezien het aantal covid-besmettingen behoorlijk is gestegen. Deze besmettingen leggen een enorme druk op de gezondheidszorg, o.a. de intensive-careafdelingen binnen de ziekenhuizen in ons land. Dit, vanwege het feit dat de intensive-careafdelingen overvol raken, terwijl er tegelijkertijd een ernstig tekort is aan ziekenhuispersoneel alsook beademingsapparaten.

6. De Lockdown maatregel is één van de public health interventies met als doel de hoge besmettingsgraad van corona tegen te gaan, althans te verminderen. Het gaat erom dat door het treffen van deze maatregel (en) gedaagde de samenleving beschermt.

7. Gedaagde ontkent en betwist met klem, dat de Lockdown maatregel geen wetenschappelijke basis heeft althans geen effect sorteert. Uit verschillende recentelijke wetenschappelijke publicaties (opgezocht bij de library www.pubmed.gov) blijkt dat de Lockdown strategie behoort tot één van de public health interventies, bij uitbraken van infectieziekten. Uit de publicaties blijkt onder andere dat deze maatregel of modificaties hiervan, vergezeld met andere public health interventies, met succes zijn toegepast in verschillende landen om de besmettingsgraden af te remmen. Vide de hierbij in fotokopie overgelegde publicaties van Imen Ayouni e.a., getiteld: *Effective public health measures to mitigate the spread of COVID-19:*
./. *a systematic review,* d.d. 29 mei 2021, **(productie 2)** en van Maria Pachetti e.a., getiteld: *Impact of lockdown on Covid-19 case fatality rate and viral mutations spread in 7 countries in Europe and*
./. *North America,* d.d. 2 september 2020 **(productie 3)**.

8. Eiser heeft op geen enkele manier kunnen onderbouwen wat het effect zou zijn wanneer de lockdown maatregel niet zou worden toegepast. Gedaagde onderstreept dat bij het uitblijven van deze maatregel het aantal besmettingen vele malen hoger zou zijn, als uitgegaan wordt van de projecties van de beschikbare gegevens aangaande corona besmettingen.

9. De door eiser aangehaalde artikelen en literatuur zijn vals aangezien deze publicaties achterhaald zijn en dus niet ter zake doende zijn. De aangehaalde literatuur slaat nergens op. Gedaagde heeft met de in punt 7 overgelegde publicaties aangetoond dat de toegepaste Lockdown maatregel gerechtvaardigd is. Door gedaagde wordt hierbij in fotokopie overgelegd de richtlijnen van de World Health Organization (WHO) d.d. 27 mei 2021 conform welke de
./. bewegingsbeperkende maatregelen (Lockdown) worden toegepast **(productie 4)**.

10. Door gedaagde is de Lockdown maatregel eerder toegepast o.a. in december 2020.
./. Gedaagde legt hierbij eveneens over een tabel **(productie 5)** die aantoont dat de toegepaste Lockdown in het weekend van 16 december 2020 wel effectief en efficiënt is geweest. Dit is te merken aan het reproductiegetal dat toen 5.230769 was, maar op januari 2021 was teruggenomen naar 0.9429993. Het reproductiegetal is niets anders dan een getal aangevende hoeveel personen andere personen kunnen besmetten binnen hun infectieuze periode. Gedaagde heeft op geen enkele wijze onrechtmatig gehandeld. Ook voert gedaagde geen angstcampagne, doch bewustwording campagne. Gedaagde heeft juist ter bescherming van de samenleving maatregelen in het kader van bestrijding van de covid-pandemie getroffen, welke maatregel (en) een wettelijke grondslag hebben en is gedaagde daartoe bevoegd.

11. De stelling van eiser als zou de reguliere gezondheidszorg wordt verwaarloosd is volledig misplaatst. Het is een notoir feit dat in alle landen met coronabesmettingen de reguliere gezondheidszorg onder druk is komen te staan. Dit is niet vreemd alsook begrijpelijk. Vandaar de toepassing van Lockdown maatregelen, die de WHO dan ook aanbeveelt.

12. Ook de stelling van eiser als zou de PCR-testen onbetrouwbaar zijn, raakt kant noch wal. Deze stelling wordt eveneens met klem weersproken door gedaagde. De PCR- testen zijn wel betrouwbaar. De betrouwbaarheid, althans de klinische betrouwbaarheid van de PCR-test is afhankelijk van een groot aantal factoren, welke letterlijk geciteerd zullen worden uit de toelichting van het Rijksinstituut voor Volksgezondheid en Milieu in Nederland (RIVM) op PCR-testen, welk
./. document hierbij in fotokopie wordt overlegd **(productie 6)**. Het gaat hierbij om de volgende factoren:

"• De analytische/technische sensitiviteit en specificiteit van de PCR-test. *De analytische/technische sensitiviteit van de PCR-test is dat deze tussen 1-10 kopieën genetisch materiaal van het SARS-CoV-2 in een PCR-reactie detecteert (1, 10, 11). Dit weten we omdat bij validatie van de PCR-test de limiet van detectie wordt bepaald (3, 12). De analytische/technische specificiteit van de PCR-test is dat deze alleen genetisch materiaal van het SARS-CoV-2 virus detecteert. Soms bevat een PCR-test nog een component, of alleen een component, die SARS-virussen detecteert in de groep van SARS-virussen waartoe SARS-CoV-2 behoort. Omdat alleen SARS-CoV-2 uit deze groep van SARS-virussen in mensen voorkomt, is deze component voor diagnostiek in mensen ook specifiek voor SARS-CoV-2. De PCR-test detecteert dus geen andere virussen en bacteriën die klachten kunnen geven die lijken op die van COVID-19 of die bij mensen zonder klachten in de luchtweg kunnen voorkomen, zoals griepvirus, verkoudheidsvirus en Chlamydia pneumoniae. Dit weten we omdat bij validatie van de PCR-test heel uitgebreid de kruisreactiviteit van de PCR-test met deze virussen en bacteriën wordt uitgetest (3, 12).*

• De hoeveelheid SARS-CoV-2 aanwezig in de bovenste luchtweg van iemand die geïnfecteerd is; het hoogst enkele dagen na infectie (ongeacht of de geïnfecteerde persoon symptomen krijgt) en houdt dan enkele dagen aan waarna het minder wordt doordat het lichaam het virus opruimt. De vooraf-kans op een positieve PCR-test is dus het hoogst als een persoon 2 tot 10 dagen na infectie wordt bemonsterd.

• De kwaliteit van het afgenomen monster om te testen met de PCR-test; het meest sensitief is om zowel een monster te nemen van de keel (orofarynx) en uit de neus (nasofarynx of tenminste hoog in de neus). Mensen die monsters afnemen worden getraind om dit goed te doen. De vooraf-kans op een positieve PCR-test is dus het hoogst als een persoon op een juiste manier wordt bemonsterd.

• Of een persoon symptomen heeft of niet; bij iemand met symptomen die passen bij COVID-19 is de vooraf-kans op een positieve PCR-test hoger dan bij een persoon die geen klachten heeft; vooral in de eerste dagen na ontstaan van symptomen. Symptomatisch testen versus asymptomatisch testen.

• Of een persoon enkele dagen voor het testen een hoge waarschijnlijkheid van besmetting heeft of niet; iemand die dicht bij een COVID-19 patiënt is geweest heeft een veel hogere vooraf-kans om PCR-test positief te worden dan iemand die willekeurig van de straat wordt 'geplukt'. Hoe langer een persoon dichtbij een COVID-19 patiënt is geweest hoe groter de vooraf-kans voor die persoon om PCR-test positief te worden. Screening met strikte casusdefinitie en bron en contactonderzoek versus algemene populatie screening.

• Hoe hoog de prevalentie is van circulatie van het virus; bij hoge prevalentie is de vooraf-kans dat bij een persoon het virus gedetecteerd wordt hoger dan bij een lage prevalentie. In het land kunnen er regionale verschillen in prevalentie zijn en daardoor dus ook verschillen in de vooraf-kans om PCR-test positief te worden."
Alle voorgaande factoren bepalen de kans of een positieve PCR-test **correct** aangeeft of een geteste persoon het genetisch materiaal van het SARS-CoV-2 virus bij zich heeft en of een negatieve PCR-test correct aangeeft of de geteste persoon het genetisch materiaal van het SARS-CoV-2 virus niet bij zich heeft. De PCR-test is derhalve betrouwbaar.

13. De stelling van eiser als zou er sprake zijn van financiële schade ten gevolge van de toegepaste Lockdown maatregel, is pertinent onjuist. De covid pandemie heeft wereldwijd geleid tot ontwrichting van samenlevingen. Dit gegeven en diverse maatregelen om de samenlevingen te beschermen hebben ongetwijfeld een impact op de financiële, mentale en sociale aspecten van de samenleving. Gedaagde heeft nimmer moedwillig financiële schade toegebracht of willen toebrengen aan wie dan ook. De stelling van eiser in deze is niet ter zake doende, aangezien het tot de primaire verantwoordelijkheid van gedaagde als centrale overheid, m.n. het Ministerie van Volksgezondheid, hoort om de gezondheid van de totale samenleving te organiseren en te garanderen.

14. Het is juist gerechtvaardigd dat gedaagde op adviezen en inzichten van de WHO en andere internationale en nationale public health deskundigen en het Outbreak Management Team maatregelen heeft getroffen, waaronder o.a. de Lockdown. De maatregel moest getroffen worden in het belang van volksgezondheid. De Lockdown is een public health interventie die mondiaal is toepast in de strijd tegen covid 19, met als doel om beweging van de mens in het openbaar te beperken en de besmettingen van persoon tot persoon te minimaliseren. De basisgedachte van de Lockdown is: 'hoe minder bewegelijke de samenleving, hoe minder besmettingen'. Gedaagde benadrukt dat de Lockdown niet zomaar wordt toegepast. Er is thans, een crisis en geen ruimte is in onze ziekenhuisinstellingen om de besmette persoon op adequaat op te vangen. De Lockdown is een tijdelijke maatregel. Vaccin is duurzaam, vandaar de campagne.

15. Uit het voorgaande blijkt dat eiser geen spoedeisend belang heeft bij de onderhavige vordering. Eiser heeft bovendien niet kunnen aantonen dat er sprake is van schade ten gevolge van gedaagde haar handelen, laat staan schade die zich in de toekomst zou kunnen manifesteren door de getroffen maatregelen door gedaagde voortvloeide uit de WUBU. Eiser dient niet-ontvankelijk verklaard te worden in zijn vordering.

16. U E.A. wordt verzocht de overgelegde producties als letterlijk herhaald en geïnsereerd te willen beschouwen.

17. Gedaagde biedt bewijs aan van al haar stellingen door alle middelen rechtens meer speciaal door getuigen zonder onverplicht bewijslast op zich te nemen.

18. Bij gedaagde bestaat geen enkel bezwaar als U E.A., indien gewenst, een comparitie van partijen zou gelasten.

Met conclusie dat U E. A. eiser **niet-ontvankelijk verklaard** in zijn vordering, althans deze hem zal worden **ontzegd als zijnde ongegrond** en niet bewezen.

Paramaribo, 11 juni 2021

Mr. C.B. Lachman

Mr. M. Babulall

Bijlagen:

1. Fotokopie van het overgelegde vonnis d.d. 24 maart 2021, A.R. No. 210733, **(productie 1)**;
2. Fotokopie van de overgelegde publicaties d.d. 29 mei 2021 van I, Ayouni e.a. en d.d. 2 september 2020 van M, Pachetti e.a. (respectievelijk **producties 2 en 3)**;
3. Fotokopie richtlijnen WHO d.d. 27 mei 2021 van een tabel **(productie 4)**;
4. Fotokopie van een tabel **(productie 5)** en
5. Fotokopie toelichting RIVM op PCR-testen **(productie 6)**.

arno. 210733

Griffie der Kantongerechten

Kantonrechter in Kort geding

A.R. no. 210733
24 maart 2021

Vonnis in de zaak van

A. DONK, KAREL, wonende aan de Powisistraat no. 175 te Paramaribo,
B. STUTGARD, RICKY, wonende aan de Harpalstraat no. 23 te Paramaribo,
procederend in persoon,
eisers in kort geding,

tegen

DE STAAT SURINAME, rechtspersoon, met name het Ministerie van Volksgezondheid, ten deze vertegenwoordigd door de Procureur-Generaal bij het Hof van Justitie, gevestigd en kantoorhoudende aan de Limesgracht 92 te Paramaribo,
gemachtigden: mr. C.B. Lachman en mr. M. Babulall, advocaten,
gedaagde in kort geding.

1. Het proces verloop:

1.1. Dit blijkt uit de volgende processtukken:
- het verzoekschrift, met producties, dat op 9 maart 2021 ter griffie der kantongerechten is ingediend,
- de conclusie van eis d.d. 11 maart 2021,
- de mondelinge conclusie van antwoord, met producties, aangetekend in het proces-verbaal van de zitting van 11 maart 2021;
- de conclusie van repliek, met producties,
- de conclusie van dupliek, met producties,
- de conclusie tot uitlating producties zijdens eisers.

1.2 De uitspraak van het vonnis in kort geding is bepaald op heden.

2. De feiten

2.1 Ingevolge de Wet van 7 augustus 2020 houdende algemene regels in verband met de uitvoering van een burgerlijke uitzonderingstoestand afgekondigd ingevolge artikel 23 jo 72 onder c van de Grondwet (SB 2020 no. 151), genoemd de Wet Uitvoering Burgerlijke Uitzonderingstoestand, zijn bij Presidentieel besluit van 25 juli 2020 (SB 2020 no. 143 / PB 16/2020) een aantal maatregelen vastgesteld.

2.2 Artikel 1 van het Presidentieel besluit luidt alsvolgt:
"Vanaf 26 juli 2020 tot nader orde worden de volgende maatregelen voor een ieder verplicht gesteld:
a. het dragen van een mond- en neusbedekking;
b. het aanhouden van 1,5 meter fysieke afstand, de zogeheten Covid afstand en
c. het regelmatig desinfecteren van de handen. "

2.3 Naar de effectiviteit en de gevolgen van het dragen van een mond- en neusbedekking is door verschillende instanties onderzoek gedaan.

3. De vordering en de grondslag daarvan

3.1 De vordering

Eisers vorderen, kort gezegd, dat de kantonrechter, bij vonnis in kort geding, uitvoerbaar bij voorraad:

Primair:

- De maatregelen voortvloeiende uit de Wet Uitvoering Burgerlijke Uitzonderingstoestand, welke omstreeks juni 2020 in werking is getreden, waarbij het dragen van een mond- en neusbedekking c.q. mondkapje voor burgers van Suriname verplicht is gesteld om verspreiding van Covid-19 tegen te gaan, opschort totdat deze middels een definitieve voorziening zal zijn opgeheven;

Subsidiair:

- De gedaagde veroordeelt om naast het aanbevelen van mondkapjes de bevolking omstandig te informeren over het bestaan van wetenschappelijk bewijs dat mondkapjes medisch niet effectief zijn en dat zij integendeel zelfs schadelijk zijn voor de gezondheid, en voorts

Primair en subsidiair:

- Gedaagde veroordeelt in de proceskosten.

3.2 De grondslag

Eisers hebben als grondslag voor het gevorderde vier gronden aangevoerd:

1. Het dragen van een mond- en neuskap draagt niet bij aan het tegengaan van de gevolgen van Covid-19

Het verplicht voorschrijven van het dragen van mond- en neusbedekking draagt niet bij aan het tegengaan van de gevolgen van Covid-19. Er bestaat geen enkel serieus bewijs dat mond- en neuskapjes helpen.

Op basis van veertig jaar wetenschappelijk onderzoek is er onvoldoende bewijs dat mond- en neuskapjes effectief zijn in het voorkomen van de verspreiding van virussen zoals het Covid-19 virus.

Eisers verwijzen naar de resultaten van de onderzoekers Ha'eri en Wiley uit 1980, onderzoekers van de Universiteit van Minnesota van oktober 2020, onderzoeken naar de effectiviteit van het dragen van maskers in de operatiekamer van 11 verschillende onderzoeksteams, van de onderzoekers van MacIntyre et al., van de Amerikaanse CDC, van de Deense RCT, van Oostenrijkse wetenschappers, van wetenschappers in de Amerikaanse staat Kansas, van professor dr. I. Kappstein van het Robert Koch Instituut, van professor Sarah Lebeer aan de Universiteit van Antwerpen, een onderzoek aan de Faculteit der Technologische Wetenschappen in Suriname, van Fikenzer et al. van juni 2020, van Yanis Roussel et al. en van de WHO zelf van onder andere juni 2020.

In meerdere rechtzaken in Nederland is door de rechter geoordeeld dat het nut van het dragen van mondkapjes beperkt en omstreden is.

2. Het dragen van mond- en neusbedekking is juist aantoonbaar schadelijk voor de gezondheid van burgers zowel fysiek als psychisch

Er is bij het dragen van een mond- en neuskap een risico op een toename van infecties van virussen, bacteriën en schimmels door langdurig en niet hygiënisch gebruik van mondkapjes, ook kunnen er allerlei andere negatieve gezondheidseffecten optreden. Voorts kan bij langdurig dragen van mondkapjes door burgers blijvende schade worden veroorzaakt. Het is niet

rechtvaardig om zo verregaand in te grijpen in de grondrechten van burgers door ze te verplichten om een mondkapje te dragen terwijl het dragen schadelijk is en niet helpt. Gedaagde heeft zich niet gehouden aan het zorgvuldigheidsbeginsel bij de besluitvorming welke geleid heeft tot het verplichten van mondkapjes.

3. De verplichting om mond- en neusbedekking te dragen is in strijd met fundamentele mensenrechten zoals opgenomen in de Grondwet en Verdragen

Het verplichten tot het dragen van mond- en neusbedekking staat op gespannen voet met verschillende grondrechten zoals opgenomen in de Grondwet en Verdragen. De verplichting tot het dragen van een mond- en neusbedekking druist in tegen het universele grondrecht van de eerbiediging van de persoonlijke levenssfeer zoals geformuleerd in artikel 16 leden 1 en 2 en artikel 17 lid 1 van de Grondwet en artikel 8 van het EVRM.

Ook is er sprake van een onrechtmatige inbreuk op het recht op leven, welk recht in artikel 14 van de Grondwet is opgenomen. De schade welke op verschillende manieren aangericht wordt aan de gezondheid van burgers door het verplicht dragen van mond- en neusbedekking tast de kwaliteit van het leven van personen aan en kan hun leven potentieel zelfs in gevaar brengen. Burgers worden gedwongen om hun gezondheid en hun leven potentieel in gevaar te brengen.

Het staat niet ter discussie dat gedaagde een belangrijke taak heeft bij de bestrijding van infectieziekten zoals Covid-19. Echter kunnen fundamentele grondrechten niet zonder meer worden ingeperkt door gedaagde. Het verplicht stellen tot het dragen van een mond- en neusbedekking is een ernstige inperking van fundamentele grondrechten. Inbreuk op grondrechten zou slechts gerechtvaardigd zijn als vaststaat dat een dergelijke inbreuk bij wet geregeld is, een legitiem doel dient, strikt noodzakelijk, proportioneel en effectief is en niet schadelijk is voor de gezondheid.

4. Er is sprake van misleiding van de samenleving

Het doel van de mondkapjesmaatregel is om de bevolking wereldwijd psychologisch te manipuleren. Men probeert opzettelijk een klimaat van continu gevaar te creëren om de bevolking angst in te boezemen, zodat de bevolking makkelijk instemt met zelfs de meest draconische maatregelen, maatregelen die thuishoren in een politiestaat. Dat verklaart ook waarom de bevolking vanaf het begin wordt overspoeld met dagelijkse berichten over het aantal Covid-19 besmettingen en doden terwijl het al vroeg duidelijk was dat het Covid-19 virus niet gevaarlijker bleek te zijn dan andere virussen in omloop. Gelijktijdig met de angst campagne vanuit de staat en de media werd elk tegengeluid wereldwijd zwaar gecensureerd, niet alleen in de reguliere media maar ook op social media. Ook in wetenschappelijke kringen werd er gecensureerd. Onder het voorwendsel van de pandemie hebben autoriteiten in sommige landen hardhandig gereageerd met veiligheidsmaatregelen en noodmaatregelen om afwijkende meningen de kop in te drukken, onafhankelijke verslaggeving het zwijgen op te leggen en activiteiten van niet-gouvernementele organisaties te beperken.

Het voorgaande geldt ook voor Suriname. Het is gedaagde samen met de media gelukt om een grimmig klimaat te scheppen waar er een constante angst heerst hetgeen door de maatregelen van gedaagde langzaam verergerd wordt.

De gedaagde heeft in strijd met artikel 7 lid 1 van de Wet Uitvoering Burgerlijke Uitzonderingstoestand de bevolking misleid door de burgers de indruk te geven dat het dragen van mondkapjes medisch effectief is terwijl er overweldigend wetenschappelijk bewijs is dat

mondkapjes medisch niet effectief zijn tegen de verspreiding van Covid-19 en zelfs schadelijk zijn voor de gezondheid. Hierdoor handelt de gedaagde onrechtmatig.

Het spoedeisend belang
Er is een spoedeisend belang. Een groot deel van de bevolking loopt als gevolg van de mondkapjes plicht het risico om daarvan grote en blijvende schade te ondervinden. Een onmiddellijke voorziening bij voorraad om een einde te maken aan het in gevaar brengen van de bevolking door gedaagde c.q. het onrechtmatig handelen van gedaagde tegen de bevolking is daarom dringend noodzakelijk.

4. Het verweer
Gedaagde heeft verweer gevoerd op welk verweer de kantonrechter, voor zover van belang, hierna terugkomt.

5. De Beoordeling
5.1 Gedaagde heeft als verweer onder andere het volgende aangevoerd: **1.** dat eisers geen belang hebben bij de vordering; zij stellen dat er fundamentele rechten geschonden zijn, echter heeft de Staat ingevolge artikel 23 van de Grondwet in verband met de Covid-19 pandemie de Wet Uitvoering Burgerlijke Uitzonderingstoestand uitgevaardigd waardoor de maatregelen wel getroffen hadden mogen worden; door gedaagde is ingesteld het Outbreak Management Team, bestaande uit medische experts en public health deskundigen; dit Outbreak Management Team geeft op basis van de geldende wetenschappelijke inzichten van onder andere de WHO, de Carfa en de CDC, adviezen aan de regering ter indamming en controle van de Covid-19 pandemie; **2.** dat eisers geen spoedeisend belang hebben; de maatregelen dateren van augustus 2020; thans zijn wij zeven maanden verder waardoor niet kan worden gesteld dat er een spoedeisend belang is; immers, dan zouden de eisers eerder de vordering ingediend moeten hebben; **3.** dat het niet uit de stellingen van eisers is gebleken dat het dragen van een mondkap nadelig is voor de gezondheid van de burgers en dat er geen gevallen bekend zijn in de Surinaamse samenleving waarbij burgers het door eisers genoemde gezondheidsnadeel hebben ondervonden van het dragen van een mondkap; dat aan die stelling dan ook voorbij gegaan moet worden; **4.** dat het niet juist is dat uit onderzoek is gebleken dat mondkapjes nadelig zijn voor de gezondheid van de burgers; het onderzoek door de eisers aangehaald uit Denemarken is bekend; ook is bekend dat dat onderzoek is gedaan onder 0,1 % van de populatie waardoor het niet representatief is; het bedoelde onderzoek wordt internationaal gekwalificeerd als niet-doorslaggevend; **5.** dat de onderzoeken door de eisers aangevoerd dateren van lang voor de Covid-19 pandemie en derhalve geen onderzoeken zijn die in verband met de pandemie zijn uitgevoerd of in verband gebracht kunnen worden met de pandemie; **6.** dat uit een onderzoek van de International Journal of Environmental Research and Public Health van 11 augustus 2020, overgelegd door gedaagde, is gebleken dat bij gezonde personen, personen zonder luchtwegklachten, het opzetten van een masker voor langere tijd zelfs, geen veranderingen laat zien in de zuurstof- en koodioxide concentratie en tevens dat het opzetten van een masker geen effect heeft op het volume per inademing en op de ademhalingssnelheid; er is een lichte stijging van drie procent in de ademweerstand gezien, doch zonder verdere gezondheidsnadelen; ook is melding gemaakt van een negatieve impact van het dragen van maskers met name bij personen met een voorgeschiedenis van hoofdpijn; bij hun bleek dat bij het lang opzetten van een masker hoofdpijn optreedt; de onderzoekers stelden echter dat de voordelen met betrekking tot de besmettingsreductie en daaraan gekoppeld de infectie-complicaties en mortaliteit, vele malen groter waren dan het ongemak van hoofdpijn; **7.** dat een toenemend aantal onderzoeken heeft uitgewezen dat het universeel beleid voor het dragen van maskers in verband kan worden gebracht met een vermindering van het aantal en het percentage van infecties en sterfgevallen; in deze onderzoeken wordt geen

onderscheid gemaakt tussen de soorten maskers, stof, chirurgisch of N95 die in de gemeenschap worden gebruikt; deze associatie wordt verstrekt om dat in veel gevallen andere mitigatie strategieën zoals bijvoorbeeld sluiting van scholen en werkplekken, aanbevelingen voor sociale afstand en handhygiëne al waren toegepast voordat het beleid voor het dragen van maskers werd ingevoerd waarna de verminderingen werden waargenomen; een studie waarin de veranderingen en toenames in percentages in 15 staten in Amerika voor en na maskerplicht werden onderzocht toonden aan dat de infecties toenamen voordat de maskerplicht was ingevoerd en daarna aanzienlijk verminderden toen de maskerplicht kwam en verminderden naarmate de maskerplicht langer van kracht was; **8.** dat uit de door gedaagde overgelegde onderzoeksrapporten en publicaties blijkt dat het dragen van mondmaskers wel effectief is bij het tegengaan van de spreiding van Covid-19, en daardoor bij het tegengaan van complicaties en mortaliteit en geen nadelig effect heeft op de gezondheid van dragers.

5.2 Eisers hebben gereageerd op het verweer van gedaagde en hebben daarbij onder andere het volgende aangevoerd: **1.** dat zij wel een belang hebben en ook een spoedeisend belang omdat de gezondheid van de burgers in het geding is; **2.** dat gedaagde de stellingen dat het dragen van mondkapjes niet effectief is en nadelig is voor de gezondheid, niet heeft weersproken; **3.** dat gedaagde slechts heeft verwezen naar de Wet betreffende de uitzonderingstoestand terwijl er fundamentele rechten geschonden worden; ook heeft een ieder het recht op gezondheid ingevolge artikel 36 lid 1 en 2, waardoor de maatregel die nadelig is voor de gezondheid niet kan worden getolereerd; **4.** dat er inderdaad in Suriname geen gegevens zijn over het nadelig effect van de mondkapjes op de gezondheid van burgers doch dat daardoor juist de vraag gesteld kan worden waarom een maatregel wordt opgelegd waarvan de effecten niet duidelijk zijn; dat geldt temeer nu er studies zijn gedaan in het buitenland waaruit het gezondheidsnadeel blijkt; eisers verwijzen daarbij nogmaals naar het onderzoek van MacIntyre et al. uit 2015; ook is uit de onderzoeken het risico op virale en bacteriële infecties gebleken en het risico op gezondheidsschade als gevolg van zuurstofgebrek of een kooldioxide-vergiftiging; **5.** dat zij erbij blijven dat er maatregelen zijn doorgevoerd zonder dat de effectiviteit ervan is bewezen en zonder dat het korte- en lange termijn effect op de gezondheid voldoende bekend is; **6.** dat het enkele feit dat enkele van de door hun aangehaalde wetenschappelijke studies van vóór de Covid-19 periode dateren, nog niet met zich meebrengt dat deze niet kunnen worden gebruikt voor het beleid van 2021; wereldwijd wordt dagelijks gebruik gemaakt van oudere wetenschappelijke studies; **7.** dat het onderzoek van Denemarken wel representatief is; er hebben zesduizend personen aan meegedaan en de studie betrof een RCT studie; RCT studies worden beschouwd als de gouden standaard voor klinisch onderzoek; de overgelegde producties van gedaagde worden niet alszodanig beschouwd; de conclusies uit het kapsalon onderzoek waar 139 personen aan meededen zou dan ook als kleinschalig moeten worden aangemerkt; **8.** dat ook het onderzoek op de USS Theodore Roosevelt niet kan worden gebruikt voor het maken van beleid omdat daar 382 personen aan hebben deelgenomen die en grotere kans op blootstelling hadden en alle informatie was gebaseerd op zelfrapportage; in dat onderzoek waren verschillende interventies gelijktijdig doorgevoerd waardoor het niet mogelijk is om te concluderen welke interventie heeft geleid tot het resultaat; **9.** dat het door de gedaagde genoemde resultaat van een verhoging van 3% ademhalingsweerstand afkomstig is uit een onderzoek met een computersimulatie; uit een onderzoek onder proefpersonen gedaan door Fikenzer et al. in juni 2020 bleek dat er wel aanzienlijke negatieve effecten optreden bij het dragen van een masker; **10.** dat het gebruik van computersimulaties ook in het begin van de pandemie hebben geleid tot verregaande maatregelen omdat met een computersimulatie was voorspeld dat er miljoenen doden zouden vallen; de voorspelling bleek niet lang daarna totaal verkeerd te zijn en niet in overeenstemming met de realiteit; **11.** dat gedaagde de maatregelen verplicht stelt doch daar zelf niet in gelooft

omdat regeringsleiders de maatregelen zelf niet naleven; zij verwijzen daarbij naar een aantal keren dat regeringsleiders zich niet aan de mondkapjesplicht hielden.

5.3 De kantonrechter overweegt met betrekking tot het belang en het spoedeisend belang dat eisers voldoende aannemelijk hebben gemaakt dat zij een spoedeisend belang hebben. Zij stellen zich onder andere op het standpunt dat de verplichting tot het dragen van mond- en neuskapjes nadelig is voor de gezondheid en dat het stellen van die verplichting in strijd is met grondrechten van de burgers. Die grondslag brengt met zich mee dat het een zaak is die spoedeisend is en waarvoor een voorziening bij voorraad gevorderd zou moeten kunnen worden, ongeacht het feit dat de verplichting reeds geruime tijd bestaat. De kantonrechter gaat daarom voorbij aan het desbetreffende verweer van gedaagde.

5.4 De kantonrechter overweegt dat de vraag die partijen verdeeld houdt de vraag betreft of er gronden zijn om de verplichting om een mond- en neusbedekking te dragen op te schorten. In hun grondslag noemen eisers – kort weergegeven - een viertal gronden namelijk:

1. Het dragen van een mond- en neuskap draagt niet bij aan het tegengaan van de gevolgen van Covid-19; er is onvoldoende bewijs dat het effectief is;

2. Het dragen van een mond- en neuskap is aantoonbaar schadelijk voor de gezondheid van burgers zowel fysiek als psychisch;

3. De verplichting om een mond- en neuskap te dragen is in strijd met fundamentele mensenrechten zoals opgenomen in de Grondwet en Verdragen

4. Gedaagde misleidt de samenleving door de burgers de indruk te geven dat het dragen van mond- en neuskapjes medisch effectief is terwijl wetenschappelijk bewezen is dat dat niet het geval is en het dragen van mond- en neuskapjes zelfs schadelijk is voor de gezondheid. De gedaagde handelt hierdoor onrechtmatig jegens haar burgers.

5.5.1 De kantonrechter stelt voorop dat het betreft een verplichting die bij Wet is opgelegd, zoals hierboven onder de feiten opgenomen, en wel in het uitvoeringsbesluit van de Wet van 7 augustus 2020 houdende algemene regels in verband met de uitvoering van een burgerlijke uitzonderingstoestand afgekondigd ingevolge artikel 23 jo 72 onder c van de Grondwet (SB 2020 no. 151).
Het betreft het Presidentieel besluit van 25 juli 2020 (SB 2020 no. 143 / PB 16/2020).

5.5.2 De kantonrechter acht het van belang allereerst de artikelen van de Grondwet te bespreken die relevant zijn voor de beoordeling van dit geschil.

5.5.3 Ingevolge artikel 80 lid 2 van de Grondwet zijn alle wetten onschendbaar, behoudens het bepaalde in de artikelen 106, 137 en 144 lid 2. In dit verband is een verwijzing naar de Wet Algemene Bepalingen (SB 1945 no. 112) ook van belang, met name artikel 12 waarin is bepaald: "De rechter moet volgens de wettelijke bepalingen rechtspreken; hij mag in geen geval hare innerlijke waarde of billijkheid beoordelen."

5.5.4 Ingevolge artikel 70 van de Grondwet is het vaststellen van wetten in formele zin opgedragen aan de Nationale Assemblee en de Regering gezamenlijk.

5.5.5 De Grondwetgever heeft met artikel 80 de toetsingsbevoegdheid van de rechter, om wetten te toetsen, afgebakend. Buiten het kader van de Grondwetsbepalingen heeft de rechter

geen bevoegdheid om de innerlijke waarde van een wet te toetsen. In artikel 80 zijn de bepalingen genoemd die een uitzondering vormen op bedoelde onschendbaarheid. Het betreft, zoals hiervoor reeds genoemd, de artikelen 106, 137 en 144 lid 2 van de Grondwet. In artikel 106 van de Grondwet is bepaald dat binnen de Republiek Suriname geldende wettelijke bepalingen geen toepassing vinden, wanneer deze toepassing niet verenigbaar zou zijn met een ieder verbindende bepalingen van overeenkomsten, die hetzij voor, hetzij na de totstandkoming van de voorschriften zijn aangegaan. In artikel 137 van de Grondwet is bepaald dat voor zover de rechter in een concreet aan hem voorgelegd geval toepassing van een bepaling van een wet strijdig oordeelt met één of meer der in hoofdstuk 5 genoemde grondrechten, de rechter die toepassing ongeoorloofd verklaart. In artikel 144 lid 2 van de Grondwet komt de bevoegdheid van het Constitutioneel Hof aan de orde. (vide tevens het vonnis van de kantonrechter in het eerste kanton d.d. 28 maart 2019; SRU-K1-2019-4)

5.6 De kantonrechter overweegt dat de vordering van eisers zo begrepen moet worden dat zij vorderen dat de bepaling met betrekking tot de verplichting van de mond- en neuskapjes wordt geschorst totdat door de rechter in een bodemprocedure of het Constitutioneel Hof een oordeel is gegeven over de vraag of de bepaling strijdig is met een ieder verbindende bepalingen van een verdrag of één of meer der in hoofdstuk 5 van de Grondwet genoemde grondrechten. Zij stellen als grondslag voorts dat inbreuk op grondrechten slechts gerechtvaardigd zou zijn als vaststaat dat een dergelijke inbreuk bij wet geregeld is, een legitiem doel dient, strikt noodzakelijk, proportioneel en effectief is en niet schadelijk is voor de gezondheid.

5.7 Eisers beroepen zich in hun grondslag op strijdigheid met de volgende grondrechten:

- het grondrecht van de eerbiediging van de persoonlijke levenssfeer zoals geformuleerd in artikel 16 leden 1 en 2 en artikel 17 lid 1 van de Grondwet;
- het grondrecht opgenomen in artikel 9 lid 1 van de Grondwet, het zelfbeschikkingsrecht, het recht van een ieder op fysieke, psychische en morele integriteit;
- het grondrecht opgenomen in artikel 14 van de Grondwet, namelijk het recht op leven.

5.8 Gedaagde heeft in haar verweer op dit verwijt aangevoerd dat artikel 23 van de Grondwet de gedaagde de bevoegdheid geeft om in geval van – onder andere – een uitzonderingstoestand de in de Grondwet genoemde grondrechten bij wet te onderwerpen aan beperkingen. De gedaagde stelt dat er sprake is van een uitzonderingstoestand omdat er een pandemie heerst die de volksgezondheid ernstig in gevaar brengt. Op 7 augustus 2020 is de Wet Uitvoering Burgerlijke Uitzonderingstoestand vastgesteld in verband met de bescherming van de volksgezondheid, de economie en de algemene veiligheid van burgers. De maatregelen waar eisers op doelen zijn enigszins beperkend, doch moesten getroffen worden in het belang van de volksgezondheid.

5.9 Eisers hebben op dat verweer gereageerd waarbij zij aanvoerden dat een ieder recht heeft op gezondheid en dat een beperking van de gezondheid van de burger niet kan worden toegestaan. Zij zijn verder gebleven bij hun stellingen dat het gebruik van mond- en neuskapjes niet effectief is en schadelijk is voor de gezondheid.

5.10 Gedaagde heeft met betrekking tot de effectiviteit van de maatregel en door eisers genoemde nadelige gevolgen voor de gezondheid aangevoerd dat de maatregel wel effectief is en dat het niet juist is dat het dragen van mondkapjes zodanige nadelige gevolgen heeft voor de gezondheid dat de maatregel daarom niet genomen had mogen worden.

5.11 Beide partijen hebben producties overgelegd om hun respectieve stellingen te onderbouwen.

5.12.1 De kantonrechter overweegt dat voor de beoordeling van het geschil, naast de hiervoor besproken Grondwetsartikelen, tevens de rechtspraak van belang is. In casu is er immers sprake van dat gedaagde gebruik maakt van haar bevoegdheid ingevolge artikel 23 van de Grondwet doch stellen eisers dat gedaagde dat op een wijze doet die ongeoorloofd is. Het toetsingskader dat in de Nederlandse rechtspraak gehanteerd is, en voor de Surinaamse rechtspraktijk ook een goed toetsingskader vormt, is onder andere te vinden in de hierna volgende uitspraak van het Gerechtshof Den Haag. Het Hof heeft daarin geoordeeld over een vordering in verband met een maatregel die bij wet was opgelegd in verband met de Covid-19 pandemie.

5.12.2 Het betreft een uitspraak van het Gerechtshof Den Haag van 26 februari 2021 (ECLI:NL:GHDHA:2021:285) waarbij het Hof onder andere alsvolgt overwoog:

"De vraag welke maatregelen moeten worden getroffen ter bestrijding van de coronacrisis en of die maatregelen proportioneel en subsidiair zijn vergt primair een politieke afweging. Dat die politieke afweging met betrekking tot de invoering van de avondklok ook heeft plaatsgevonden, blijkt zowel uit de toelichting bij de Voortduringswet als uit het besluit van het kabinet om voorafgaand aan het instellen van de avondklok de Tweede Kamer te raadplegen. De civiele rechter – en zeker de rechter in kort geding – moet zich daarom terughoudend opstellen bij de beoordeling van de keuzes die de Staat binnen de grenzen van zijn beoordelings- en beleidsvrijheid maakt. Alleen als evident is dat de Staat onjuiste keuzes maakt en de Staat dus in redelijkheid niet voor het gevoerde beleid heeft kunnen kiezen, of wanneer de Staat een bevoegdheid aanwendt zonder dat daarvoor in de gegeven omstandigheden een wettelijke grondslag bestaat, is plaats voor rechterlijk ingrijpen....."

" In deze procedure is de vraag aan de orde of er sprake is van buitengewone omstandigheden die invoering van de avondklok noodzakelijk maken.
6.7.
Het begrip buitengewone omstandigheden is in de wet of de wetsgeschiedenis .....niet gedefinieerd. Naar het oordeel van het hof is het zonder meer duidelijk dat er sprake is van buitengewone omstandigheden..... Ondanks vele (vaak vergaande) maatregelen is het Covid-19 virus nog steeds niet uitgedoofd en is dit aan het muteren in (veelal) nog besmettelijkere varianten. Het wachten is uiteindelijk op voldoende vaccinatiemogelijkheden, maar zover is het nu nog niet, terwijl bovendien onzeker is of de thans bestaande vaccins onverminderd werken bij de nieuwe varianten.
6.8.
Volgens de regering is de situatie zeer zorgelijk, omdat twee epidemiologische situaties zich naast elkaar ontwikkelen, te weten het 'oude' Covid-19 virus en de veel besmettelijkere buitenlandse varianten die naar verwachting de boventoon zullen gaan voeren. Alles op alles moet worden gezet om het aantal besmettingen zo laag mogelijk te houden en zo te voorkomen dat Nederland wordt overspoeld met een derde golf bovenop de tweede. De regering baseert zich hierbij op het OMT (met specifieke deskundigheid), dat in verband hiermee dringend adviseert tot invoering van de avondklok omdat geen gelijkwaardige alternatieven voorhanden zijn.
6.9.
Naar het oordeel van het hof mag het kabinet in beginsel op de adviezen van het OMT afgaan. Niet voor niets is dit orgaan verantwoordelijk voor het tot stand komen van het best mogelijke professionele advies over de te nemen crisismaatregelen.7 De omstandigheid dat niet exact gewogen kan worden in hoeverre de tevens dringend geadviseerde bezoekbeperking mede effect sorteert, maakt niet dat daarmee de noodzaak van de avondklok ontbreekt of is vervallen.

De Staat heeft voldoende onderbouwd dat de avondklok ook effect heeft, althans dat hij hier in redelijkheid van mag uitgaan.....".
"..... heeft nog gesteld dat het invoeren van de avondklok niet noodzakelijk is omdat het aantal besmettingen terugloopt, evenals de ziekenhuis- en IC-bezetting, terwijl het aantal besmettingen bovendien niet gelijk staat aan even zovele zieken en het om een 'vrij onschuldig' virus gaat. ..... miskent hiermee dat het OMT ondanks de verminderde druk op de zorg uitvoerig en wetenschappelijk onderbouwd heeft toegelicht dat verder ingrijpen noodzakelijk is, met name in verband met de toename van de nieuwe varianten. Dit ter voorkoming van het risico – dit is geen zekerheid en hoeft en kan ook geen zekerheid (te) zijn – van versneld oplopende ernstige besmettingen en daarmee (over)belasting van de zorg. De stelling dat de "donkere wolk" die door het OMT is geschetst "nog nooit regen heeft opgeleverd" is een miskenning van de feitelijke toestand waarin Nederland sinds ongeveer een jaar verkeert en waarvan het kabinet mag oordelen dat die zodanig is dat een verergering moet worden voorkomen....."
6.11.
"Al met al heeft de Staat daarom in redelijkheid kunnen oordelen dat er sprake was van buitengewone omstandigheden die invoering van de avondklok noodzakelijk maakten. .....
Uiteraard dienen de beginselen van proportionaliteit en subsidiariteit bij de daadwerkelijke inzet van de Wbbbg wel in acht te worden genomen. Het hof zal hierna deze aspecten toetsen.

Proportionaliteit en subsidiariteit
6.12.
Niet in geschil is dat met de invoering van de avondklok diverse grondrechten worden beperkt, die onder meer zijn verankerd in internationale verdragen. Het gaat daarbij om het recht op bewegingsvrijheid (artikel 2 Vierde Protocol EVRM), het recht op eerbiediging van de persoonlijke levenssfeer (artikel 8 EVRM en artikel 10 Grondwet - Gw) en indirect de vrijheid van vergadering, betoging en het belijden van godsdienst en levensovertuiging (artikel 9 en artikel 10 EVRM en artikel 6 en artikel 9 Gw).
6.13.
Deze grondrechten bieden ruimte voor een inperking daarvan (onder meer) als dat noodzakelijk is voor de bescherming van de volksgezondheid. De Staat is tot deze bescherming verplicht op grond van artikel 22 Gw en de artikelen 2 en 8 EVRM. Een dergelijke inperking is mogelijk voor zover deze (i) een legitiem doel dient, (ii) bij de wet is voorzien en (iii) noodzakelijk is in een democratische samenleving. In dat laatste criterium ligt besloten dat de inperking van de grondrechten proportioneel moet zijn en dat er geen andere (lichtere) middelen moeten zijn om het beoogde doel te verwezenlijken. De Staat heeft hierbij een grote beoordelingsvrijheid (a wide margin of appreciation).
6.14.
Vast staat dat de inperking (i) een legitiem doel dient en (ii) bij wet is voorzien. De Staat heeft aangevoerd (iii) dat de maatregel ook proportioneel is. .....
6.15.
Naar het oordeel van het hof is, gelet op de klemmende situatie waar de Staat blijkens het voorgaande vanuit mocht gaan, de maatregel van deze avondklok (iii) proportioneel en voldoet deze ook aan de eisen van subsidiariteit. Afwachten hoe de situatie zich ontwikkelt, ...heeft de Staat in redelijkheid niet willen en hoeven doen. ...."

5.12.3 De kantonrechter acht op grond van de hiervoor genoemde wetgeving en rechtspraak het volgende kader van belang bij de beoordeling:

- er moet sprake zijn van buitengewone omstandigheden;
- de beginselen van proportionaliteit en subsidiariteit moeten in acht genomen worden bij het doorvoeren van maatregelen waarbij grondrechten worden beperkt;
- de civiele rechter, en zeker de rechter in kort geding, moet zich terughoudend opstellen bij de beoordeling van de keuzes die de gedaagde binnen de grenzen van zijn beoordelings- en beleidsvrijheid maakt, omdat de vraag welke maatregelen moeten worden getroffen ter bestrijding van de coronacrisis en of die maatregelen proportioneel en subsidiair zijn primair moet worden beantwoord door de regering en de wetgevende macht; alleen als het evident is dat de gedaagde bij het beperken van de grondrechten onjuiste keuzes maakt, dus in redelijkheid niet voor het gevoerde beleid heeft kunnen kiezen, is er plaats voor rechterlijk ingrijpen.

5.13 De kantonrechter overweegt dat er sprake is van buitengewone omstandigheden, evenals in de casus van het hiervoor bedoeld vonnis van het Hof. Daarom was gedaagde genoodzaakt de uitzonderingstoestand af te kondigen. Beoordeeld moet worden of de beginselen van proportionaliteit en subsidiariteit in acht zijn genomen en of er sprake is van een situatie waarbij gedaagde bij het beperken van de grondrechten onjuiste keuzes heeft gemaakt waarbij in redelijkheid niet voor het gevoerde beleid gekozen had kunnen worden.

5.14 De kantonrechter overweegt dat de stellingen van eisers hierop neerkomen dat gedaagde onjuiste keuzes heeft gemaakt. De twee gronden die zij daarbij aanvoeren staan in verband met de proportionaliteit. Zij stellen in hun grondslag dat inbreuk op grondrechten slechts gerechtvaardigd zou zijn als vaststaat dat een dergelijke inbreuk strikt noodzakelijk, proportioneel en effectief is en niet schadelijk is voor de gezondheid.

5.15.1 Eisers stellen allereerst dat het dragen van mond- en neuskapjes niet effectief is. Zij stellen dat de verplichting om die reden niet doorgevoerd had mogen worden. In hun stellingen wijzen zij erop dat nu de maatregel niet effectief is, deze niet mocht worden doorgevoerd, temeer niet nu deze maatregel een inbreuk vormt op de grondrechten. Deze stellingen betreffen het proportionaliteitsbeginsel.

5.15.2 De gedaagde heeft op deze grond verweer gevoerd. Zij heeft aangevoerd dat het wel is gebleken dat de maatregel effectief is. Om haar verweer te onderbouwen heeft zij acht en twintig producties overgelegd waaronder een publicatie van de Centers for Disease Control and Prevention van november 2020 waarin is geconcludeerd dat verschillende onderzoeken leiden tot de slotsom dat het gebruik van mond- en neuskapjes leidt tot de vermindering van de spreiding van het Covid-19 virus en een tussentijdse richtlijn van de WHO van 1 december 2020 (pagina 8 en verder) waarin wordt geadviseerd over te gaan tot het dragen van maskers in de gevallen van "community or cluster transmission".

5.15.3 De kantonrechter overweegt dat enerzijds eisers, blijkens de opsomming onder de grondslag, circa dertien onderzoeken hebben aangevoerd voor het onderbouwen van hun stelling. Anderzijds heeft gedaagde haar stelling onderbouwd met een achtentwintigtal publicaties, eveneens resultaten van wetenschappelijk onderzoek. De kantonrechter overweegt dat het evident is dat er in de wetenschappelijke wereld verschillende meningen bestaan over de effectiviteit en de gevolgen van het gebruik van mond- en neuskapjes. De kantonrechter overweegt dat, ondanks de meningsverschillen, uit het door gedaagde gevoerd verweer en de overgelegde producties, voldoende aannemelijk is geworden dat de inzichten van de WHO en andere internationale en nationale public health deskundigen, en het Outbreak Management

Team, op wiens adviezen de besluiten van de gedaagde zijn gebaseerd, tot de conclusie leiden dat de maatregel wel effectief is. Zoals ook in de hiervoor genoemde rechtspraak is overwogen, is de kantonrechter van oordeel dat gedaagde in beginsel op de adviezen van het Outbreak Management Team mag afgaan. De gedaagde heeft voldoende onderbouwd dat de maatregel effect heeft, althans dat zij hier in redelijkheid van mag uitgaan.

5.16.1 Eisers stellen ten tweede dat het dragen van mond- en neuskapjes schadelijk is voor de gezondheid van burgers, zowel fysiek als psychisch. Daardoor zou de verplichting om mond- en neuskapjes te dragen niet als maatregel mogen zijn doorgevoerd. Zij hebben om deze stelling te onderbouwen verwezen naar verschillende onderzoeken met betrekking tot het effect van de mondkapjes op het zuurstof- en kooldioxidegehalte in het bloed en het verhogen van het risico van virale en bacteriële besmettingen.

5.16.2 De gedaagde heeft ook op deze grond verweer gevoerd. Zij heeft aangevoerd dat het niet is gebleken dat het dragen van een mond- en neuskap een noemenswaardig effect heeft op het zuurstof- en kooldioxidegehalte in het bloed. Verder heeft zij aangevoerd dat er weliswaar ongemakken zijn gebleken doch dat deze ongemakken niet opwegen tegen het positieve effect dat het dragen van mond- en neuskapjes heeft op het indammen van de verspreiding van de pandemie en de daarmee gepaard gaande complicaties en mortaliteit. Om die reden hebben de WHO en andere internationale en nationale public health deskundigen, en het Outbreak Management Team, geadviseerd het dragen van een mond- en neuskap wel te verplichten. Ook ten aanzien van deze weren zijn door gedaagde enkele publicaties met onderzoeksresultaten overgelegd waaronder een publicatie van de American Thoracic Society waarin resultaten van een onderzoek zijn opgenomen betreffende de fysiologische effecten van het gebruik van mond- en neuskapjes. In die publicatie is de conclusie opgenomen dat er geen noemenswaardige gezondheidsproblemen ontstaan voor wat betreft het zuurstof- en kooldioxidegehalte in het bloed bij het dragen van een mond- en neuskap. Ook is in die publicatie ingegaan op het feit dat er geen redenen zijn om bezorgd te zijn over de veiligheid van het gebruik van de mond- en neuskapjes. Voorts is overgelegd een publicatie van de International Journal of Environmental Research en Public Health waarin is ingegaan op de fysiologische effecten van het dragen van een mond- en neuskap, waaronder het ontstaan van hoofdpijn, pijn aan het gezicht, acne, jeuk en huiduitslag. In die publicatie wordt echter geconcludeerd dat de hiervoor genoemde effecten veelal kunnen worden vermeden door een ander soort mond- en neuskap te gebruiken. In het artikel wordt gesteld dat het voordeel dat bereikt wordt door het gebruik van mond- en neuskapjes veel zwaarder wegen dan de nadelen die zijn genoemd. In de tussentijdse richtlijn van de WHO van december 2020 is op pagina 6 ingegaan op de nadelige effecten van het gebruik van mond- en neuskapjes en is op pagina 5 ingegaan op maatregelen die getroffen kunnen worden om de nadelige gevolgen van het dragen van een mond- en neuskap te vermijden.

5.16.3 De kantonrechter overweegt dat uit het door gedaagde gevoerd verweer en de overgelegde producties, voldoende aannemelijk is geworden dat de inzichten van de WHO en andere internationale en nationale public health deskundigen, en het Outbreak Management Team, op wiens adviezen de besluiten van de gedaagde zijn gebaseerd, tot de conclusie leiden dat er geen sprake is van zodanige nadelige gevolgen op de gezondheid door het dragen van een mond- en neuskap, dat de maatregel niet had mogen worden doorgevoerd. Evenals hiervoor overwogen, is de kantonrechter van oordeel dat gedaagde in beginsel op de adviezen van het Outbreak Management Team mag afgaan. De gedaagde heeft voldoende onderbouwd dat de maatregel niet leidt tot zodanige nadelige effecten voor de gezondheid van de dragers van een mond- en neusbedekking, dat de maatregel niet had mogen worden doorgevoerd, althans dat zij hier in redelijkheid van mag uitgaan.

5.17.1 De kantonrechter overweegt dat op grond van het hiervoor overwogene, de grondslag van eisers voor wat betreft de punten 1, 2 en 3 niet aannemelijk is geworden, met name de grondslag dat de maatregel niet had mogen worden doorgevoerd omdat de maatregel grondrechten beperkt terwijl de maatregel niet effectief is en schadelijk is voor de gezondheid.

5.17.2 De kantonrechter zal het deel van de grondslag, genoemd onder punt 4 van de grondslag, met betrekking tot de misleiding van de samenleving niet beoordelen nu dat deel van de grondslag niet valt onder de uitzondering op de onschendbaarheid van wetten zoals genoemd in artikel 80 lid 2 van de Grondwet.

5.18 De kantonrechter zal op grond van het voorgaande de gevraagde voorzieningen weigeren.

5.19 De kantonrechter zal de overige stellingen en weren van partijen niet verder bespreken nu deze niet langer relevant zijn en eisers, als de in het ongelijk gestelde partij, veroordelen in de proceskosten.

6. De beslissing

6.1 Weigert de gevraagde voorzieningen;
6.2 Veroordeelt eisers in de kosten van dit geding aan de zijde van gedaagde gevallen en tot aan deze uitspraak begroot op nihil.

Aldus gewezen en uitgesproken door mr. A.C. Johanns, kantonrechter in kort geding, ter openbare terechtzitting van het kantongerecht in het eerste kanton te Paramaribo van woensdag 24 maart 2021, in tegenwoordigheid van de griffier.

w.g. O. Apai w.g. A.C. Johanns

EISERS IN KORT GEDING ZIJN IN PERSOON BIJ DE UITSPRAAK TER TERECHTZITTING VERSCHENEN EN DE GEDAAGDE IS BIJGESTAAN DOOR HAAR GEMACHTIGDEN VERSCHENEN.

Voor eensluidend afschrift
De Griffier,
(Sub)
24/3/2021
Mr. O.S. Apai

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Effective public health measures to mitigate the spread of COVID-19: a systematic review

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Abstract

Background: In December 2019, a novel coronavirus (2019-nCoV) was recognized in Wuhan, China. It was characterised by rapid spread causing a pandemic. Multiple public health interventions have been implemented worldwide to decrease the transmission of the 2019 novel coronavirus disease (COVID-19). The objective of this systematic review is to evaluate the implemented public health interventions to control the spread of the outbreak of COVID-19. **Methods:** We systematically searched PubMed, Science Direct and MedRxiv for relevant articles published in English up to March 16, 2021. We included quasi experimental studies, clinical trials, cohort studies, longitudinal studies, case-control studies and interrupted time series. We included the studies that investigated the effect of the implemented public health measures to prevent and control the outbreak of 2019 novel coronavirus disease (COVID-19).

Results: The database search using the predefined combinations of Mesh terms found 13,497 studies of which 3595 in PubMed, 7393 in Science Direct 2509 preprints in MedRxiv. After removal of the duplicates and the critical reading only 18 articles were included in this systematic review and processed for data extraction.

Conclusions: Public health interventions and non-pharmaceutical measurements were effective in decreasing the transmission of COVID-19. The included studies showed that travel restrictions, borders measures, quarantine of travellers arriving from affected countries, city lockdown, restrictions of mass gathering, isolation and quarantine of confirmed cases and close contacts, social distancing measures, compulsory mask wearing, contact tracing and testing, school closures and personal protective equipment use among health workers were effective in mitigating the spread of COVID-19.

Keywords: Public heath interventions, Non-pharmaceutical measures, Prevention, COVID-19, Systematic review

Introduction

In the twenty-first century, two highly pathogenic human coronaviruses (HCoVs) severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) emerged from animal reservoirs to cause global epidemics. In December 2019, yet another pathogenic HCoV, 2019 novel coronavirus (2019-nCoV), was recognized in Wuhan, China, and has caused serious illness and death [1]. This novel coronavirus is characterised by rapid spread and high contagiousness [2] which caused a pandemic as it was spreading rapidly between and within the countries. As of 18 March 2021 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused more than 121.8 million cases and 2.69 deaths [3]

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affecting 221 countries and territories. Since the beginning of the COVID-19 pandemic several public health interventions have been implemented worldwide to reduce the transmission of the SARS-CoV-2. In previous experiences, like the 1918–19 H1N1 influenza pandemic where no treatments or vaccines were available to treat or prevent the disease multiple non-pharmaceutical interventions were successful at reducing case numbers and have shown to be effective when implemented early in the epidemic. Those interventions include travel bans and restrictions, schools and workplace closures, isolating infected persons, quarantine of exposed persons, social distancing and cancellation of mass gathering events. Those interventions have shown to be effective ways to respond to the outbreak when implemented early in the epidemic [4–9]. However the effectiveness of those interventions whether applied alone or simultaneously still unclear and results from previous modelling studies are inconsistent [10].

Within this systematic review we aimed to evaluate the public health interventions and the non-pharmaceutical control measures that have been implemented worldwide to mitigate and control the spread of the outbreak of 2019 novel coronavirus disease (COVID-19).

Methods

Search strategy and selection criteria

We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11]. The protocol of this systematic review was published on PROSPERO (registration number CRD42020196018). Given the nature of this research study no approval by an institutional review board was necessary. We systematically searched PubMed, Science Direct and MedRxiv for relevant articles published in English up to March 16, 2021 using the following combinations of terms in PubMed: ((("public health"[MeSH Terms]) OR "preventive medicine"[MeSH Terms])) AND "covid 19"[MeSH Terms]; (health knowledge, attitudes, practice [MeSH Terms]) AND covid 19[MeSH Terms]; ((("covid 19"[MeSH Terms]) AND ("epidemiology"[MeSH Terms])) OR (public health interventions [Title/Abstract])) OR (epidemiological assessment [Title/Abstract]); ((("covid 19"[MeSH Terms]) AND ("social distancing"[Title/Abstract])) OR ("quarantine"[MeSH Terms])) OR ("isolation"[Title/Abstract]); ("covid 19"[MeSH Terms]) AND ("contact tracing"[MeSH Terms]); ("covid 19"[MeSH Terms]) AND ("lockdown"[-Title/Abstract]). In Science Direct and MedRxiv we used the following terms: "Public Health measures" and "covid-19".

Study eligibility and quality assessment

We included articles published only in English language up to March 16, 2021, clinical trials, quasi experimental studies, cohort studies, longitudinal studies, case-control studies, and interrupted time series. The studies that investigated the effect of the non-pharmaceutical interventions such as social distancing, lockdown, quarantine, mobility and travel restrictions, border control measures, contact tracing, isolation of cases that have been implemented to mitigate, prevent and control the outbreak of 2019 novel coronavirus disease (COVID-19). We excluded articles published in a language other than English; narrative literature reviews, policy reviews, case studies, case reports, case series, cross-sectional studies, ecological studies, commentaries, editorials, letters, point of views, simulation studies, modelling studies, prediction studies, qualitative studies,systematic reviews and meta-analysis.

The database search was conducted by one author (AI) who did the tiles and abstracts screening in order to identify the eligible studies for full text review with referral to (MJ) and (DW). Both authors (AI, DW) did the full text review of the studies that potentially met eligibility criteria and checked their relevance with referral to a third author (MJ) in case of discordance. Any discrepancy between the reviewers was resolved by discussion.

Data analysis

Two authors (AI, DW) did the data extraction using a standardized form to collect the relevant data from each article. The form included study identification features (authors, article title, country of origin), study characteristics (aim of the study, study design), characteristics of the studied population, public health interventions that has been implemented (description of the intervention(s) and control(s) if applicable), outcomes and authors' conclusions. The included studies were evaluated for quality and risk of bias using the Effective Public Health Practice Project (EPHPP) quality assessment tool quantitative studies [12]. All studies were independently assessed for quality by two reviewers (AI, DW), with disagreements resolved by discussion until full consensus was reached with referral to (MJ) and (ZN). Level of evidence and grade of recommendation of the included studies were assessed according to the Scottish Intercollegiate Guidelines Network (SIGN) system [13].

Results

The database search in PubMed and Science Direct using the predefined combinations of Mesh terms found 13,497 studies of which 3595 in PubMed, 7393 in Science Direct 2509 preprints in MedRxiv. After removal of the duplicates 12,433 articles remained. During the

screening stage one article was excluded as it was retracted and 12,139 records were excluded on basis of title and abstract. After the critical reading of the 293 remaining articles, 275 articles were excluded seeing that they didn't meet the eligibility criteria and only 18 articles were included in this systematic review and processed for data extraction. Fig. 1 summarized the described outcomes. The characteristics of the included studies and the main results were summarized Table 1 including the following items: authors, country, study design, objective, methods and main outcomes. For the quality assessment results the quality of 14 (77.77%) included studies [14–16, 19–21, 23–29, 31] was moderate, the quality of two studies [18, 22] was strong and the quality was weak for the two remaining studies [17, 30] (Table 2). As for the results of the level of evidence and grade of recommendation assessment, six studies had low level of evidence and low grade of recommendation [16, 17, 19, 21, 24, 30]. Ten studies had moderate level of evidence and low grade of recommendation [14, 15, 20, 22, 23, 25–29], one study had moderate level of evidence and moderate grade of recommendation [18] and only one study had high level of evidence and high grade of recommendation [31] (Table 3). Three studies [16, 22, 26] have found that travel entry restrictions and bans, borders control measures and quarantine of travellers especially the ones arriving from affected countries along with other interventions was effective in reducing the spread of COVID-19. Seven studies [14, 15, 23, 24, 27, 30, 31] have shown that city lockdown, stay at home orders, traffic suspension and restrictions of mass gathering are strongly associated with reduced growth rate of COVID-19 confirmed cases and reduction in the epidemic growth. Moreover in their study Salvatore M et al. [23] found that lockdown was partly effective due to state level variations which should be considered in

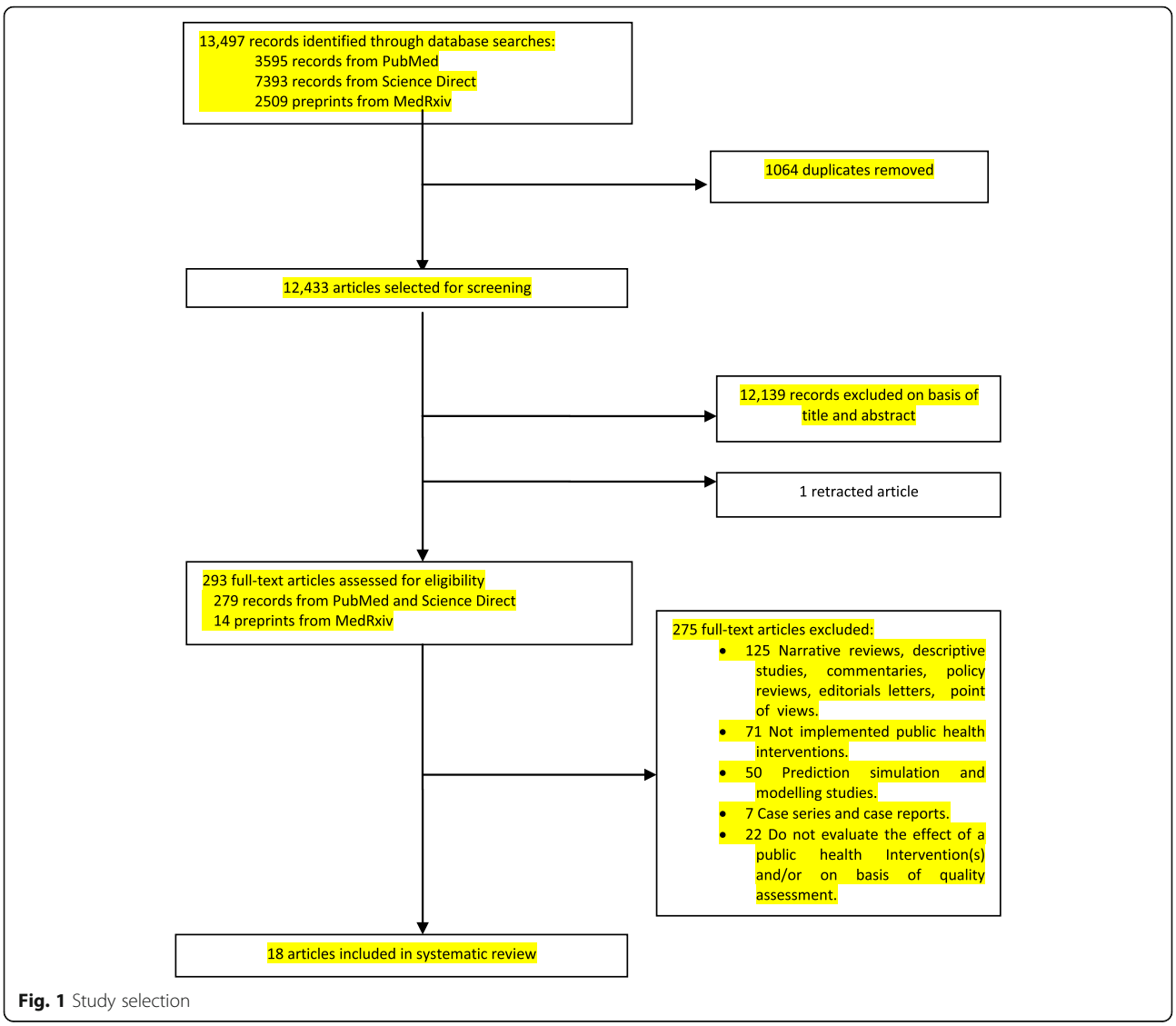

Fig. 1 Study selection

Table 1 Characteristics of included studies and main outcomes

Authors, country	Study design	Objective	Methods	Main outcomes
Pan A et al [14]**, China**	Interrupted time series	Evaluate the association of several public health interventions on the control of COVID 19 outbreak over 5 periods according to key interventions.	32, 583 laboratory-confirmed COVID-19 cases. Time periods and Interventions: 1st period: time before January 10, 2020 without specific intervention. 2nd period: January 10 to 22, 2020, no strong intervention, massive migration, first human-to-human transmission on January 20 and hospitals started to be crowded.3rd period: between January 23 and February 1, 2020 city lockdown, traffic suspension, home quarantine, social distancing measures including compulsory mask wearing in public places and cancellation of social gatherings.4th period: February 2 to 16, 2020 intensified measures with centralized quarantine and treatment, improved medical resources and stay at home policy.5th period: February 17th to March 8th 2020, centralized quarantine and community universal survey. Rt: effective reproduction number is the mean number of secondary cases generated by typical case at primary case is an indicator that measures SARS-CoV-2 before and after the intervention.	The daily confirmed case rate per million people increased from 2.0 (95% CI, 1.8–2.1) before January 10, to 45.9 (95% CI, 44.6–47.1) in the 2nd period, to 162.6 (95% CI, 159.9–165.3) in the 3rd period and then decreased to 77.9 (95% CI, 76.3–79.4) in the 4th period. After February 16, it decreased to 17.2 (95% CI, 16.6–17.8). Rt varied in the first period, gradually increased in the 2nd period with a peak of 3.82 on January 24, and then declined. It fell below 1.0 on February 6, 2020, and further decreased to below 0.3 on March 1, 2020.
Wang K-W et al [15]**, China**	Interrupted time series	Estimate the effects of wartime control measures after early imported COVID-19 cases in Jiangsu from Hubei Province.	Time series observations from January 2 2 to February 18, 2020. Wartime control measures: Collect estimate, report and release emergency information every day. Put cities with epidemic on lockdown to limit population mobility. Restrict or stop crowd gathering. Migrant management such as on-site isolation for confirmed COVID-19 cases and contact tracing. Traffic health quarantine.	From January 22to February 18, 2020 the number of confirmed cases increased from 1 to 631. No new confirmed cases were identified after February 18th.
Cowling BJ et al [16]**, Hong Kong**	Cohort Study	Quantify behavioural changes in population of Hong Kong during the COVID-19 outbreak and describe effect of public health interventions on COVID-19 and influenza transmission.	Public health interventions: Travel and border entry restrictions and bans, testing, tracing, flexible working arrangements, school closures, quarantine and isolation orders that has been issued for cases and their contacts and travellers arriving from affected countries, cancellation of many conferences, some religious organizations and local mass gatherings and social distancing. Rt: effective reproduction number, mean number of secondary infections that result from a primary case of infection at time t.	Public health interventions and population behaviour changes such social distancing and personal protective measures implemented in Hong Kong since January 2020 is associated with reduced spread of COVID-19. Contact tracing, quarantine and social distancing played an important role in suppressing transmission adding to case identification with isolation.

Table 1 Characteristics of included studies and main outcomes *(Continued)*

Authors, country	Study design	Objective	Methods	Main outcomes
Jüni P et al [17]**, 144 geopolitical areas**	Cohort Study	Determine whether epidemic growth is associated with climate or public health interventions.	Prospective cohort study of 144 geopolitical areas with at least 10 cases and local transmission excluding China, South Korea, Iran and Italy. Determination of the association between epidemic growth and latitude, temperature, humidity, school closures, restrictions of mass gatherings and measures of social distancing during an exposure period from March 7 to 13, 2020) using weighted random-effects regression.	Few or no associations of epidemic growth with latitude and temperature, weak negative association with relative and absolute humidity. Strong associations for implemented public health interventions.
Wang J et al [18]**, China**	Longitudinal Study	Estimate the incidence of 2019nCoV infection among people who are under home quarantine in Shenzhen province, China.	Stratified multistage random sampling method has been used to recruit participants and collect demographic information and laboratory results of people under home quarantine. Descriptive analysis was conducted to estimate the basic characteristics and to calculate the Incidence of novel coronavirus (2019-nCoV) infection among people under home quarantine. In order to report the outcomes of categorical variables proportions and frequencies were used. Mean and range were used to express continuous variables.	Testing for a total of 2004 people was conducted and three of these tested positive for 2019nCoV.The incidence of COVID-19 in the sample was 1.5‰ (95% CI: 0.31‰–4.37‰). None of the three patients had obvious symptoms during the time of home quarantine. Also, they did not report any history of contacts with confirmed cases. Home quarantine has been effective in preventing the early transmission of COVID-19.
Cheng VC-C et al [19]**, China**	Cohort Study	Assess the effect of community-wide mask usage to control COVID-19 in Hong Kong Special Administrative Region (HKSAR). Analyze the incidence of COVID19 in geographical areas with or without community-wide masking.	During the first 100 days epidemiological analysis was performed for confirmed cases especially the ones that acquired COVID-19 during mask-off and mask-on settings. The incidence of COVID-19 per million populations in HKSAR with community-wide masking was compared to that of non-mask-wearing countries which are comparable with HKSAR in terms of population density, healthcare system, BCG vaccination and social distancing measures but not community-wide masking.	Epidemiological measures by the HKSAR government: border controls from day 36, followed by imposing home quarantine order for 14 days to all entrees from mainland China from day 40. Then, the quarantine order was progressively imposed to all entrees into HKSAR from day 80. All entrees were compulsorily tested for SARS-CoV-2 from day 100. In addition to isolation of confirmed cases, contact tracing and quarantine, closure of affected or high risk premises, and social distancing measures such as home-office and school closure were instituted. 961 cases of COVID-19 were confirmed in HKSAR on day 100. From day 31 to 71 there were 111 cases predominantly local cases and from day 72 there were 840 cases predominantly imported cases with local clusters of cases. Among the 961 confirmed cases, there were 11 clusters of 113 persons that were directly engaged in mask-off activities. There were only three clusters involving 11 persons engaged in mask-on settings at the workplace there were significantly more COVID-19 clusters involving mask-off settings.

Table 1 Characteristics of included studies and main outcomes *(Continued)*

Authors, country	Study design	Objective	Methods	Main outcomes
Thu TPB et al [20]**, The U.S., Spain, Italy, The U. K, France, Germany, Russia, Turkey, Iran and China.**	Longitudinal Study	Present the effect of social distancing interventions on the spread of COVID-19 in the cases of 10 highly infected countries.	The relationships between the social distancing interventions and the statistics of COVID-19 confirmed-cases and deaths were analyzed in order to elucidate the effectiveness of the social distancing interventions on the spread of COVID-19 in 10 highly infected countries including The U.S., Spain, Italy, The U.K., France, Germany, Russia, Turkey, Iran and China.	It took between 1 to 4 weeks since the point of highest level of social distancing measures promulgation until the numbers of daily confirmed-cases and daily deaths showed signs of decreasing. The effectiveness of the social distancing measures on the spread of COVID-19 was different between the 10 studied countries. This variation is due to the difference in the level of promulgated social distancing measures and in the difference in the COVID-19 spread situation at the time of promulgation in these countries. The growth rate of daily confirmed-cases at the time of promulgating the social distancing measures partly influences the decline rates of daily confirmed-cases after the spread reached its peak.
Seong H et al [21]**, South Korea**	Cohort Study	Compare the epidemiologic features of the second and third waves of the coronavirus disease 2019 (COVID-19) pandemic in South Korea.	COVID-19 data were collected between 6 May and 30 December 2020. The degree of social activity was estimated using an Internet search trend analysis program for leisure-related keywords, including 'eating-out', 'trip' and 'get directions' (transportation). Demographics, transmission chains, case fatality rates, social activity levels and public health responses were compared between the second (13 August–18 September 2020) and third (4 November 2020–present) waves.	The 3rd wave was characterized by delayed strengthening of social distancing measures (3 vs.15 days), longer duration (36 vs. > 56 days) and a higher case fatality rate (0.91% vs.1.26%) compared to the 2nd WAVE. There were significant differences in transmission chains between the two waves ($P < 0.01$). In comparison with the second wave, the proportion of local clusters (24.8% vs. 45.7%) was lower in the third wave, and personal contact transmission (38.5% vs. 25.9%) and unknown routes of transmission (23.5% vs. 20.8%) were higher in the third wave. In conclusion early and timely interventions with strengthened social distancing policies should be implemented to suppress and control the COVID-19 pandemic effectively.
Lam HY et al [22]**, Hong Kong**	Longitudinal Study	Review the epidemiology of the confirmed COVID-19 cases reported between January to May 2020 Assess the overall effectiveness of the various public health Interventions.	Description and comparison of the epidemiological and clinical characteristics of the cases recorded in different phases of the epidemic. Using the changes in the daily number of confirmed cases and the interval from symptom onset to hospital admission the effectiveness of the public health interventions implemented were reviewed.	Several public health interventions such as enhanced surveillance, border control, and social distancing, were introduced in phases in response to the rapid spread of the coronavirus locally and globally. Overall, the combination of public health interventions taken in Hong Kong were associated with a stabilization of case numbers and absence of a community-wide COVID-19 outbreak during the 4.5 m following the reporting of the first case.

Table 1 Characteristics of included studies and main outcomes *(Continued)*

Authors, country	Study design	Objective	Methods	Main outcomes
Salvatore M et al [23]**, India**	Longitudinal Study	Evaluate the effect of four-phase national lockdown from March 25 to May 31 in response to the COVID-19 pandemic in India.	Participants Confirmed COVID-19 cases nationally and across 20 states that accounted for > 99% of the current cumulative case counts in India until 31 May 2020. Exposure Lockdown (non-medical intervention).	Results The estimated effective reproduction number R for India was 3.36 (95% CI 3.03 to 3.71) on 24 March, whereas the average of estimates from 25 May to 31 May stands at 1.27 (95% CI 1.26 to 1.28). Patterns of change over lockdown periods indicate the lockdown has been partly effective in slowing the spread of the virus at the national level. However, there exist large state-level variations and identifying these variations can help in both understanding the dynamics of the pandemic and formulating effective public health interventions.
Meo SA et al [24]**, 27 countries**	Cohort Study	Assess the impact of 15 days before, 15 days during, and 15 days after the lockdown on the the prevalence and mortality rate in 27 countries during COVID-19 pandemic.	27 countries were randomly selected and the information on the trends in the prevalence and mortality due to COVID-19 pandemic in was taken from World Health. Organization and lockdown data were obtained from studied countries and their ministries. Analysis of the impact of lockdown for 15 days before, 15 days during, and 15 days after the lockdown on the prevalence and mortality due to the COVID-19 pandemic in 27 countries.	Daily cases of SARS-COV-2 and the growth factor results declined and the growth rate per day both declined to an impressive negative level in the case of the growth rate per day by the time period of 15 days after the lockdown period, these two metrics of infection spreading did not fall sufficiently to control the pandemic. Lockdown policies should adhere to optimizing behaviour such as social distancing measures and community wide mask wearing that can affect spreading the COVID-19 pandemic. Lockdown alone will not be effective.
Xu T-L et al [25]**, China**	Longitudinal Study	Summarize the containment measures taken in China, as well as the effect of the practices on SARS-CoV-2 transmission.	The measures taken by the governments was tracked and sorted on a daily basis from the websites of governmental authorities. The measures were reviewed and summarized by categorizations, figures and tables. The population shift levels, daily local new diagnosed cases, daily mortality and daily local new cured cases were used for measuring the effect of the interventions.	Practices were categorized into active case surveillance, rapid case diagnosis and management, strict follow-up and quarantine of persons with close contacts. Together with these measures, daily local new diagnosed cases, and mortality rates were decreased and the daily local new cured cases were increased in China. China's practices are effective in controlling transmission of SARS-CoV-2.
Zeng K et al [26]**, United States, Spain, and Italy, with Taiwan, South Korea, and Singapore**	Longitudinal study	Compare the measures taken against the spread of COVID-19 in the United States, Spain, and Italy, with Taiwan, South Korea, and Singapore, especially related to the use of digital tools for contact tracing.	COVID-19 death rate information were taken from the European Centre for Disease Prevention and Control (ECDC), accessed through the Our World in Data database and were evaluated based on population size per 100,000 people from December 31, 2019, to September 6, 2020. All policies and interventions were obtained from their respective governmental websites.	Strong association between lower death rates per capita and countries that implemented early mask use and strict border control measures that included mandatory quarantine using digital tools. There was a significant difference in the number of deaths per 100,000 when comparing Taiwan, South Korea, and Singapore with the United States, Spain, and Italy. These findings suggest that early intervention with the use of digital tools had a strong correlation with the successful containment of COVID-19.

Table 1 Characteristics of included studies and main outcomes *(Continued)*

Authors, country	Study design	Objective	Methods	Main outcomes
				Infection rates and subsequent deaths in Italy, Spain, and the United States could have been much lower with early community mask wearing and more importantly timely border control interventions using modern digital tools.
Wong CKH et al [27]**, 54 countries and 4 epicentres of the COVID-19 pandemic (Wuhan, New York State, Lombardy, and Madrid),**	Longitudinal study	Describe and evaluate the impact of national containment interventions and policies such as stay-at-home orders, curfews, and lockdowns on decelerating the increase in daily new cases of COVID-19 rates in 54 countries and 4 epicentres of the pandemic worldwide.	The effective dates of the national containment interventions were reviewed of 54 countries and 4 epicenters of the COVID-19 pandemic (Wuhan, New York State, Lombardy, and Madrid) and cumulative numbers of confirmed COVID-19 cases and daily new cases provided by health authorities were searched. Data were drawn from an open, crowdsourced, daily-updated COVID-19 data set provided by Our World in Data. Moreover the trends in the percent increase in daily new cases from 7 days before to 30 days after the dates on which containment measures went into effect by continent, World Bank income classification, type of containment interventions, effective date of containment interventions and number of confirmed cases on the effective date of the containment measures were examined as well.	122,366 patients with confirmed COVID-19 infection from 54 countries and 24,071 patients from 4 epicentres on the effective dates on which stay-at-home orders, curfews, or lockdowns were implemented from January 23 to April 11, 2020 were included in this study. Stay-at-home, curfew, and lockdown interventions commonly started in countries with approximately 30, 20%, or 10% increases in daily new cases. All three interventions were found to lower the percent increase in daily new cases to < 5 within one month. 20% had an average percent increase in daily new cases of 30–49 over the seven days prior to the implementation of the containment measures; the percent increase in daily new cases in these countries was curbed to 10 and 5 a maximum of 15 days and 23 days after the implementation of containment interventions, respectively. Different national containment interventions were associated with a decrease in daily new cases of confirmed COVID-19 infection. Stay-at-home orders, curfews, and lockdowns curbed the percent increase in daily new cases to < 5 within a month.
Siedner MJ et al [28]**, USA**	Longitudinal study	Estimate the change in COVID-19 case growth before and after implementation of statewide social distancing measures in the US.	The primary exposure was time before (14 days prior to and through 3 days after) versus after (beginning 4 days after, to up to 21 days after) implementation of the first state-wide social distancing interventions. State-wide restrictions on internal movement were examined as a secondary exposure. The COVID-19 case growth rate was the primary outcome. The COVID-19-attributed mortality growth rate was the secondary outcome.	Statewide social distancing interventions were associated with a decrease in the COVID-19 case growth rate that was statistically significant. Statewide social distancing interventions were also associated with a decrease in the COVID-19-attributed mortality growth rate beginning 7 days after implementation; however this decrease was no longer statistically significant by 10 days.
Krishnamachari B et al [29]**, USA (preprint)**	Cohort Study	Examine the effects of government implemented social distancing measures on the cumulative incidence rates of COVID-19 in the United States on a state level and in the 25 most populated cities	Assessed social distancing variables: days to closing of non-essential business; days to stay home orders; days to restrictions on gathering, days to restaurant closings and days to school closing. Using negative binomial	The effect of social distancing interventions may differ between states and cities and between locations with different population densities. Individual approaches are needed to containment of an epidemic, with an awareness of their own

Table 1 Characteristics of included studies and main outcomes *(Continued)*

Authors, country	Study design	Objective	Methods	Main outcomes
			regression, adjusted rate ratios and 95% confidence intervals were calculated in order to compare two levels of a binary variable: "above median value," and "median value and below" for days to implementing a social distancing interventions. For city level data, the effects of these social distancing variables were assessed as well in high (above median value) vs low (median value and below) population density cities. For the state level analysis, days to school closing was associated with cumulative incidence, with an adjusted rate ratio of 1.59 (95% CI:1.03,2.44), $p = 0.04$ at 35 days.	structure in terms of crowding and socio-economic variables.
Singh BB et al [30]**, India (preprint)**	Longitudinal study	Evaluation of the public health interventions using the effective reproduction number (Rt), in key lockdown periods in India.	Laboratory-confirmed COVID-19 infections rates per day and effective reproduction number (Rt) were estimated for 4 periods (Pre-lockdown and Lockdown Phases 1 to 3) according to nationally implemented phased interventions. Adoption of these measures was estimated using Google mobility data. Estimates at the national level and for 12 Indian states most affected by COVID-19 are presented. Using data are publicly available from Google a domain-specific mobility index was constructed using India's mobility report (Google Inc., Mountain View, CA, USA). domain-specific mobility index was constructed for the country and 12 Indian states.	Median mobility in India decreased in all contact domains, with the lowest being 21% in retail/recreation (95% CI 13–46%), except home which increased to 129% (95% CI 117–132%) compared to the 100% baseline value. The Indian government imposed strict contact mitigation, followed by a phased relaxation, which slowed the spread of COVID-19 epidemic progression in India.
Kepp KP et al [31]**, Denmark (preprint)**	Quasi experimental study	Analyse the unique case-controlled epidemiological dataset arising from the selective lockdown of parts of Northern Denmark, but not others, as a consequence of the spread of mink-related mutations in November 2020.	A quasi-natural experiment in the Danish region of Northern Jutland. 7 of the 11 municipalities of the region went into extreme lockdown in early November after the discovery of mutations of Sars-CoV-2 while the four other municipalities retained the moderate restrictions of the remaining country. Incidentally, the infection numbers in the two groups were compared.	While infection levels decreased, they did so before lockdown was effective. Infection numbers decreased as well in other municipalities without mandates. Control of infection pockets possibly together with voluntary social behaviour was apparently effective before the mandate which explains why the infection decline occurred before and in both the mandated and non-mandated areas. The findings of this study suggest that efficient infection surveillance and voluntary compliance make full lockdowns unnecessary at least in some circumstances.

implementing lockdown. Adding to that Meo SA et al. [24] demonstrated that lockdown alone will not be effective unless it is implemented with other interventions such as social distancing and community wide mask wearing and in their quasi experimental study Kepp KP et al. [31] suggested that efficient infection surveillance and voluntary compliance may make full lockdowns unnecessary at least in some circumstances. Six studies

Table 2 Quality assessment of the included studies

Article	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdrawals and drop-outs	Global rating
Pan A et al [14]	Moderate	Moderate	N/A	N/A	weak	N/A	Moderate
Wang K-W et al [15]	Moderate	Moderate	N/A	N/A	weak	N/A	Moderate
Cowling BJ et al [16]	Moderate	Moderate	weak	N/A	Moderate	N/A	Moderate
Jüni P et al [17]	Moderate	Moderate	Weak	N/A	weak	N/A	weak
Wang J et al [18]	Strong	Moderate	N/A	N/A	Moderate	Strong	Strong
Cheng VC-C et al [19]	Moderate	Moderate	Weak	N/A	Moderate	N/A	Moderate
Thu TPB et al [20]	Moderate	Moderate	N/A	N/A	Moderate	N/A	Moderate
Seong H et al [21],	Moderate	Moderate	Weak	N/A	Moderate	N/A	Moderate
Lam HY et al [22]	Moderate	Moderate	N/A	N/A	Moderate	N/A	Strong
Salvatore M et al [23]	Moderate	Moderate	N/A	N/A	Weak	N/A	Moderate
Meo SA et al [24]	Moderate	Moderate	Weak	N/A	Moderate	N/A	Moderate
Xu T-L et al [25]	Moderate	Moderate	N/A	N/A	Moderate	N/A	Moderate
Zeng K et al [26]	Moderate	Moderate	N/A	N/A	Weak	N/A	Moderate
Wong CKH et al [27]	Moderate	Moderate	N/A	N/A	Weak	N/A	Moderate
Siedner MJ et al [28]	Moderate	Moderate	N/A	N/A	Weak	N/A	Moderate
Krishnamachari B et al [29]	Moderate	Moderate	Moderate	N/A	Weak	Moderate	Moderate
Singh BB et al [30]	Weak	Moderate	N/A	N/A	Weak	N/A	Weak
Kepp KP et al [31]	Moderate	Strong	Strong	Weak	Moderate	N/A	Moderate

Table 3 Level of evidence of the included studies and grade of recommendation

Article	*Type of study*	*Level of evidence*	*Grade of recommendation*
Pan A et al [14]	Interrupted time series	2+	C
Wang K-W et al [15]	Interrupted time series	2+	C
Cowling BJ et al [16]	Cohort Study	2-	C
Jüni P et al [17]	Cohort Study	2-	C
Wang J et al [18]	Longitudinal Study	2++	B
Cheng VC-C et al [19]	Cohort Study	2-	C
Thu TPB et al [20]	Longitudinal Study	2+	C
Seong H et al [21],	Cohort Study	2-	C
Lam HY et al [22]	Longitudinal Study	2+	C
Salvatore M et al [23]	Longitudinal Study	2+	C
Meo SA et al [24]	Cohort Study	2-	C
Xu T-L et al [25]	Longitudinal Study	2+	C
Zeng K et al [26]	Longitudinal study	2+	C
Wong CKH et al [27]	Longitudinal study	2+	C
Siedner MJ et al [28]	Longitudinal study	2+	C
Krishnamachari B et al [29]	Cohort Study	2+	C
Singh BB et al [30]	Longitudinal study	2-	C
Kepp KP et al [31]	Quasi experimental study	1+	A

[14–16, 18, 25, 26] found that identification of cases with isolation, quarantine of close contacts adding to home quarantine have been effective in suppressing transmission of COVID-19. Social and physical distancing measures have been proven in eight of the included studies [14, 16, 17, 20–22, 28, 29] to decrease the transmission of COVID-19. Thu TPB et al. [20] showed in their study that the time of promulgating the social distancing measures partly influences the intervention outcomes, adding to that population densities, crowding and socioeconomic variables as it was suggested by Krishnamachari B et al [29] Three studies [14, 19, 26] showed that compulsory mask wearing and community wide masking may contribute to the control of COVID-19 when they are implemented with other non-pharmaceutical control measures. In addition to that three studies [16, 18, 19] demonstrated that testing in conjunction with active case finding and contact tracing especially when implemented with isolation of cases and close contacts and social distancing are effective in reducing the transmission of COVID-19 and particularly important in maintaining suppression. Two studies [16, 17] suggested that school closures together with the restrictions of mass gathering and physical distancing measures may have an effect in reducing the transmission of SARS-COV-2.Pan A et al [14], found in their study conducted in Wuhan, China that the rate of cases among health workers was substantially higher than in the general population in the period with there is no strong public health interventions which indicated a high risk of nosocomial infections and which might be inadequate use of personal protective equipment and lower awareness. However after increasing awareness and wider use of personal protective equipment adding to hospital-level prevention and management in parallel with the implementation of strong public heath interventions the rate of confirmed cases quickly decreased and furthermore no new case were reported among local health workers which prove that protecting heath care workers is an important measure in controlling an outbreak of a high transmissible infectious disease. Finally Zeng K et al. [26] and Seong H et al. [21] suggested that early community mask wearing and timely border control interventions using modern digital tools in addition to early and timely measures with strengthened social distancing interventions should be implemented to suppress and control the COVID-19 pandemic effectively.

Discussion

We found that public health interventions and non-pharmaceutical control measures were effective in reducing the transmission of COVID-19 and were associated with reduced epidemic growth. The identified studies showed that travel restrictions, borders measures, quarantine of travellers arriving from affected countries, city lockdown, restrictions of mass gathering, isolation and quarantine of confirmed cases and close contacts, social distancing measures, compulsory mask wearing, contact tracing and testing, school closures and personal protective equipment use among health workers were effective in mitigating the spread of COVID-19 with varying degrees. Our results are in line with the findings of other studies [32–34] that demonstrated that public health measures and non-pharmaceutical control strategies are effective in mitigating the current pandemic of COVID-19 and in some countries aggressive and extreme interventions are probably needed to bring the epidemic under control and to prevent very large number of deaths and excess hospitals capacities.

Travel and entry restrictions, borders measures and quarantine of travellers arriving from affected countries were effective in controlling the spread of infection caused by SARS-CoV 2. Those interventions have been shown to be effective as well in other studies [6, 35], which suggest that travel restrictions and border control measures including surveillance targeting inbound travellers from affected countries and 14-day quarantine for arriving passengers adding to other public health interventions were associated with a stabilization of case numbers.

City lockdown, restriction of mass gathering physical distancing and stay at home policies has been shown to be effective as well in reducing the spread of SARS-CoV2 in the current study. Further studies support these findings and showed that lockdown measurements and stay at home orders were efficient in controlling and slowing down the spread of the epidemic [36–39] were strongly associated with the containment of COVID-19 [40]. A rapid review of modelling studies [41] found that quarantine is crucial in decreasing incidence and mortality in the pandemic of COVID-19. Moreover in order to ensure effectiveness it is very important implement quarantine measures especially in combination with other public health interventions at the early stage of the epidemic. Adding to that, in their study Marco Vinceti et al [42] showed the less rigid lockdown measurements led to an insufficient reduction in transmission to reverse the outbreak and with a tighter lockdown mobility and person to person transmission decreased enough to bring down transmission straight off below the level required to counteract spread of SARS-CoV-2 infection. In addition to that physical distancing strategies and restriction of human mobility [43, 44] has been showed to have a notable effect on controlling the spread of the COVID-19 outbreak.

Isolation and quarantine measures of contacts and close contacts adding to contact tracing are crucial to control the outbreak of COVID-19 and reduce the

human to human transmission. Those results are consistent with the findings of other studies [45–48] which indicate successful contact tracing and isolation of cases and close contacts are highly important to control the outbreak and to ensure a lower reproduction number below 1. These interventions might be more effective if combined with other measures such as physical distancing, self-isolation and testing. Testing is a key intervention in mitigating the spread of COVID-19 especially when it is applied in conjunction with tracing and isolation of cases and close contacts [49].

Compulsory mask wearing and community wide masking policies are essential in controlling the pandemic of COVID-19. Authors of a rapid systematic review [50] on the efficacy of face masks suggest that masking wearing could be beneficial in the context of COVID-19 outbreak especially universal community mask use and in the health care settings as well. Findings from a systematic review and meta-analysis [51] showed that mask wearing by health workers and non-health workers and in the general community is and efficient in preventing the infection by SARS-CoV2. Another study [52] showed that wearing masks in public is crucial as a preventive measure to ensure a significant reduction in the daily infected cases. In addition to that a prospective cohort study [53] found that the risk of infection by SARS-CoV-2 is increase among frontline health workers, therefore adequate strategies should be implemented to ensure the availability of personal protective equipments in order to protect health workers from COVID-19. Moreover timing is very important while implementing non-pharmaceutical interventions which should be initiated early when the numbers of COVID-19 cases are low as it was demonstrated in an observational study conducted by Qureshi A I et al [54]

School closures had been found to be effective in reducing the transmission of COVID-19, recently this intervention has been widely discussed; some studies [55, 56] found that school closures were associated with a reduction in the transmission of COVID-19 and in the mortality rate as well. However, other studies [57, 58] showed that school closures don't have any mitigating impact on the transmission of COVID-19 as children are likely to be asymptomatic and they don't seem to be greater transmitters in comparison with adults.

Further studies [59, 60] found additional tools that help prevent and control the COVID-19 pandemic such as internet hospitals and virtual care which presents a promising potential in the control of the COVID-19 outbreak as they are capable of reducing the emergency room visits, reducing the risk of nosocomial cross-infection by treating patients remotely, prevent the shortage of health care resources and promote personal prevention measures such as social distancing, mask wearing and hand hygiene. A systematic review [61] showed that telehealth is capable of minimizing the risk of COVID-19 transmission by decreasing the physical contacts adding to providing continuous community care.

This systematic review has several limitations, the included studies have heterogeneous methodology and most of them lack a control group and a vigorous study design. Although most of the included studies have moderate quality and for the remaining studies; two studies have low quality and only two studies have strong quality. Also, most of the included studies have moderate level of evidence and low grade of recommendation, six studies have low level of evidence and low grade of recommendation, only one study has moderate level of evidence and grade of recommendation and only one study as well has high level of evidence and grade of recommendation. In addition to that most of the public health interventions are implemented simultaneously or within a short period of time which means that it is difficult to evaluate the effect of each intervention alone accurately, consequently we can either underestimate or overestimate their impact on the COVID-19 pandemic. Future research studies which have rigorous methodology especially experimental and quasi experimental studies are needed to properly evaluate the outcomes of these public health interventions and non-pharmaceutical measures.

Conclusion

With no effective treatment and vaccine against SARS-CoV-2, public health measures and non-pharmaceutical interventions are vital to reduce the infection and mortality rate. Some interventions are not efficient enough when implemented alone and could not contain the outbreak, thus, depending on the country and the phase of the epidemic multiple interventions are needed to be applied together in order to bring the outbreak under control.

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Raw data

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Authors' contributions

A.I wrote the main manuscript with referral to M.J. A. I did the database search with referral to M. J and D.W. A. I and D. W did the full text review with referral to M.J. A. I, D.W and M. J did the data extraction. A. I and M. J independently assessed all the included articles for quality with referral to M. J and Z.N. A. I, BF. S and G. R prepared Tables 1, 2 and 3. All authors reviewed the manuscript, discussed the findings and approved its final version.

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Availability of data and materials
Protocol of this systematic review could be found at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=196018

Declarations

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Not applicable.

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References
1. Paules CI, Marston HD, Fauci AS. Coronavirus Infections-More Than Just the Common Cold. JAMA. 2020;323(8):707–8.
2. Sanche S, Lin YT, Xu C, Romero-Severson E, Hengartner N, Ke R. High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis juill. 2020;26(7):1470–7. https://doi.org/10.3201/eid2607.200282.
3. [En ligne]. Coronavirus Update (Live): 121,880,695 Cases and 2,694,054 Deaths from COVID-19 Virus Pandemic - Worldometer; [cité le 18 mars 2021]. Disponible: https://www.worldometers.info/coronavirus/
4. novel-coronavirus-guidelines-non-pharmaceutical-measures_0.pdf [En ligne]. [cité le 29 mars 2021]. Disponible: https://www.ecdc.europa.eu/sites/default/files/documents/novel-coronavirus-guidelines-non-pharmaceutical-measures_0.pdf
5. Nunan D, Brassey J. What is the evidence for mass gatherings during global pandemics? A rapid summary of best-available evidence. 8. https://www.cebm.net/covid-19/what-is-the-evidence-for-mass-gatherings-during-global-pandemics/.
6. Hossain MP, Junus A, Zhu X, Jia P, Wen T-H, Pfeiffer D, et al. The effects of border control and quarantine measures on the spread of COVID-19. Epidemics. 2020;32:100397. https://doi.org/10.1016/j.epidem.2020.100397.
7. Considerations relating to social distancing measures in response to COVID-19 – second update. 12. https://www.ecdc.europa.eu/en/publications-data/considerations-relating-social-distancing-measures-response-covid-19-second.
8. Lai S, Ruktanonchai NW, Zhou L, Prosper O, Luo W, Floyd JR, et al. Effect of non-pharmaceutical interventions to contain COVID-19 in China. Nature sept. 2020;585(7825):410–3. https://doi.org/10.1038/s41586-020-2293-x.
9. Patiño-Lugo DF, Vélez M, Velásquez Salazar P, Vera-Giraldo CY, Vélez V, Marín IC, et al. Non-pharmaceutical interventions for containment, mitigation and suppression of COVID-19 infection. Colomb Médica CM [en ligne]. [cité le 29 mars 2021];51(2). Disponible: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7518730/
10. Bo Y, Guo C, Lin C, Zeng Y, Li HB, Zhang Y, et al. Effectiveness of non-pharmaceutical interventions on COVID-19 transmission in 190 countries from 23 January to 13 April 2020. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2021;102:247–53.
11. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100.
12. [En ligne]. Quality assessment tool for quantitative studies; [cité le 23 mars 2021]. Disponible: https://www.nccmt.ca/knowledge-repositories/search/14
13. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ. 2001;323(7308):334–6.
14. Pan A, Liu L, Wang C, Guo H, Hao X, Wang Q, et al. Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. JAMA. 2020;323(19):1915–23.
15. Wang K, Gao J, Wang H, Wu X, Yuan Q, Guo F, et al. Epidemiology of 2019 novel coronavirus in Jiangsu Province, China after wartime control measures: A population-level retrospective study. Travel Med Infect Dis. 2020;35:101654.
16. Cowling BJ, Ali ST, Ng TWY, Tsang TK, Li JCM, Fong MW, et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. Lancet Public Health. 2020;5(5):e279–88. https://doi.org/10.1016/S2468-2667(20)30090-6.
17. Jüni P, Rothenbühler M, Bobos P, Thorpe KE, da Costa BR, Fisman DN, et al. Impact of climate and public health interventions on the COVID-19 pandemic: a prospective cohort study. CMAJ Can Med Assoc J J Assoc Medicale Can. 2020;192(21):E566–73.
18. Wang J, Liao Y, Wang X, Li Y, Jiang D, He J, et al. Incidence of novel coronavirus (2019-nCoV) infection among people under home quarantine in Shenzhen, China. Travel Med Infect Dis. 2020;37:101660.
19. Cheng VC-C, Wong S-C, Chuang VW-M, So SY-C, Chen JH-K, Sridhar S, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. J Infect juill. 2020;81(1):107–14. https://doi.org/10.1016/j.jinf.2020.04.024.
20. Thu TPB, Ngoc PNH, Hai NM, Tuan LA. Effect of the social distancing measures on the spread of COVID-19 in 10 highly infected countries. Sci Total Environ. 2020;742:140430.
21. Seong H, Hyun HJ, Yun JG, Noh JY, Cheong HJ, Kim WJ, et al. Comparison of the second and third waves of the COVID-19 pandemic in South Korea: importance of early public health intervention. Int J Infect Dis. 2021;104:742–5. https://doi.org/10.1016/j.ijid.2021.02.004.
22. Lam HY, Lam TS, Wong CH, Lam WH, Leung CME, Au KWA, et al. The epidemiology of COVID-19 cases and the successful containment strategy in Hong Kong-January to may 2020. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2020;98:51–8.
23. Salvatore M, Basu D, Ray D, Kleinsasser M, Purkayastha S, Bhattacharyya R, et al. Comprehensive public health evaluation of lockdown as a non-pharmaceutical intervention on COVID-19 spread in India: national trends masking state-level variations. BMJ Open. 2020;10(12):e041778.
24. Meo SA, Abukhalaf AA, Alomar AA, AlMutairi FJ, Usmani AM, Klonoff DC. Impact of lockdown on COVID-19 prevalence and mortality during 2020 pandemic: observational analysis of 27 countries. Eur J Med Res. 2020;25(1):56.
25. Xu T-L, Ao M-Y, Zhou X, Zhu W-F, Nie H-Y, Fang J-H, et al. China's practice to prevent and control COVID-19 in the context of large population movement. Infect Dis Poverty. 2020;9(1):115.
26. Zeng K, Bernardo SN, Havins WE. The Use of Digital Tools to Mitigate the COVID-19 Pandemic: Comparative Retrospective Study of Six Countries. JMIR Public Health Surveill. 2020;6(4):e24598.
27. Wong CKH, Wong JYH, Tang EHM, Au CH, Lau KTK, Wai AKC. Impact of National Containment Measures on Decelerating the Increase in Daily New Cases of COVID-19 in 54 Countries and 4 Epicenters of the Pandemic: Comparative Observational Study. J Med Internet Res. 2020;22(7):e19904.
28. Siedner MJ, Harling G, Reynolds Z, Gilbert RF, Haneuse S, Venkataramani AS, et al. Social distancing to slow the US COVID-19 epidemic: Longitudinal pretest-posttest comparison group study. PLoS Med. 2020;17(8):e1003244.
29. Krishnamachari B, Morris A, Zastrow D, Dsida A, Harper B, Santella AJ. Effects of Government Mandated Social Distancing Measures on Cumulative Incidence of COVID-19 in the United States and its Most Populated Cities. medRxiv. Cold Spring Harbor Laboratory Press; 2020;2020.05.22.20110460. https://www.medrxiv.org/content/10.1101/2020.05.22.20110460v1.full.
30. Singh BB, Lowerison M, Lewinson RT, Vallerand IA, Deardon R, Gill JP, et al. Public health interventions in India slowed the spread of COVID-19 epidemic dynamics. medRxiv. Cold Spring Harbor Laboratory Press; 2020;2020.06.06.20123893.
31. Kepp KP, Bjørnskov C. Lockdown Effects on Sars-CoV-2 Transmission – The evidence from Northern Jutland. medRxiv. Cold Spring Harbor Laboratory Press; 2021;2020.12.28.20248936.
32. Zhang N, Cheng P, Jia W, Dung C-H, Liu L, Chen W, et al. Impact of intervention methods on COVID-19 transmission in Shenzhen. Build Environ août. 2020;180:107106. https://doi.org/10.1016/j.buildenv.2020.107106.
33. Yu X. Impact of mitigating interventions and temperature on the instantaneous reproduction number in the COVID-19 pandemic among 30 US metropolitan areas. One Health. 2020;10:100160. https://doi.org/10.1016/j.onehlt.2020.100160.
34. Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ. Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study. Lancet Public Health. 2020;5(7):e375–85. https://doi.org/10.1016/S2468-2667(20)30133-X.

35. Kucharski AJ, Russell TW, Diamond C, Liu Y, Edmunds J, Funk S, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. Lancet Infect Dis. 2020;20(5):553–8. https://doi.org/10.1016/S1473-3099(20)30144-4.
36. Peng T, Liu X, Ni H, Cui Z, Du L. City lockdown and nationwide intensive community screening are effective in controlling the COVID-19 epidemic: analysis based on a modified SIR model. PLoS One. 2020;15(8):e0238411. https://doi.org/10.1371/journal.pone.0238411.
37. Lau H, Khosrawipour V, Kocbach P, Mikolajczyk A, Schubert J, Bania J, et al. The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China. J Travel Med. 2020;27(3). https://pubmed.ncbi.nlm.nih.gov/32181488/.
38. Lyu W, Wehby GL. Comparison of Estimated Rates of Coronavirus Disease 2019 (COVID-19) in Border Counties in Iowa Without a Stay-at-Home Order and Border Counties in Illinois With a Stay-at-Home Order. JAMA Netw Open. 2020;3(5):e2011102.
39. Sjödin H, Wilder-Smith A, Osman S, Farooq Z, Rocklöv J. Only strict quarantine measures can curb the coronavirus disease (COVID-19) outbreak in Italy, 2020. Eurosurveillance. 2020;25(13) [cité le 26 mars 2021]. Disponible: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7140595/.
40. Tian H, Liu Y, Li Y, Wu C-H, Chen B, Kraemer MUG, et al. An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. Science. 2020;368(6491):638–42.
41. Mayr V, Nußbaumer-Streit B, Gartlehner G. Quarantine Alone or in Combination with Other Public Health Measures to Control COVID-19: A Rapid Review (Review). Gesundheitswesen Bundesverb Arzte Offentlichen Gesundheitsdienstes Ger. 2020;82(6):501–6.
42. Vinceti M, Filippini T, Rothman KJ, Ferrari F, Goffi A, Maffeis G, et al. Lockdown timing and efficacy in controlling COVID-19 using mobile phone tracking. EClin Med. 2020;25:100457. https://doi.org/10.1016/j.eclinm.2020.100457.
43. Chu DK, Duda S, Solo K, Yaacoub S, Schunemann H. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. J Vasc Surg. 2020;72(4):1500. https://doi.org/10.1016/j.jvs.2020.07.040.
44. Zhou Y, Xu R, Hu D, Yue Y, Li Q, Xia J. Effects of human mobility restrictions on the spread of COVID-19 in Shenzhen, China: a modelling study using mobile phone data. Lancet Digit Health. 2020;2(8):e417–24.
45. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Health avr. 2020;8(4):e488–96. https://doi.org/10.1016/S2214-109X(20)30074-7.
46. Kucharski AJ, Klepac P, Conlan AJK, Kissler SM, Tang ML, Fry H, et al. Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. Lancet Infect Dis oct. 2020;20(10):1151–60. https://doi.org/10.1016/S1473-3099(20)30457-6.
47. Zhou F, Li J, Lu M, Ma L, Pan Y, Liu X, et al. Tracing asymptomatic SARS-CoV-2 carriers among 3674 hospital staff:a cross-sectional survey. EClinicalMedicine. 2020;26:100510. https://doi.org/10.1016/j.eclinm.2020.100510.
48. Pan Q, Gao T, He M. Influence of isolation measures for patients with mild symptoms on the spread of COVID-19. Chaos Solitons Fractals. 2020;139:110022. https://doi.org/10.1016/j.chaos.2020.110022.
49. Grassly NC, Pons-Salort M, Parker EPK, White PJ, Ferguson NM. Imperial College COVID-19 Response Team. Comparison of molecular testing strategies for COVID-19 control: a mathematical modelling study. Lancet Infect Dis. 2020;20(12):1381–9.
50. MacIntyre CR, Chughtai AA. A rapid systematic review of the efficacy of face masks and respirators against coronaviruses and other respiratory transmissible viruses for the community, healthcare workers and sick patients. Int J Nurs Stud. 2020;108:103629. https://doi.org/10.1016/j.ijnurstu.2020.103629.
51. Liang M, Gao L, Cheng C, Zhou Q, Uy JP, Heiner K, et al. Efficacy of face mask in preventing respiratory virus transmission: a systematic review and meta-analysis. Travel Med Infect Dis. 2020;36:101751. https://doi.org/10.1016/j.tmaid.2020.101751.
52. Zeng N, Li Z, Ng S, Chen D, Zhou H. Epidemiology reveals mask wearing by the public is crucial for COVID-19 control. Med Microecol. 2020;4:100015. https://doi.org/10.1016/j.medmic.2020.100015.
53. Nguyen LH, Drew DA, Joshi AD, Guo C-G, Ma W, Mehta RS, et al. Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study. medRxiv [En ligne]. 25 mai 2020 [cité le 26 mars 2021]; Disponible: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7273299/
54. Qureshi AI, Suri MFK, Chu H, Suri HK, Suri AK. Early mandated social distancing is a strong predictor of reduction in peak daily new COVID-19 cases. Public Health. 2021;190:160–7. https://doi.org/10.1016/j.puhe.2020.10.015.
55. Auger KA, Shah SS, Richardson T, Hartley D, Hall M, Warniment A, et al. Association Between Statewide School Closure and COVID-19 Incidence and Mortality in the US. JAMA. 2020;324(9):859–70.
56. Kurita J, Sugawara T, Ohkusa Y. Estimated effectiveness of school closure and voluntary event cancellation as COVID-19 countermeasures in Japan. J Infect Chemother Off J Jpn Soc Chemother. 2021;27(1):62–4. https://doi.org/10.1016/j.jiac.2020.08.012.
57. Iwata K, Doi A, Miyakoshi C. Was school closure effective in mitigating coronavirus disease 2019 (COVID-19)? Time series analysis using Bayesian inference. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2020;99:57–61.
58. Rajmil L. Role of children in the transmission of the COVID-19 pandemic: a rapid scoping review. BMJ Paediatr Open. BMJ Special J. 2020;4(1):e000722.
59. Gong K, Xu Z, Cai Z, Chen Y, Wang Z. Internet Hospitals Help Prevent and Control the Epidemic of COVID-19 in China: Multicenter User Profiling Study. J Med Internet Res. 2020;22(4):e18908.
60. Khairat S, Meng C, Xu Y, Edson B, Gianforcaro R. Interpreting COVID-19 and Virtual Care Trends: Cohort Study. JMIR Public Health Surveill. 2020;6(2):e18811.
61. Monaghesh E, Hajizadeh A. The role of telehealth during COVID-19 outbreak: a systematic review based on current evidence. BMC Public Health. 2020;20(1):1193.

Publisher's Note

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Impact of lockdown on Covid-19 case fatality rate and viral mutations spread in 7 countries in Europe and North America

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Abstract

Background: Severe acute respiratory syndrome CoV-2 (SARS-CoV-2) caused the first coronavirus disease 2019 (COVID-19) outbreak in China and has become a public health emergency of international concern. SARS-CoV-2 outbreak has been declared a pandemic by WHO on March 11th, 2020 and the same month several Countries put in place different lockdown restrictions and testing strategies in order to contain the spread of the virus.

Methods: The calculation of the Case Fatality Rate of SARS-CoV-2 in the Countries selected was made by using the data available at https://github.com/owid/covi-19-data/tree/master/public/data. Case fatality rate was calculated as the ratio between the death cases due to COVID-19, over the total number of SARS-CoV-2 reported cases 14 days before. Standard Case Fatality Rate values were normalized by the Country-specific ρ factor, i.e. the number of PCR tests/1 million inhabitants over the number of reported cases/1 million inhabitants. Case-fatality rates between Countries were compared using proportion test. Post-hoc analysis in the case of more than two groups was performed using pairwise comparison of proportions and *p* value was adjusted using Holm method. We also analyzed 487 genomic sequences from the GISAID database derived from patients infected by SARS-CoV-2 from January 2020 to April 2020 in Italy, Spain, Germany, France, Sweden, UK and USA. SARS-CoV-2 reference genome was obtained from the GenBank database (NC_045512.2). Genomes alignment was performed using Muscle and Jalview software. We, then, calculated the Case Fatality Rate of SARS-CoV-2 in the Countries selected.

Results: In this study we analyse how different lockdown strategies and PCR testing capability adopted by Italy, France, Germany, Spain, Sweden, UK and USA have influenced the Case Fatality Rate and the viral mutations spread. We calculated case fatality rates by dividing the death number of a specific day by the number of patients with confirmed COVID-19 infection observed 14 days before and normalized by a ρ factor which takes into account the diagnostic PCR testing capability of each Country and the number of positive cases detected. We notice the stabilization of a clear pattern of mutations at sites nt241, nt3037, nt14408 and nt23403. A novel nonsynonymous SARS-CoV-2 mutation in the spike protein (nt24368) has been found in genomes sequenced in Sweden, which enacted a soft lockdown strategy.

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Conclusions: Strict lockdown strategies together with a wide diagnostic PCR testing of the population were correlated with a relevant decline of the case fatality rate in different Countries. The emergence of specific patterns of mutations concomitant with the decline in case fatality rate needs further confirmation and their biological significance remains unclear.

Keywords: SARS-CoV-2, Case fatality rate, Mutation, Europe, US, COVID-19, Lockdown strategy, Testing capacity

Background

SARS-CoV-2, the etiologic agent of the current global pandemic, is an enveloped positive-sense single-stranded RNA (+ssRNA) virus, that belongs to the *Betacoronavirus* genus and to the Coronaviridae family, which is broadly distributed in humans and other mammals [1–3]. Also, during the last decades, other newly emerged coronaviruses have caused respiratory infections with pandemic potential, such Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV).

Similarities of clinical features between previous *Betacoronavirus* infections and SARS-CoV-2 have been noted. Moreover, full genome sequencing has shown that it is closely related to SARS-CoV, both viruses have about 80% similarity and their genomes consist of six major open-reading frames (ORFs) plus a number of other accessory genes. Also, molecular modelling indicated similarities between their receptor-binding domains. The spike protein, that presents the most immunogenic determinants of the virus, has been shown to bind the same SARS-CoV receptor (the angiotensin converting enzyme 2 receptor, ACE2) in order to invade cells, suggesting a similar pathogenic mechanism.

As of April 30th, 2020 there were approximately 3.1 M confirmed cases of COVID-19 worldwide and more than 217.000 infection-related deaths. SARS-CoV and MERS-CoV have caused more than 10,000 cumulative cases in the past two decades, with mortality rates of 9,6% for SARS-CoV and 37% for MERS-CoV, respectively [4–7].

Although SARS-CoV-2 is less lethal than MERS-CoV, as many as 20% of the infected people develop rapidly a severe disease characterized by interstitial pneumonia and acute respiratory distress syndrome that can ultimately lead to death. This is particularly reported in elderly and in people with underlying medical conditions. However, most of the patients remain asymptomatic or develop mild symptoms, like fever and dry cough, followed then by breathing difficulties (dyspnea), and bilateral ground-glass opacities on chest CT scans, indicating that the target cells are located in the lower airways [8].

Nowadays, the main goal is to identify an effective treatment and a vaccine against SARS-CoV-2 and to found effective diagnostics, sociological and public health strategies to reduce the spread of the virus, ensuring a faster economic recovery.

This study aims to compare the effectiveness of the different lockdown strategies, the need of a considerable diagnostic PCR testing capability as well as the impact of the representative viral strains isolated in each Country presented here. To this purpose, we focused our study on Italy, Spain, France, Germany, UK, Sweden and United States, broadening our previous analysis of SARS-CoV-2 variants [9]. The characterization of SARS-CoV-2 variants might also significantly contribute to the design of effective therapies, vaccines and novel diagnostics tools.

Methods

Case fatality rate (CFR) represents the proportion of cases who eventually die from a disease over the diagnosed cases of disease (https://ourworldindata.org/mortality-risk-covid). Once an epidemic has ended, CFR is calculated as (deaths cases/infected cases). However, while an epidemic is still ongoing, as it is the case with the current novel coronavirus outbreak, this formula does not represent the true case fatality rate and might be off by orders of magnitude. Diagnosis of viral infection will precede recovery or deaths by days to weeks and the number of death should therefore be compared to the past case counts—accounting for this delay increasing the estimate of the case fatality rate [10].

To calculate CFR, we used the following formula:

$$\text{CFR} = \text{deaths at day x / cases at day x} - \{T\}$$

where T: average time period from case confirmation to death.

Therefore, in our study, CFR was calculated as the ratio between the death cases due to COVID-19, over the total number of SARS-CoV-2 reported cases 14 days before, as previously described [11]. We normalized these rates among different Countries, considering the different policies in terms of number of testing/million inhabitants, and at the same time considering the different incidence of the infection taking into account the number of cases/million inhabitants. A corrective Country-specific ρ factor was defined as the ratio between the number of PCR tests/1 million inhabitants and the number of reported cases/1 million inhabitants (data obtained from https://www.worldometers.info/coronavirus/#countries).

Standard CFR values were normalized by the Country-specific ρ factor. CFR between Countries were compared using proportion test. Post-hoc analysis in the case of more than two groups was performed using pairwise comparison of proportions and p-value was adjusted using Holm method.

We also analyzed 487 full-length genomic sequences of SARS-CoV-2 from GISAID database. Sequenced specimens were collected from December 2019 to April 2020, from the following Countries: Germany, Italy, Spain, France, UK, Sweden and USA. NC_045512.2 genome deposited in the GenBank has been used as SARS-CoV-2 reference genome. Muscle and Jalview software were used for genomes alignment and analysis.

Results and discussions

CFR comparison in different Countries

Mortality calculations during the epidemics are difficult, mostly due to calculation biases: during the initial period of the epidemic, many patients were diagnosed with COVID-19 only after developing critical illness or even at the time of death, whereas asymptomatic or paucisymptomatic patients were untested, leading to an underestimation of the denominator [11]. Additional significant biases affect mortality curves: to name a few, the parameters used for death counting, the rigidity of lockdown measures, population age. Over time Countries started adopting better policies for diagnostic PCR testing and lockdown strategies, and consequently the spread of the virus was better monitored and the data were more carefully determined. We chose to analyze the Country-specific data relative to the number of COVID-19 deaths in April 2020, when some of the initial biases were likely attenuated, using the method described [11]. The number of deaths of a specific day was divided by the total number of infected cases reported 14 days before. This method considers the fact that 14 days are the average lag time estimated between the first symptoms to death [12]. The data analyzed for Italy, France, Germany, Spain, UK, Sweden and USA are reported in Fig. 1a. For all Countries we observed a decrease in the CFR values over time, with the exception of Germany (that maintains a very low value overall) and Sweden (where no decrease is observed). We identified two critical elements that might affect CFR among these Countries: (a) the number of PCR tests made and (b) the total number of positive cases for each Country. Since the second parameter (b) depends on the first parameter (a), we introduced a corrective Country-specific factor $\rho = a/b$, that was later used to normalize the CFR previously calculated (Table 1). Data obtained through this normalization model are reported in Fig. 1b. By taking only the data calculated on the 30th of April and representing them in a bubble plot (Fig. 2), we clearly identify the presence of three clusters of Countries. Group 1 includes Germany and has a very low normalized CFR (0.31% CI

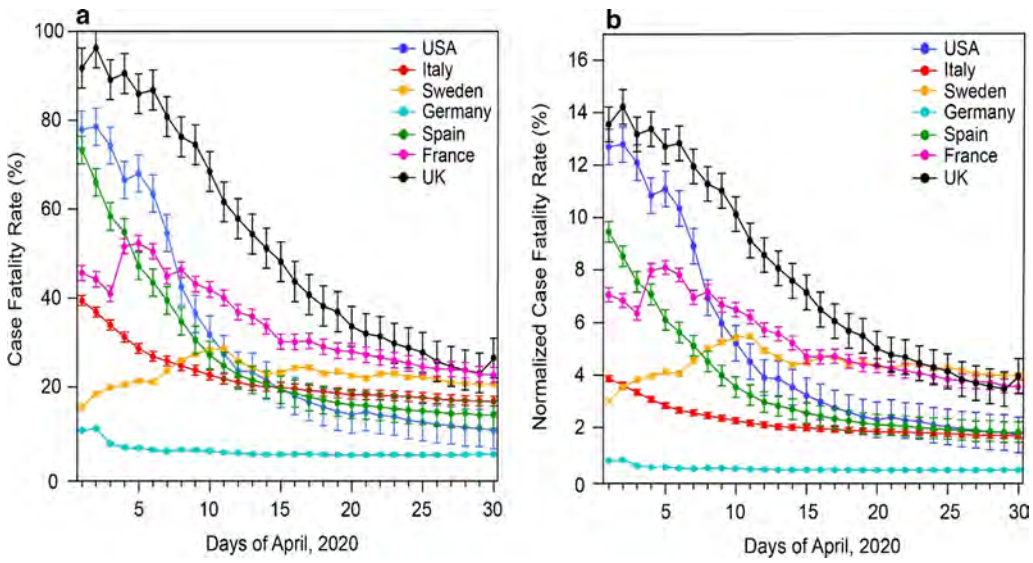

Fig. 1 **a** Calculated case fatality rate curves for USA, Italy, Sweden, Germany, Spain, France and UK as explained by Baud and colleagues [11]. Bars indicate the 95% of confidence interval. **b** Case fatality rate of **a** normalized by the ρ factor, i.e. by the number of PCR tests performed per 1 M population over positive cases per 1 M population up to the 30th of April, 2020. Bars indicate the 95% of confidence interval. The normalization leads to the formation of three main groups: group 1 includes Germany, group 2 includes Italy, USA and Spain and group 3 includes UK, France and Sweden

Table 1 Country-specific data showing number of PCR tests and cases per million inhabitants and corrective factor ρ = a/b

	Italy	Spain	France	Germany	UK	Sweden	USA
PCR Tests/1 M inhabitans (a)	36244	41332	16856	30400	19026	11833	22545
Cases/1 M inhabitans (b)	3505	5311	2596	1984	2807	2250	3665
Corrective factor (ρ)	10.34	7.78	6.49	15.32	6.78	5.26	6.15

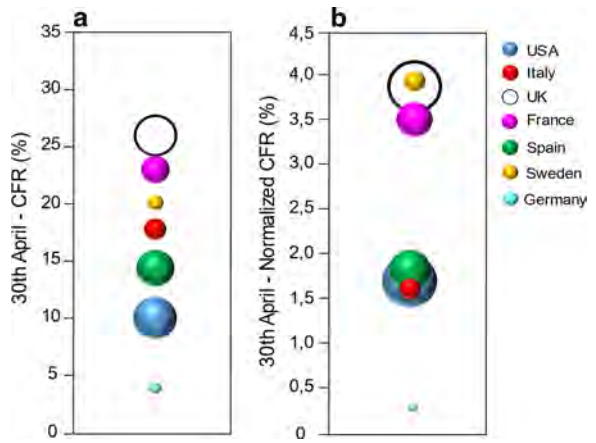

Fig. 2 Bubble plot representation of the 30th of April Case Fatality Rate (**a**) and of the 30th of April Normalized Case Fatality Rate of USA (in light blue), Italy (in red), of UK (black line), France (in magenta), Spain (in green), Sweden (in yellow) and Germany (in cyan). In **a**, the CFRs are distributed within a large range of values, whereas in **b** the normalized CFRs values are clustered in three well-distinct groups: Germany forms the first group, Italy, Spain and USA the second group and, finally, Sweden, UK and France the third group with the higher normalized CFR value

(95%) [0.29 : 0.33] on April 30th 2020). Group 2 includes Italy, USA and Spain and has an intermediate value of normalized CFR (1.62% CI (95%) [1.51:1.72]; 1.65% CI (95%) [0.97:2.33]; 1.76% CI (95%) [1.36:2.15], respectively, on April 30th 2020). Group 3 includes France, Sweden and UK (3.49% CI (95%) [3.23:3.76]; 3.92% CI (95%) [3.83:4.02]; 3.90% CI (95%) [3.25:4.27], on April 30th 2020). The difference among cluster's CFR (respectively 0.31% vs 1.68% vs 3.78%) was statistically significant ($p < 0.001$). Also, all pairwise comparisons were significant (p-adjusted with Holm method < 0.001).

This result could be furtherly refined by considering the variability of the lag time due to patients age, i.e. older people (>70 y.o.) have a lower lag time [12] compared to others. However, even if the daily number of death patients divided per age is available for each Country, we could not provide in this study a further normalization of the CFR taking into account patients age, since a similar daily database of infected people divided per age is not publicly available. Anyway, since the infection mostly leads to death older people or those that have ongoing severe illnesses (i.e. cardiovascular diseases, diabetes, cancer), we can speculate that the overall estimation of the CFR is driven by this class of patients. Therefore, the observed CFR curves observed among different Countries through the introduction of an innovative corrective factor ρ, might be explained mainly by the different policies that were enacted by each Country. To further support this hypothesis, we note that in Countries of group 3 where lockdown was not put in place (i.e. Sweden) or it was adopted late, and less SARS-CoV-2 PCR tests were executed (i.e. in UK and France), normalized CFR is higher than in the other groups. Although further data are needed to refine the CFR estimation, we improved the CFR estimate by using a new corrective factor which considers two important variables (number of positives and number of PCR tests performed). In fact, several sources of variability affect CFR but for modifiable confounding factors, a standardization process could help to reduce the biases, improving the interpretability and comparability of CFR across Countries.

Lockdown impact on viral mutation spread

A database of 487 genome sequences isolated from patients infected with SARS-CoV-2 in Italy, Spain, Germany, France, UK, Sweden and USA has been randomly collected from the GISAID database, aligned and compared to the SARS-CoV-2 reference genome. A total of 27 genomes were considered in January 2020, 91 in February 2020, 210 in March 2020 and, finally, 159 genomes in April 2020. We analyzed 54 genome samples collected in Italy, 61 in Spain, 62 in Germany, 52 in France, 80 in UK, 50 in Sweden and 128 in the United States (Table 2).

We studied the evolution of the mutation patterns in the selected Countries from January to April 2020, and we reported only the recurrent mutations occurring more than 10 times in the time range considered, as described elsewhere [9]. The occurrence of each mutation in a specific Country has been normalized by the number of genomes collected in that geographic area for each timeframe, dividing the silent by the non-silent mutations (Fig. 3). Interestingly, the number of nonsynonymous mutations increases over time during the spread out of Asia, and appears to stabilize in April (Fig. 3, top panel).

Table 2 Sequenced genomes selection for different geographic areas and time of collection

	Italy	Spain	France	Germany	UK	Sweden	USA	Tot
January 2020	3	0	8	1	2	0	13	27
February 2020	5	7	11	12	25	2	29	91
March 2020	36	35	24	23	27	25	40	210
April 2020	10	19	9	26	26	23	46	159
Tot	54	61	52	62	80	50	128	487

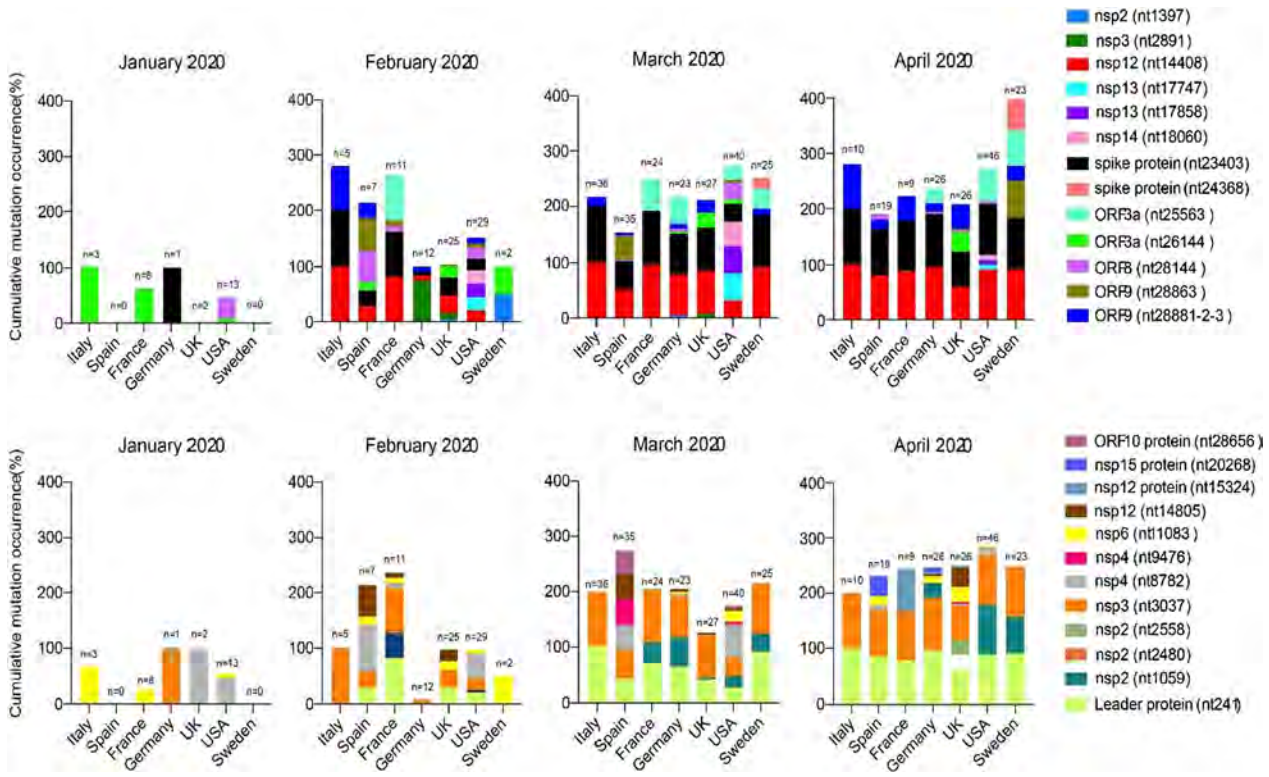

Fig. 3 SARS-CoV-2 recurrent mutations occurrence over time, divided per geographic area. The graph reports evolution of nonsynonymous (top) and silent (bottom) mutation patterns from January 2020 to April 2020 in Italy, Spain, France, Germany, UK, Sweden and in the USA. The frequency of each mutation in each country and for each month was normalized to 100%, i.e. to the total number of genomes analyzed in that frameshift and collected in that specific country. Recurrent nonsynonymous mutation pattern is characterized by the occurrence of mutations at nt14408, nt 23403 and nt28881–28882–28883 (RdRp and spike protein, respectively), while the most found silent mutations are at nt241 and nt3037 (localized in the leader protein and in the nsp3)

The pattern of nonsynonymous mutations changes quite dramatically from January to February, when such mutations appeared for the first time. More in detail, part of the genomes analyzed in January 2020 belong to patients infected in China or to patients in close contact to those travelling or coming back from Asia. In February, most Countries decided to suspend flights at first from and to China and, after, only few communications were maintained between nations and during that month locally transmitted outbreak cases occurred. We observed a pattern of recurrent mutations which reached a homogeneous distribution across the different Countries in March 2020. This observation is confirmed also in April 2020 in all the analyzed Countries. It is likely that lockdown policies implemented in this period greatly reduced further viral spread from Asia and hampered mixing of SARS-CoV-2 strains among Countries. We observed a similar pattern for silent mutations (Fig. 3, bottom panel).

Overall, our data show a number of silent mutations (nt241, nt3037) and nonsynonymous mutations

(nt14408, nt23403 and nt28881–28882–28883) (Fig. 3). Among the nonsynonymous mutations, we note the occurrence of an already observed mutation at position 14408, which is located in the viral RNA-dependent RNA-polymerase (RdRp gene), a key component of the replication/transcription machinery [9]. This mutation (Fig. 3, depicted in red) emerged in February 2020 and is quite homogeneously distributed across all the Countries analyzed. This is also observed for a mutation occurring in the spike protein (nt23403, Fig. 3, depicted in black) and to a minor extent for a mutation in the nucleocapsid phosphoprotein (nt28881–28882–28883, Fig. 3, depicted in blue). The occurrence of the mutation in the RdRp (nt14408) is always associated with that of the spike protein (nt23403), of the nsp3 mutation (nt3037) and of the mutation in the leader protein (nt241). A different pattern of hotspot mutations characterized viral genomes detected in patients from the United States. In February we initially detected three novel mutations (in position 17747, 17858 and 18060), that were not found elsewhere. These mutations were found predominantly in the viral genomes sequenced in Washington State (USA). The occurrence of this isolated pattern over time reflects the viral spreading of a more "European-like" strain (nt241, nt3037, nt14408 and nt23403) in the rest of the US. Overall, the occurrence of this "European-like" group varies from 32.5% of analyzed genomes (in USA) to 100% (in Italy). Our data confirm the previous observations made by Korber et al. [13], when the authors hypothesized that this mutation group, associated with the G clade, could enhance viral fitness, possibly due to the nt23403 mutation that triggers a significant amino acid substitution in a strongly immunogenic linear epitope of Spike protein, which might affect neutralizing antibodies sensitivity.

Emerging of new mutations

We noted the emergence of other recurrent mutation sites over time, both nonsynonymous (nt25563, nt28863) and silent (nt2480, nt2558, nt9476, nt15324, nt20268 and nt28656). The nonsynonymous mutations occur in the ORF3a and ORF9 (nucleocapsid phosphoprotein), causing the amino acid mutation Q56H (glutamine to histidine) and S197L (serine to leucine). All these mutations are found in most Countries and they are not exclusively reported in a specific geographic area. An additional recurrent mutation has been detected exclusively in genomes from Swedish at nt24368 (G to T transition); this mutation, which is located in the spike protein sequence, appeared in March (carried by 20% of genomes analyzed) and its frequency more than doubled in April (52% of genomes analyzed). This mutation triggers an amino acid substitution at position 936, from an aspartic acid to a tyrosine, with a significant shift in terms of isoelectric point from 2.85 to 5.64. D936 residue in SARS-CoV-2 Spike protein corresponds to the E918 residue of the homologue protein of SARS-CoV, and it is located in the heptad repeat 1 (HR1) domain [14, 15]. Heptat repeat 1 interacts with heptad repeat 2 (HR2) domain and form a six-helix bundle fusion core, able to bring viral and cellular membranes in close proximity, promoting fusion and infection of host cell [16, 17]. This makes HR1 and HR2 good target candidates for drug design. Recently, D936 (site of the recurrent mutation) has been proved to bind to R1185 of the heptad repeat 2 (HR2) domain through a salt bridge. Additional studies are required to further characterize if G936 mutant, present in April in more than half of Swedish genomes analyzed, could provide some beneficial advantages in terms of viral fitness, as observed for mutation nt23403 [13]. Among the Countries in the different groups there are no significant differences in the distribution of mutations, since the recurrent mutation pattern is comparable among different Countries (Fig. 3, top panel). The only significant difference is the newly emerged mutation nt24368, that in our database was detected only in the genomes analyzed in Sweden.

Conclusions

By normalizing the CFR by the ρ factor, we divided the analyzed Countries in three groups with an increased estimated CFR: group 1 is represented by Germany, group 2 by Italy, Spain and USA and group 3 by Sweden, France and UK. Groups 1 and 2 include Countries that adopted strict lockdown strategies and/or have a wide testing capability, whereas group 3 is formed by Countries that have adopted lockdown restrictions later (or have not at all) and/or did not perform an extensive diagnostic PCR testing. A decreasing trend of case fatality rate has been observed among most Countries. There are several direct factors that might contribute to this decline, such as health service's ability to cope with COVID-19 patients, increased and improved viral testing and tracing, efficacy of the different lockdown strategies, herd immunity development, influence of age on the affected population, variation in viral contagiousness and lethality. We observe that, after the rapid emergence and diffusion of recurrent mutations in February and March, a specific mutation pattern has stabilized by April 2020 in all the Countries analyzed. This pattern is comprised of mutations nt241, nt3037, nt14408 and nt23403. In Sweden we report the occurrence of a unique nonsynonymous mutation in the spike protein (nt24368) which has been found in more than 50% of genomes. The emergence of specific patterns of mutations concomitant with the decline in case fatality rate needs further confirmation

and the biological significance of such mutations remains unclear.

Abbreviations
CFR: case fatality rate; UK: United Kingdom; WHO: World Health Organization.

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Authors' contributions
MP, BM and FG performed the analysis. MP and BM wrote the paper. FB, SA, MC, CM, RI and DZ revised the manuscript. RI, BM and DZ conducted the investigation. All authors read and approved the final manuscript.

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Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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References

1. Su S, Wong G, Shi W, Liu J, Lai ACK, Zhou J, Liu W, Bi Y, Gao GF. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol. 2016. https://doi.org/10.1016/j.tim.2016.03.003.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W, China Novel Coronavirus Investigating and Research Team. Novel coronavirus from patients with pneumonia in China. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001017.
3. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi ZL. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020. https://doi.org/10.1038/s41586-020-2012-7.
4. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, Tong S, Urbani C, Comer JA, Lim W, Rollin PE, Dowell SF, Ling AE, Humphrey CD, Shieh WJ, Guarner J, Paddock CD, Rota P, Fields B, DeRisi J, Yang JY, Cox N, Hughes JM, LeDuc JW, Bellini WJ, Anderson LJ, SARS Working Group. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med. 2003. https://doi.org/10.1056/NEJMoa030781.
5. Kuiken T, Fouchier RA, Schutten M, Rimmelzwaan GF, van Amerongen G, van Riel D, Laman JD, de Jong T, van Doornum G, Lim W, Ling AE, Chan PK, Tam JS, Zambon MC, Gopal R, Drosten C, van der Werf S, Escriou N, Manuguerra JC, Stöhr K, Osterhaus AD. Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. Lancet. 2003. https://doi.org/10.1016/S0140-6736(03)13967-0.
6. Drosten C, Günther S, Preiser W, van der Werf S, Brodt HR, Becker S, Rabenau H, Panning M, Kolesnikova L, Fouchier RAM, Berger A, Burguière AM, Cinatl J, Eickmann M, Escriou N, Grywna K, Kramme S, Manuguerra J, Müller S, Rickerts V, Stürmer M, Vieth S, Klenk H, Osterhaus ADME, Schmitz H, Doerr HW. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med. 2003. https://doi.org/10.1056/NEJMoa030747.
7. de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, Fouchier RA, Galiano M, Gorbalenya AE, Memish ZA, Perlman S, Poon LL, Snijder EJ, Stephens GM, Woo PC, Zaki AM, Zambon M, Ziebuhr J. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. J Virol. 2013. https://doi.org/10.1128/JVI.01244-13.
8. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020. https://doi.org/10.1016/S0140-6736(20)30183-5.
9. Pachetti M, Marini B, Benedetti F, Giudici F, Mauro E, Storici P, Masciovecchio C, Angeletti S, Ciccozzi M, Gallo RC, Zella D, Ippodrino R. Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant. J Transl Med. 2020. https://doi.org/10.1186/s12967-020-02344-6.
10. Battegay M, Kuehl R, Tschudin-Sutter S, Hirsch HH, Widmer AF, Neher RA. 2019-Novel Coronavirus (2019-nCoV): estimating the case fatality rate—a word of caution. Swiss Med Wkly. 2020. https://doi.org/10.4414/smw.2020.20203.
11. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. Lancet Infect Dis. 2020. https://doi.org/10.1016/S1473-3099(20)30195-X.
12. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
13. Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, Foley B, Giorgi EE, Bhattacharya T, Parker MD, Partridge DG, Evans CM, de Silva TI, LaBranche CC, Montefiori DC. Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2. Biorxiv. 2020. https://doi.org/10.1101/2020.04.29.069054.
14. Chan WE, Chuang CK, Yeh SH, Chang MS, Chen SS. Functional characterization of heptad repeat 1 and 2 mutants of the spike protein of severe acute respiratory syndrome coronavirus. J Virol. 2006. https://doi.org/10.1128/JVI.80.7.3225-3237.
15. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, Zhang Q, Shi X, Wang Q, Zhang L, Wang X. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020. https://doi.org/10.1038/s41586-020-2180-5.
16. Bosch BJ, Martina BE, Van Der Zee R, Lepault J, Haijema BJ, Versluis C, Heck AJ, De Groot R, Osterhaus AD, Rottier PJ. Severe acute respiratory syndrome coronavirus (SARS-CoV) infection inhibition using spike protein heptad repeat-derived peptides. Proc Natl Acad Sci USA. 2004. https://doi.org/10.1073/pnas.0400576101.
17. Xia S, Liu M, Wang C, Xu W, Lan Q, Feng S, Qi F, Bao L, Du L, Liu S, Qin C, Sun F, Shi Z, Zhu Y, Jiang S, Lu L. Inhibition of SARS-CoV-2 (previously 2019-nCoV) infection by a highly potent pan-coronavirus fusion inhibitor targeting its spike protein that harbors a high capacity to mediate membrane fusion. Cell Res. 2020. https://doi.org/10.1038/s41422-020-0305-x.

Publisher's Note

Critical preparedness, readiness and response actions for COVID-19

Interim guidance

27 May 2021

World Health Organization

Key points

- Countries should continue to take all necessary public health and social measures to slow further spread of SARS-CoV-2, to prevent infections, especially in people vulnerable to severe disease or death, and avoid having their health systems overwhelmed.
- Variants of SARS-CoV-2 are circulating, some with increased transmissibility. However, the preparedness, readiness and response actions that are needed remain the same.
- Countries should administer COVID-19 vaccines according to their National Deployment and Vaccination Plans.
- Countries should be able to deliver the COVID-19 care pathway for patients, including life-saving therapies of corticosteroids and oxygen for those with severe disease, regardless of transmission scenario.
- There are seven transmission scenarios for COVID-19: no cases, sporadic cases, clusters of cases and four levels of community transmission. Countries should assess the transmission scenarios at sub-national levels.
- Countries should respond to all transmission scenarios while including communities in decision making processes to enhance adherence to public health and social measures
- Prioritization of resources for each technical area will depend on which transmission scenario(s) a country is facing, as well as the response capacity.
- There is still much to understand about COVID-19 and its impact in different contexts. Preparedness, readiness and response actions will continue to be driven by rapidly accumulating scientific and public health knowledge.

Introduction

This document is an update to the interim guidance entitled 'Critical preparedness, readiness and response actions for COVID-19', originally published on 22 March 2020 and last updated on 5 November 2020. This version provides updated guidance on contact tracing, laboratory testing, infection prevention and control, public health and social measures and health services, in the context of COVID-19 vaccination implementation. The full list of WHO technical guidance documents available for COVID-19 has also been updated.

This document outlines critical preparedness, readiness and response actions that are necessary, depending on the SARS-CoV-2 transmission scenario. Where possible, the transmission scenario should be assessed at the lowest administrative level (e.g., province, state, district, community) within each country.

Background

Since January 2020, the scientific knowledge on SARS-CoV-2 (the virus that causes COVID-19), how it spreads, and the public health, economic and social impacts of the COVID-19 pandemic have continued to evolve. Many countries continue to demonstrate that SARS-CoV-2 transmission can be controlled. Variants of SARS-CoV-2 have been detected, including four which have been defined as variants of concern. However, the preparedness, readiness and response actions that are needed remain the same. These actions have saved lives and provided countries with more time to enhance emergency response systems; to increase capacity to detect cases and care for patients; to ensure hospitals have the necessary staff, supplies, including structures and systems, to ensure treatment for COVID-19 and non-COVID-19 conditions.

On 31 December 2020, WHO issued the first emergency use listing (EUL) of a COVID-19 vaccine. Since then, five more vaccines have received EUL. Vaccines and vaccination are now part of the global response for COVID-19, and the Strategic Advisory Group of Experts on Immunization recommends the prioritisation of vaccination for high-risk individuals. While vaccination plans are being implemented, countries should continue to take all necessary public health and social measures (PHSM) to slow further spread, to avoid having their health systems overwhelmed and to prevent infections, especially among older persons and those with chronic conditions who are at higher risk of severe outcomes and death.

The overarching aim of the Strategic Preparedness and Response Plan for COVID-19 continues to be to suppress transmission of SARS-CoV-2 and prevent associated illness and death. In February 2021, the SPRP was updated to include vaccination into the global response. The 2021 global strategic objectives are:

- **Suppress transmission** through rollout of equitable COVID-19 vaccines and vaccination, through the implementation of recommended effective and evidence-based public health and social measures, and infection prevention and control measures, including detecting and testing suspected cases; investigating clusters of cases; tracing contacts;

supported quarantine of contacts; isolating probable and confirmed cases; implementing measures to protect high-risk groups.

- **Reduce exposure** by enabling communities to adopt risk-reducing behaviours and practice infection prevention and control, including avoiding crowds and maintaining physical distance from others; practicing proper hand hygiene; through at the appropriate times; the correct and rational use of masks; and improving indoor ventilation.
- **Empower communities** to lead or be part of the response decision-making process by reinforcing risk communication and community engagement approaches that can reinforce local solutions, increase trust and social cohesion, and ultimately a reduction in the negative impacts of COVID-19.
- **Counter misinformation and disinformation** by managing the infodemic, communicating with, engaging, and empowering communities, while also enriching the information eco-system online and offline through relevant, actionable and localized guidance that communicates, and by communicating risks and science for specific target populations, as needed.
- **Protect the vulnerable through vaccination**, ensuring vaccine deployment readiness in all countries and all populations, by communicating, implementing, and monitoring COVID-19 vaccination campaigns, by engaging health workers, and by building vaccine acceptance and demand based on priority groups, taking into account gender and equity perspectives to leave no one behind.
- **Reduce mortality and morbidity from all causes** by ensuring that patients with COVID-19 are diagnosed early and given quality care and treated in a COVID-19 Care pathway with access to corticosteroids and oxygen for patients with severe disease; that health systems can surge to maintain and meet the increasing demand for both COVID-19 care and other essential health services; that core health systems are strengthened; that demand-side barriers to care are addressed; and by ensuring that all priority groups in every country are vaccinated.
- **Accelerate equitable access** to new COVID-19 tools including vaccines, diagnostics and therapeutics, and support safe and rational allocation and implementation in all countries.

This update recognises that all countries have increased their level of preparedness, alert and response to implement national COVID-19 plans, and that there is no one-size-fits-all approach to managing cases and outbreaks of COVID-19. As such, each country should continually assess its risk and rapidly implement the necessary measures at the appropriate scale to reduce both SARS-CoV-2 transmission, COVID-19 morbidity and mortality, as well as the broader economic, public and social impacts.

Scenarios

The transmission scenarios defined by WHO are outlined in Table 1: no (active) cases (including both zero transmission and the absence of detected and reported cases), imported/ sporadic cases, clusters of cases and community transmission. The community transmission (CT) classification is now divided into four levels, from low incidence (CT1) to very high incidence (CT4).

This is described in further detail in Considerations in adjusting public health and social measures in the context of COVID-19. Further explanation of these categories and when to adjust public health and social measures can also be found in WHO guidance Public health criteria to adjust public health and social measures in the context of COVID-19 and Considerations for implementing a risk-based approach to international travel in the context of COVID-19.

Table 1: Definition of the categories for transmission classification

Category name	**Definition** *Countries/territories/areas with:*
No (active) cases	No new cases detected for at least 28 days (two times the maximum incubation period), in the presence of a robust* surveillance system. This implies a near-zero risk of infection for the general population.
Imported / Sporadic cases	Cases detected in the past 14 days are all imported, sporadic (e.g. laboratory acquired or zoonotic) or are all linked to imported/sporadic cases, and there are no clear signals of further locally acquired transmission. This implies minimal risk of infection for the general population.
Clusters of cases	Cases detected in the past 14 days are predominantly limited to well-defined clusters that are not directly linked to imported cases, but which are all linked by time, geographic location **and** common exposures. It is assumed that there are a number of unidentified cases in the area. This implies a low risk of infection to others in the wider community if exposure to these clusters is avoided.

Category name	**Definition** *Countries/territories/areas with:*
Community transmission – level 1 (CT1)	**Low incidence** of locally acquired, widely dispersed cases detected in the past 14 days, with many of the cases not linked to specific clusters; transmission may be focused in certain population sub-groups. Low risk of infection for the general population.
Community transmission – level 2 (CT2)	**Moderate incidence** of locally acquired, widely dispersed cases detected in the past 14 days; transmission less focused in certain population sub-groups. Moderate risk of infection for the general population.
Community transmission – level 3 (CT3)	**High incidence** of locally acquired, widely dispersed cases in the past 14 days; transmission widespread and not focused in population sub-groups. High risk of infection for the general population.
Community transmission – level 4 (CT4)	**Very high incidence** of locally acquired, widely dispersed cases in the past 14 days. Very high risk of infection for the general population.

* Note that in situations where COVID-19 surveillance is not robust, a lack of identified cases should not be interpreted as an absence of transmission.

Countries could experience one or more of these scenarios at the sub-national level and should define the transmission scenario and response actions at the lowest administrative level. Transmission scenarios may also move in both directions, such that “No cases” includes both never having had a COVID-19 case and having no active cases.

Countries should prepare to be able to respond to all transmission scenarios, following the framework laid out in the Strategic Preparedness and Response Plan for COVID-19. Prioritization of resources for each technical area will depend on which transmission scenario(s) a country is managing.

There is still much to understand about COVID-19 and its impact in different contexts. Preparedness, readiness and response actions will continue to be driven by rapidly accumulating scientific and public health knowledge. Table 2 describes the preparedness, readiness and response actions for COVID-19 for each transmission scenario. Hyperlinks to WHO technical guidance are provided. All technical guidance for WHO can be found on the WHO website.

Table 2. Critical preparedness, readiness and response actions for each transmission scenario for COVID-19

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
Transmission scenario	No reported cases.	One or more cases, imported or locally detected, without evidence of local transmission.	Cases limited to well-defined clusters, related by time, geographic location and common exposures	Outbreaks with the inability to relate confirmed cases through chains of transmission for a large number of cases, or by increasing positive tests through sentinel samples (routine systematic testing of respiratory samples from established laboratories.
Aim	Suppress transmission and prevent spread.	Suppress transmission and prevent spread.	Suppress transmission and prevent spread.	Suppress transmission, reduce case numbers, end community outbreaks.
Priority areas of work				
Emergency response mechanisms	Activate emergency response mechanisms. Review and maintain emergency response mechanisms.	Scale up emergency response mechanisms.	Scale up emergency response mechanisms.	Scale up emergency response mechanisms.
Risk communication and community engagement (RCCE) and infodemic management	Engage the public through RCCE and ensure people and communities participate in sharing trustworthy information, lead community actions and nurture trust in public health and social measures, through two-way communication. - Establish/revise RCCE working group - Assess situation and develop detailed RCCE plan, including resources, clear roles and responsibilities - Assess RCCE capacity and prepare training - Prepare risk perception assessment (formative research) - Prepare feedback loop mechanism - Set up monitoring system - Address rumours and misinformation with trustworthy information and facts shared through trusted channels and sources	Engage the public through RCCE and ensure people and communities participate in sharing trustworthy information, lead community actions and nurture trust in public health and social measures, through two-way communication. - Assess and revise RCCE plan according to situation with RCCE working group. - Provide training for surge staff - Engage communities as needed, with a focus on enhancing community dialogue and trust - Assess initial risk perception assessment (formative research) - Implement feedback loop mechanism - Monitor process	Engage the public through RCCE and ensure people and communities participate in sharing trustworthy information, lead community actions and nurture trust in public health and social measures, through two-way communication. - Assess and revise RCCE plan according to situation with RCCE working group. - Reinforce community-led activities to motivate individual and social responsibility to slow down transmission, alleviate stretched health systems and protect the most vulnerable - Provide training for surge staff - Engage communities as needed, with a focus on enhancing community dialogue and trust	Engage the public through RCCE and ensure people and communities participate in sharing trustworthy information, lead community actions and nurture trust in public health and social measures, through two-way communication. - Assess and revise RCCE plan according to situation with RCCE working group - Reinforce community-led activities to motivate individual and social responsibility to slow down transmission, alleviate stretched health systems and protect the most vulnerable - Continue risk perception assessment (formative research) - Implement feedback loop mechanism

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
	- Engage people and communities in designing strategies on how to take up and sustain the recommended individual and public health and social measures, including vaccination. - Ready communities for introduction of vaccines, treatments and tests. - Build resilience within communities to prepare for a shift in case scenarios and to ward off complacency of public health and social measures.	- Address rumours and misinformation with trustworthy information and facts shared through trusted channels and sources - Engage people and communities in designing strategies on how to take up and sustain the recommended individual and public health and social measures, including vaccination. - Ready communities for introduction of vaccines, treatments and tests. - Build resilience within communities to prepare for a shift in case scenarios and to ward off complacency of public health and social measures.	- Assess initial risk perception assessment (formative research) - Implement feedback loop mechanism - Monitor process to guide implementation of RCCE plan - Address rumours and misinformation with trustworthy information and facts shared through trusted channels and sources; amplify information and support from trusted community leaders and influencers including though trusted media - Engage people and communities in designing strategies on how to take up and sustain the recommended individual and public health and social measures, including vaccination. - Ready communities for introduction of vaccines, treatments and tests. - Build resilience within communities to prepare for a shift in case scenarios and to ward off complacency of public health and social measures.	- Engage communities as needed, with a focus on enhancing community dialogue and trust - Monitor process to guide implementation of RCCE plan - Address rumours and misinformation with trustworthy information and facts shared through trusted channels and sources; amplify information and support from trusted community leaders and influencers including though trusted media - Engage people and communities in designing strategies on how to take up and sustain the recommended individual and public health and social measures, including vaccination. - Ready communities for introduction of vaccines, treatments and tests. - Build resilience within communities to prepare for a shift in case scenarios and to ward off complacency of public health and social measures.
Surveillance	Actively test for COVID-19 among suspected cases; rapid isolation of cases. Implement testing for COVID-19 using existing community-based surveillance, respiratory disease surveillance systems, hospital-based surveillance, event-based surveillance and investigation of clusters. Include variants of concern in surveillance capacities, including sequencing where available. Implement or maintain enhanced surveillance for residential facilities and for vulnerable groups.	Actively test for COVID-19 among suspected cases; rapid isolation of cases. Implement COVID-19 surveillance using existing community-based surveillance, respiratory disease surveillance systems, hospital-based surveillance, event-based surveillance and investigation of clusters. Include variants of concern in surveillance capacities, including sequencing where available. Implement enhanced surveillance for residential facilities and for vulnerable groups.	Actively test for COVID-19 among suspected cases; rapid isolation of cases. Expand COVID-19 surveillance using existing community-based surveillance, respiratory disease surveillance systems, hospital-based surveillance, event-based surveillance and investigation of clusters. Include variants of concern in surveillance capacities, including sequencing where available. Implement enhanced surveillance for residential facilities and for vulnerable groups.	Actively test for COVID-19 among suspected cases; where possible, especially in newly infected areas; rapid isolation of cases and apply self-initiated isolation for symptomatic individuals. Adapt existing surveillance systems to monitor disease activity. Continue event-based surveillance and investigation of clusters. Include variants of concern in surveillance capacities, including sequencing where available. Implement enhanced surveillance for residential facilities and for vulnerable groups.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
	Develop national strategy for genomic surveillance for SARS-CoV-2 variants.	Where possible, track vaccination status of infected individuals in order to contribute to awareness of vaccine effectiveness Develop national strategy for genomic surveillance for SARS-CoV-2 variants.	Where possible, track vaccination status of infected individuals in order to contribute to awareness of vaccine effectiveness Develop national strategy for genomic surveillance for SARS-CoV-2 variants.	Where possible, track vaccination status of infected individuals in order to contribute to awareness of vaccine effectiveness Implement genomic surveillance for SARS-CoV-2 variants.
Contact tracing and management	Prepare for surge in contact tracing needs.	Conduct contact tracing and monitoring; quarantine of contacts.	Conduct contact tracing, monitoring; quarantine of contacts. Conduct cluster investigations.	Conduct contact tracing and monitoring where possible; quarantine of contacts. Conduct cluster investigations. Contact tracing capacity may be stretched and should therefore prioritize the identification and investigation of clusters, high risk settings and those at risk of severe disease.
Public health and social measures (PHSM)	Prepare to adjust public health and social measures based on an analysis of the level of transmission, the capacity of the health system to respond and other contextual factors. Ensure that basic risk mitigation measures in relation to international travel are in place (such as travel advice, self-monitoring for international travellers, and environmental controls and public health and social measures at points of entry and on board conveyances). Conduct systematic and regular risk assessments to inform the introduction, adjustment or discontinuation of supplementary measures (such as screening, testing and quarantine of international travellers) for all travel routes. Advise against the use of COVID-19 vaccination as a condition for travellers to enter or exit the country, or to attend gatherings.	Adjust public health and social measures based on an analysis of the level of local transmission, the capacity of the health system to respond and other contextual factors. Ensure that basic risk mitigation measures in relation to international travel are in place (such as travel advice, self-monitoring for international travellers, and environmental controls and public health and social measures at points of entry and on board conveyances). Conduct systematic and regular risk assessments to inform the introduction, adjustment or discontinuation of supplementary measures (such as screening, testing and quarantine of international travellers) for all travel routes. Advise against the use of COVID-19 vaccination as a condition for travellers to enter or exit the country, or to attend gatherings.	Adjust public health and social measures based on an analysis of the level of local transmission, the capacity of the health system to respond and other contextual factors. Ensure that basic risk mitigation measures in relation to international travel are in place (such as travel advice, self-monitoring for international travellers, and environmental controls and public health and social measures at points of entry and on board conveyances). Conduct systematic and regular risk assessments to inform the introduction, adjustment or discontinuation of supplementary measures (such as screening, testing and quarantine of international travellers) for all travel routes. Advise against the use of COVID-19 vaccination as a condition for travellers to enter or exit the country, or to attend gatherings.	Adjust public health and social measures based on an analysis of the level of local transmission, the capacity of the health system to respond and other contextual factors. Ensure that basic risk mitigation measures in relation to international travel are in place (such as travel advice, self-monitoring for international travellers, and environmental controls and public health and social measures at points of entry and on board conveyances). Conduct systematic and regular risk assessments to inform the introduction, adjustment or discontinuation of supplementary measures (such as screening, testing and quarantine of international travellers) for all travel routes. Advise against the use of COVID-19 vaccination as a condition for travellers to enter or exit the country, or to attend gatherings.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
	Any decision to restrict, modify, postpone, cancel, or proceed with holding a mass gathering should be based on a rigorous risk-assessment exercise, tailored to the event, positioned within the context of the public health and social measures (PHSMs) implemented in the hosting country or area where the event is planned.	No gatherings should occur unless the basic precautionary measures are observed. Any decision to restrict, modify, postpone, cancel, or proceed with holding a mass gathering should be based on a rigorous risk-assessment exercise, tailored to the event, positioned within the context of the public health and social measures (PHSMs) implemented in the hosting country or area where the event is planned.	No gatherings should occur unless the basic precautionary measures are observed. Any decision to restrict, modify, postpone, cancel, or proceed with holding a mass gathering should be based on a rigorous risk-assessment exercise, tailored to the event, positioned within the context of the public health and social measures (PHSMs) implemented in the hosting country or area where the event is planned.	No gatherings should occur unless the basic precautionary measures are observed. Any decision to restrict, modify, postpone, cancel, or proceed with holding a mass gathering should be based on a rigorous risk-assessment exercise, tailored to the event. In case of high or very high risk, postponing or cancelling an event should always be considered, positioned within the context of the public health and social measures (PHSMs) implemented in the hosting country or area where the event is planned.
Infection prevention and control (IPC) – health care setting	Identify national and facility level IPC focal points. (Re)train staff in IPC and clinical management specifically for COVID-19. Implement IPC strategies and measures to prevent or control transmission in health care settings. Use appropriate personal protective equipment (PPE) by health workers providing direct care to patients with COVID-19. Develop plan to forecast essential supply needs and a strategic allocation plan for severe shortages if disruption in PPE supply is anticipated. Prepare strategies for detecting, preventing and managing SARS-CoV-2 infections among health workers.	Identify national and facility level IPC focal points. (Re)train staff in IPC and clinical management specifically for COVID-19. Implement IPC strategies and measures to prevent or control transmission in health care settings. Use appropriate PPE by health care workers providing direct care to patients with COVID-19. Implement essential supply forecasting and strategic planning for severe shortages if disruption in PPE supply is anticipated or experienced. Implement guidance on mask use for health facilities. Implement strategies for detecting, preventing and managing SARS-CoV-2 infections among health workers.	Identify national and facility level IPC focal points. (Re)train staff in IPC and clinical management specifically for COVID-19. Implement IPC strategies and measures to prevent or control transmission in health care settings. Use appropriate PPE by health care workers providing direct care to patients with COVID-19. Implement essential supply forecasting and strategic planning for severe shortages if disruption in PPE supply is anticipated or experienced. Implement guidance on mask use for health facilities. Consider universal masking in health care facilities at this level. Implement strategies for detecting, preventing and managing SARS-CoV-2 infections among health workers.	Identify national and facility level IPC focal points. Retrain staff in IPC and clinical management specifically for COVID-19. Reinforce IPC strategies and measures to prevent or control transmission in health care settings. Use of appropriate PPE by health workers providing direct care to patients with COVID-19. Implement essential supplies forecasting and strategic planning for severe shortages if disruption in PPE supply is anticipated or experienced. Implement guidance on mask use for health facilities. Consider universal masking in health care facilities at this level. Implement strategies for detecting, preventing and managing SARS-CoV-2 infections among health workers.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
	Prepare for surge in health care facility needs, including respiratory support, IPC, IPC and PPE supplies, screening of health workers for infection and mental health support for health workers. Implement environmental and engineering controls, including adequate ventilation and environmental cleaning.	Prepare for surge in health care facility needs, including respiratory support, IPC, IPC and PPE supplies, screening of health workers for infection and mental health support for health workers. Implement environmental and engineering controls, including adequate ventilation and environmental cleaning.	Prepare for surge in health care facility needs, including respiratory support, IPC, IPC and PPE supplies, screening of health workers for infection and mental health support for health workers. Implement environmental and engineering controls, including adequate ventilation and environmental cleaning.	Implement health facilities surge plans, including respiratory support, IPC, IPC and PPE supplies, screening of health workers for infection and mental health support for health workers. Implement environmental and engineering controls, including adequate ventilation and environmental cleaning.
Infection prevention and control (IPC) – community settings	Anyone with symptoms suggestive of COVID-19 and those caring for sick persons at home should use medical masks and be mindful of other IPC recommendations such as environmental cleaning and ventilation.	Anyone with symptoms suggestive of COVID-19 and those caring for sick patients at home should use medical masks and be mindful of other IPC recommendations such as environmental cleaning and ventilation. Maintain physical distancing of at least 1 meter, wear a mask when physical distance of at least 1 meter cannot be maintained. Encourage outdoor activities over indoor activities, where possible. Perform frequent hand hygiene with alcohol-based hand sanitizer or soap and water. Ensure adequate ventilation in indoor settings. Avoid three C settings: **Crowded** places with many people nearby; **close-contact** settings, especially where people have close-range conversations; and **confined** and enclosed spaces with poor ventilation. Increase access to outdoor air through natural ventilation.	Anyone with symptoms suggestive of COVID-19 and those caring for sick patients at home should use medical masks and be mindful of other IPC recommendations such as environmental cleaning and ventilation Maintain physical distancing of at least 1 meter, wear a mask when physical distance of at least 1 meter cannot be maintained. Encourage outdoor activities over indoor activities, where possible. Encourage the use of medical masks by individuals/people with higher risk of severe complications from COVID-19 (people aged >60 years and/or with comorbid conditions); use of fabric mask for the general public where physical distancing of at least 1 m cannot be achieved, or if indoors where ventilation cannot be assessed or is known to be poor. Encourage the use of fabric mask for households, in indoor settings, when there is visitor who is not a member of the household.	Anyone with symptoms suggestive of COVID-19 and those caring for sick patients at home should use medical masks and be mindful of other IPC recommendations such as environmental cleaning and ventilation. Maintain physical distancing of at least 1 meter, wear a mask when physical distance of at least 1 meter cannot be maintained. Encourage outdoor activities over indoor activities, where possible. Encourage the use of medical masks by individuals/people with higher risk of severe complications from COVID-19 (people aged >60 years and/or with comorbid conditions); use of fabric mask for the general public where physical distancing of at least 1 m cannot be achieved, or if indoors where ventilation cannot be assessed or is known to be poor. Encourage outdoor activities over indoor activities, where possible. Encourage the use of fabric mask for households, in indoor settings, when there is visitor who is not a member of the household.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
			Ensure adequate ventilation in indoor settings. Perform frequent hand hygiene with alcohol-based hand sanitizer or soap and water. Avoid three C settings: **Crowded** places with many people nearby; **close-contact** settings, especially where people have close-range conversations; and **confined** and enclosed spaces with poor ventilation. Increase access to outdoor air through natural ventilation.	Ensure adequate ventilation in indoor settings. Perform frequent hand hygiene with alcohol-based hand sanitizer or soap and water. Avoid three C settings: **Crowded** places with many people nearby; **close-contact** settings, especially where people have close-range conversations; and **confined** and enclosed spaces with poor ventilation. Increase access to outdoor air through natural ventilation.
Laboratory and diagnostics	Test according to the national strategy, using available and approved diagnostic tests. Nucleic acid amplification testing (NAAT), for example RT-PCR, is the reference method for detection of active SARS-CoV-2 infections.[1] Identify facilities at national or international laboratories for referral of positive specimens for sequencing.	Test according to the national strategy, using available and approved diagnostic tests. Nucleic acid amplification testing (NAAT), for example RT-PCR, is the reference method for detection of active SARS-CoV-2 infections.[1] Genomic sequencing of SARS-CoV-2 should be used to detect and monitor SARS-CoV-2 variants. At least a subset of representative, quality and timely NAAT positive samples should be sequenced at national facilities or at international reference laboratories. The following additional cases can be prioritized for further characterization through sequencing: - Infection in previously infected individuals - Infection in previously vaccinated individuals - Diagnostic test failure or target drop out	Test according to the national strategy, using available and approved diagnostic tests. Nucleic acid amplification testing (NAAT), for example RT-PCR, is the reference method for detection of active SARS-CoV-2 infections.[1] Genomic sequencing of SARS-CoV-2 should be used to detect and monitor SARS-CoV-2 variants. At least a subset of representative, quality and timely NAAT positive samples should be sequenced at national facilities or at international reference laboratories. The following additional cases can be prioritized for further characterization through sequencing: - Infection in previously infected individuals - Infection in previously vaccinated individuals - Diagnostic test failure or target drop out	Test according to the national strategy, using available and approved diagnostic tests. Nucleic acid amplification testing (NAAT), for example RT-PCR, is the reference method for detection of active SARS-CoV-2 infections.[1] If diagnostic capacity is insufficient, implement prioritized testing and measures that can reduce spread (e.g. isolation), including priority testing with Ag-RDTs or (wherever possible) with RT-PCR of: - people who are at risk of developing severe disease and vulnerable populations, who will require hospitalization and advanced care for COVID-19 - health workers (including emergency services and non-clinical staff) regardless of whether they are a contact of a confirmed case (to protect health workers and reduce the risk of nosocomial transmission)

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
		- Individuals with prolonged viral replication and shedding All genetic sequence data should be shared by uploading to a publicly accessible database.	- Individuals with prolonged viral replication and shedding All genetic sequence data should be shared by uploading to a publicly accessible database.	- the first symptomatic individuals in a closed setting (e.g. schools, long term living facilities, prisons, hospitals) or fragile settings (e.g. humanitarian operations, refugee/migrant camp and non-camp settings) to quickly identify outbreaks and ensure containment measures Genomic sequencing of SARS-CoV-2 should be used to detect and monitor SARS-CoV-2 variants in areas of widespread transmission. At least a subset of representative, quality and timely NAAT positive samples should be sequenced at national facilities or at international reference laboratories. The following additional cases can be prioritized for further characterization through sequencing: - Infection in previously infected individuals - Infection in previously vaccinated individuals - Diagnostic test failure or target drop out - Individuals with prolonged viral replication and shedding Sequence a subset of representative, quality and timely NAAT positive samples from sentinel surveillance sites. All genetic sequence data should be shared by uploading to a publicly accessible database.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
Case management strategy	Set up or maintain screening and triage protocols at all points of access to the health system. Prepare to treat COVID-19 affected patients, this includes patients that may go on to develop Post COVID-19 condition. Set up or maintain COVID-19 hotline and referral system; ready hospitals for potential surge. Ensure supply chain management system in place for therapeutics (i.e. corticosteroids), oxygen supply and availability. Ensure national guidelines are adapted on regular basis to align with WHO Living Guidances. Ensure health workers are trained in clinical management, this includes clinical and technical staff. Ensure structures for caring for COVID-19 patients adhere to guidance available on design and ventilation.	Screen and triage patients at all points of access to the health system. Care for all suspected and confirmed patients according to disease severity and acute care need. Care for all suspected and confirmed patients that go on to develop Post COVID-19 condition. Ready hospitals for surge; ready communities for surge, including by setting up community facilities for isolation of mild/moderate cases; establish protocol for home isolation. Ensure supply chain management system in place for therapeutics (i.e. corticosteroids), oxygen supply and availability. Ensure national guidelines are adapted on regular basis to align with WHO Living Guidances. Ensure health workers are trained in clinical management, this includes clinical and technical staff. Ensure structures for caring for COVID-19 patients adhere to guidance available on design and ventilation.	Screen and triage patients at all points of access to the health system. Care for all suspected and confirmed patients according to disease severity and acute care needs. Care for all suspected and confirmed patients that go on to develop Post COVID-19 condition Activate surge plans for health facilities, activate community facilities; activate protocols for home isolation. Ensure supply chain management system in place for therapeutics (i.e. corticosteroids), oxygen supply and availability. Ensure national guidelines are adapted on regular basis to align with WHO Living Guidances. Ensure health workers are trained in clinical management, this includes clinical and technical staff. Ensure structures for caring for COVID-19 patients adhere to guidance available on design and ventilation.	Screen and triage patients at all points of access to the health system. Care for all suspected and confirmed patients according to disease severity and acute care needs. Care for all suspected and confirmed patients that go on to develop Post COVID-19 condition Activate and continue to scale up surge plans for health facilities, community facilities and home care, including enhancement of COVID-19 referral system. Ensure supply chain management system in place for therapeutics (i.e. corticosteroids), oxygen supply and availability. Ensure national guidelines are adapted on regular basis to align with WHO Living Guidances. Ensure health workers are trained in clinical management, this includes clinical and technical staff. Ensure structures for caring for COVID-19 patients adhere to guidance available on design and ventilation.
Case management recommendations by case severity and risk factors	Test suspect COVID-19 cases according to the diagnostic strategy. For mild and moderate cases with no risk factors, there are three options for care and isolation: - Health facilities, if resources allow - Community facilities (i.e. stadiums, gymnasiums, hotels) with access to rapid health advice (i.e., adjacent COVID-19 designated health post, telemedicine) - Self-isolation at home according to WHO guidance with consideration of alternative delivery platforms such as telemedicine or community outreach teams. For moderate cases with risk factors, and all severe/critical cases: hospitalization (in-patient treatment), with appropriate isolation/cohorting. The decision of location should be made on a case-by-case basis and will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease and conditions at home, including the presence of vulnerable persons in the household.			

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
Health services	Maintain all health services. Prepare or review health system capacity and surge strategies. Designate an essential health services (EHS) focal point to the national COVID-19 incident management team (IMT). Generate a country-specific list of core EHS and map to (HR and material) resource needs. Establish triggers or thresholds for phased reallocation of capacity and dynamic adaptation of services as the pandemic evolves. Establish or review mechanisms to monitor the ongoing delivery of EHS. Initiate rapid trainings to expand health worker capacity in key areas (including screening triage and emergency care). Maintain and reinforce surveillance for vaccine-preventable diseases; develop or review strategies for delivering immunization services.	Maintain all health services, with strategic shifts in service delivery to limit transmission (e.g. limiting facility-based encounters where appropriate, modifying patient flow for safety). Implement health system capacity and surge strategies. Generate and complete a country-specific list of core EHS and map to (HR and material) resource needs. Evaluate readiness to shift to priority EHS. Establish mechanisms of coordination and communication among the IMT and service providers. Ensure that 24-hour acute care services are available at all first-level hospital emergency (or similar) units and ensure public awareness. Conduct rapid capacity assessments (HR and material resources). Suspend user fees at the point of care for EHS for all patients. Maintain and reinforce surveillance for vaccine-preventable diseases; implement strategies for delivering immunization services.	Maintain all health services, with strategic shifts in service delivery to limit transmission (e.g. limiting facility-based encounters where appropriate, modifying patient flow for safety). Enhance health system capacity and surge strategies. Prepare to initiate strategic shifts for prioritization. Implement protocols for targeted referral and counter-referral pathways. Schedule appointments, limit visitors and create unidirectional patient and staff flow to ensure sufficient distancing. Implement tools and information systems to support teleconsultations. Coordinate additional funding for health workers to ensure timely payment of salaries, overtime, sick leave and incentive or hazard pay. Maintain and reinforce surveillance for vaccine-preventable diseases; implement strategies for delivering immunization services.	Maintain all health services as possible. In CT4, or whenever service capacity is overwhelmed, implement strategic shifts to prioritize EHS. Intensify health system capacity and surge strategies. Continue to monitor delivery of EHS at community and facility level, identify barriers to access and anticipate restoring suspended services based on changing needs. Establish weekly reporting from major distribution points on critical products that may be at risk of shortages. Coordinating primary care support, adjust hospital admission and discharge protocols as appropriate to limit duration of inpatient stays. Document adaptive responses implemented during the pandemic phase that should be considered for longer-term integration into health system operations. Maintain surveillance for vaccine-preventable diseases; implement strategies for delivering immunization services.
Societal response	Develop all-of-society and business continuity plans. Review and update all-of-society and business continuity plans as evidence becomes available.	Implement all-of-society plans, repurpose government and ready business continuity plans.	Implement all-of-society plans, repurpose government, business continuity and community services plans.	Implement all-of-society plans, repurpose government, business continuity and community services plans.

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
Vaccine introduction	Operationalize COVID-19 National Deployment and Vaccination Plan Identify and plan a national vaccine access/procurement approach (e.g. COVAX Facility, bilateral purchase agreement, procurement through UN agency, self-procurement), ensuring access to vaccines, ancillary supplies, and Personal Protective Equipment (PPE). Train health workers for safe COVID-19 vaccination delivery Support the adoption of efficient and expedited regulatory pathways for approval and regulatory oversight of COVID-19 vaccines including risk-based pharmacovigilance and post marketing surveillance of products. Assess required logistical procedures, as well as dry storage and cold chain capacity and infrastructure needs at all levels with regards to the COVID-19 vaccines characteristics and develop a plan to fill the identified supply and logistics gaps. Ensure a vaccination monitoring and safety monitoring systems exists and coordinating committee is in place. Include COVID-19 vaccine programme costs (vaccine, operating costs, human resources and capital costs) in government budgetary and/or planning documents approved by the appropriate authority; Identify funding gaps in operational costs and if needed apply to multilateral back funding and in-country donor funding.	Operationalize COVID-19 National Deployment and Vaccination Plan Identify and plan a national vaccine access/procurement approach (e.g. COVAX Facility, bilateral purchase agreement, procurement through UN agency, self-procurement), ensuring access to vaccines, ancillary supplies, and Personal Protective Equipment (PPE). Train health workers for safe COVID-19 vaccination delivery Support the adoption of efficient and expedited regulatory pathways for approval and regulatory oversight of COVID-19 vaccines including risk-based pharmacovigilance and post marketing surveillance of products. 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Include COVID-19 vaccine programme costs (vaccine, operating costs, human resources and capital costs) in government, budgetary and/or planning documents approved by the appropriate authority; Identify funding gaps in operational costs and if needed apply to multilateral back funding and in-country donor funding.

WHO Technical Guidance for COVID-19

Country-level coordination, planning, and monitoring

- COVID-19 Partners Platform based on Operational Planning Guidance
- Training modules: Operational Planning Guidelines and COVID-19 Partners Platform
- National capacities review tool for a novel coronavirus

Critical preparedness, readiness and response actions for COVID-19

- Responding to community spread of COVID-19
- Overview of Public Health and Social Measures in the context of COVID-19
- Considerations for implementing and adjusting public health and social measures in the context of COVID-19
  - Considerations for public health and social measures in the workplace in the context of COVID-19
  - Considerations for school-related public health measures in the context of COVID-19
  - Considerations for mass gatherings in the context of COVID-19
- Considerations for implementing a risk-based approach to international travel in the context of COVID-19
- Preparedness for cyclones, tropical storms, tornadoes, floods and earthquakes during the COVID-19 pandemic
- Investing in and building longer-term health emergency preparedness during the COVID-19 pandemic
- Practical actions in cities to strengthen preparedness for the COVID-19 pandemic and beyond
- Guidance for conducting a country COVID-19 intra-action review (IAR)
- Strategic Advisory Group of Experts on Immunization (SAGE): COVID-19 vaccines technical documents
- Emergency use listing for COVID-19
- Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines

Surveillance, rapid response teams, and case investigation

- Public health surveillance for COVID-19
  - COVID-19 Case definition
  - Global surveillance of COVID-19: WHO process for reporting aggregated data
- Considerations in the investigation of cases and clusters of COVID-19
- Considerations for quarantine of contacts of COVID-19 cases
- Surveillance strategies for COVID-19 human infection
- Contact tracing in the context of COVID-19
  - Digital tools for COVID-19 contact tracing
  - Ethical considerations to guide the use of digital proximity tracking technologies for COVID-19 contact tracing
- Operational considerations for COVID-19 surveillance using GISRS
- Medical certification, ICD mortality coding, and reporting mortality associated with COVID-19

Guidance for national laboratories

- Diagnostic testing for SARS-CoV-2
- Laboratory testing strategy recommendations for COVID-19
- Laboratory biosafety related to coronavirus disease (COVID-19)
- Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus
- Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays
- SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide
- COVID-19 Target product profiles for priority diagnostics to support response to the COVID-19 pandemic
- Laboratory assessment tool for laboratories implementing SARS-CoV-2 testing
- SARS-CoV-2 genomic sequencing for public health goals: interim guidance
- Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health
- Operational considerations to expedite genomic sequencing component of GISRS surveillance of SARS-CoV-2

Clinical care for COVID-19 patients

- Clinical management of COVID-19
- Therapeutics and COVID-19
- Drugs to Prevent COVID-19
- Clinical care of severe acute respiratory infections – Tool kit
- Home care for patients with suspected or confirmed COVID-19 and management of their contacts
- Operational considerations for case management of COVID-19 in health facility and community
- Severe Acute Respiratory Infections Treatment Centre
- Recommendations: Prehospital Emergency Medical Services (EMS) COVID-19
- Use of chest imaging in COVID-19
- Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease (COVID-19)
- Global COVID-19 Clinical Characterization Case Record Form
  - Rapid core case report form
  - Pregnancy case report form
  - Case Report Form for suspected cases of multisystem inflammatory syndrome (MIS) in children and adolescents temporally related to COVID-19
  - Post COVID-19 case report form

Infection Prevention and Control for COVID-19

- Infection prevention and control during health care when COVID-19 is suspected or confirmed
- Rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages
- Advice on the use of masks in the context of COVID-19
- Advice on the use of masks for children in the community in the context of COVID-19
- Considerations for quarantine of contacts of COVID-19 cases
- Water, sanitation, hygiene and waste management for COVID-19
- Infection prevention and control for the safe management of a dead body in the context of COVID-19

- Infection prevention and control for long-term care facilities in the context of COVID-19Infection prevention and control for long-term care facilities in the context of COVID-19
- Cleaning and disinfection of environmental surfaces in the context of COVID-19
- Surveillance protocol for SARS-CoV-2 infection among health workers
- Prevention, identification and management of health worker infection in the context of COVID-19
- Health workers exposure risk assessment and management in the context of COVID-19 virus
- Home care for patients with suspected novel coronavirus (nCoV) infection presenting with mild symptoms and management of contacts
- Aide-memoire: Infection prevention and control (IPC) principles and procedures for COVID-19 vaccination activities

Essential resources planning

- COVID-19 Essential Supplies Forecasting Tool
- FAQ: COVID-19 Essential Supplies Forecasting Tool (COVID-19 ESFT)
- Adapt Surge Planning Support Tool
- Health Workforce Estimator
- Reagent calculator for portal
- List of priority medical devices for COVID-19 case management
- Technical specifications for invasive and non-invasive ventilators for COVID-19
- Oxygen sources and distribution for COVID-19 treatment centres
- Technical specifications for Pressure Swing Adsorption (PSA) Oxygen Plants

Essential health services

- Maintaining essential health services: operational guidance for the COVID-19 context
- Community-based health care, including outreach and campaigns, in the context of the COVID-19 pandemic
- Harmonized health service capacity assessments in the context of the COVID-19 pandemic
  - Rapid hospital readiness checklist
  - Biomedical equipment for COVID-19 case management - inventory tool
  - Diagnostics, therapeutics, vaccine readiness, and other health products for COVID-19
  - Ensuring a safe environment for patients and staff in COVID-19 health-care facilities
  - Infection prevention and control health-care facility response for COVID-19
  - Continuity of essential health services: Facility assessment tool
- Recommendations to Member States to improve hand hygiene practices to help prevent the transmission of the COVID-19 virus
- Guiding principles for immunization activities during the COVID-19 pandemic
  - FAQ: Immunization in the context of COVID-19 pandemic
- Framework for decision-making: implementation of mass vaccination campaigns in the context of COVID-19
- Preventing and managing COVID-19 across long-term care services: Policy brief
  - Preventing and managing COVID-19 across long-term care services: Web annex
- Considerations for implementing mass treatment, active case-finding and population-based surveys for neglected tropical diseases in the context of the COVID-19 pandemic
- Considerations for the provision of essential oral health services in the context of COVID-19

Risk communication and community engagement

- Risk communication and community engagement Toolkit
- 10 Steps to community readiness – what countries should do to prepare communities for a COIVD-19 vaccine, treatment or new test
- COVID-19 Global Risk Communication and Community Engagement Strategy
- Risk communication and community engagement readiness and response to coronavirus disease (COVID-19)
- Mental health considerations during COVID-19 outbreak
- COVID-19 risk communication package for healthcare facilities
- A guide to preventing and addressing social stigma associated with COVID-19

Guidance for COVID-19 in schools, workplaces and institutions

- Key messages and actions for COVID-19 prevention and control in schools
- IASC: COVID-19 prevention and control in schools
- Getting your workplace ready for COVID-19
- COVID-19 and Food Safety: Guidance for competent authorities responsible for national food safety control systems
- COVID-19 and food safety: Guidance for food businesses
- Operational considerations for COVID-19 management in the accommodation sector
- Preparedness, prevention and control of COVID-19 in prisons and other places of detention
- Rights, roles and responsibilities of health workers, including key considerations for occupational safety and health

Humanitarian operations, camps and other fragile settings

- IASC: Scaling-up COVID-19 Outbreak in Readiness and Response Operations in Camps and Camp-like Settings (jointly developed by IFRC, IOM, UNHCR and WHO)
- Preparedness, prevention and control of coronavirus disease (COVID-19) for refugees and migrants in non-camp settings
- Public health and social measures for COVID-19 preparedness and response in low capacity and humanitarian settings
- Preparedness for cyclones, tropical storms, tornadoes, floods and earthquakes during the COVID-19 pandemic

Operational support and logistics

- Disease commodity package

Travel, points of entry and border health

- Considerations for implementing a risk-based approach to international travel in the context of COVID-19
- Management of ill travellers at Points of Entry – international airports, seaports and ground crossings – in the context of COVID-19 outbreak
- Operational considerations for managing COVID-19 cases/outbreak on board ships
- Operational considerations for managing COVID-19 cases or outbreak in aviation
- Controlling the spread of COVID-19 at ground crossings
- Promoting public health measures in response to COVID-19 on cargo ships and fishing vessels
- Interim position paper: considerations regarding proof of COVID-19 vaccination for international travellers

Mass gatherings

- Key planning recommendations for Mass Gatherings in the context of the current COVID-19 outbreak
- Mass gatherings COVID-19 risk assessment
  - Risk assessment tool
  - Decision tree
  - Considerations for risk assessment for sports federations/sports event organizers
  - Risk assessment tool for sports events
- Practical considerations and recommendations for religious leaders and faith-based communities in the context of COVID-19
  - Risk assessment tool
  - Decision tree
- Safe Ramadan practices in the context of the COVID-19
- Safe Eid al Adha practices in the context of COVID-19

Reducing animal-human transmission of emerging pathogens

- Origin of SARS-CoV-2
- Recommendations to reduce risk of transmission of emerging pathogens from animals to humans in live animal markets or animal product markets

Early investigation protocols (the Unity Studies)

- The First Few X (FFX) Cases and contact investigation protocol for COVID-19 infection
- Household transmission investigation protocol for COVID-19 infection
- Prospective cohort protocol for assessment of potential risk factors for COVID-19 infection among health care workers in a health care setting
- Case-control protocol for assessment of potential risk factors for COVID-19 infection among health care workers in a health care setting
- Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection
- Surface sampling of coronavirus disease COVID-19 virus: A practical "how to" protocol for health care and public health professionals

Online training courses available for COVID-19

- Introduction to COVID-19
- eProtect Respiratory Infections
- Critical Care for Severe Acute Respiratory Infections
- WHO Medical emergency checklist
- Severe Acute Respiratory Infection (SARI) treatment facility design
- Resuscitation area designation tool
- Infection Prevention and Control for COVID-19
  - Infection Prevention and Control core components and multimodal strategies
  - Standard precautions: Hand hygiene
  - Standard precautions: Waste management
  - Standard precautions: Environmental cleaning and disinfection
  - Standard precautions: Injection safety and needle-stick injury management
  - Decontamination and sterilization of medical devices
  - How to put on and remove personal protective equipment
- Country preparedness and response planning
- Mass gatherings risk assessment training
- Occupational health and safety for health workers in the context of COVID-19
- Long-term care facilities in the context of COVID-19
- Controlling the spread of COVID-19 at ground crossings
- Operational considerations for managing COVID-19 cases and outbreaks in aviation
- Operational considerations for managing COVID-19 cases and outbreaks on board ships
- Management of ill travellers at point of entry in the context of the COVID-19 outbreak

WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication

WHO reference number: WHO/2019-nCoV/Community_Actions/2021.1

Datum	dagelijkse R	avondklok	weekend		Weekgem	berekening	Weekgem zonder effect
10 dec.	1	23-5	geen		2.142857		
11 dec.	1.545455	23-5	geen		2.428571		
12 dec.	2.083333	23-5	geen		3.571429		
13 dec.	2.416667	23-5	geen		4.142857		
14 dec.	2.615385	21-5	geen		4.857143		
15 dec.	7.857143	21-5	geen		7.857143		
16 dec.	5.230769	21-5	weekend 19-05		9.714286		
17 dec.	6.066667	21-5	weekend 19-05		13		
18 dec.	7.058824	21-5	weekend 19-05		17.14286	17.14/2.42=7.06	
19 dec.	6.48	21-5	weekend 19-05		23.14286		
20 dec.	6.862069	21-5	weekend 19-05		28.42857		
21 dec.	6.588235	21-5	weekend 19-05		32		
22 dec.	5.236364	21-5	weekend 19-05		41.14286		
23 dec.	4.897059	21-5	weekend 19-05		47.57143		
24 dec.	4.197802	21-5	weekend 19-05		54.57143		
25 dec.	3.508333	21-5	weekend 19-05		60.14286	60.14/17.14=3.51	121.3512
26 dec.	2.635802	21-5	weekend 19-05		61		7.08*17.14
27 dec.	2.140704	21-5	weekend 19-05		60.85714		
28 dec.	1.919643	21-5	weekend 19-05		61.42857		
29 dec.	1.489583	21-5	weekend 19-05		61.28571		
30 dec.	1.342342	21-5	weekend 19-05		63.85714		
31 dec.	1.04712	21-5	weekend 19-05		57.14286		
1-Jan	0.942993	21-5	weekend 19-05		56.71429		

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Over de betrouwbaarheid van de PCR-test voor SARS-CoV-2

Analytische/technische betrouwbaarheid

De analytische/technische **sensitiviteit** van de PCR-test is dat deze tussen 1-10 kopieën genetisch materiaal van het SARS-CoV-2 in een PCR reactie detecteert (1, 10, 11). Dit weten we omdat bij validatie van de PCR-test de limiet van detectie wordt bepaald (3, 12).

De analytische/technische **specificiteit** van de PCR-test is dat deze alleen genetisch materiaal van het SARS-CoV-2 virus detecteert. Soms bevat een PCR-test nog een component, of alleen een component, die SARS virussen detecteert in de groep van SARS virussen waartoe SARS-CoV-2 behoort. Omdat alleen SARS-CoV-2 uit deze groep van SARS virussen in mensen voorkomt, is deze component voor diagnostiek in mensen ook specifiek voor SARS-CoV-2. De PCR-test detecteert dus geen andere virussen en bacteriën die klachten kunnen geven die lijken op die van COVID-19 of die bij mensen zonder klachten in de luchtweg kunnen voorkomen, zoals griepvirus, verkoudheidsvirus en *Chlamydia pneumoniae*. Dit weten we omdat bij validatie van de PCR-test heel uitgebreid de kruisreactiviteit van de PCR-test met deze virussen en bacteriën wordt uitgetest (3, 12).

Er is een **kwaliteitscontrole programma** wat vanuit de WHO referentielaboratoria in Nederland, gevestigd bij het RIVM en het Erasmus MC, de kwaliteit van de gebruikte PCR-testen in Nederlandse laboratoria bewaakt (13, 14). Deze kwaliteitscontrole betreft controle op zowel de analytische/technische sensitiviteit als de analytische/technische specificiteit van de uitgevoerde PCR-testen, inclusief de efficiëntie van extractie van genetisch materiaal van het virus uit klinische monsters. Verdere informatie over de PCR-test staat hier: https://www.rivm.nl/coronavirus-covid-19/testen (10).

Klinische betrouwbaarheid

De PCR-test bepaalt of een getest persoon genetisch materiaal van het SARS-CoV-2 bij zich heeft en daarmee of een persoon met het virus geïnfecteerd is. Een persoon die het SARS-CoV-2 virus bij zich heeft kan daar ziek van worden of niet. Het percentage van met SARS-CoV-2 geïnfecteerde personen wat ziek wordt is niet precies bekend; schattingen voor geen tot milde symptomen lopen uiteen van 5 tot 80% (5). Een recente meta-analyse geeft een samenvattend percentage voor asymptomatische infectie van 15.6% (95% CI, 10.1%-23.0%), waarbij er grote verschillen kunnen zijn tussen specifieke groepen SARS-CoV-2 positieve personen (4).

In het huidige document wordt geen onderscheid gemaakt tussen PCR-test positief en besmettelijk en PCR-test positief en niet besmettelijk. Een beschouwing hierover staat hier: https://www.rivm.nl/sites/default/files/2020-11/Toelichting%20PCR_RIVM.pdf (11).

De klinische betrouwbaarheid van de PCR-test is afhankelijk van een groot aantal factoren:

- De **analytische/technische sensitiviteit en specificiteit** van de PCR-test (zie hierboven)
- De hoeveelheid SARS-CoV-2 aanwezig in de bovenste luchtweg van iemand die geïnfecteerd is; het hoogst enkele dagen na infectie (ongeacht of de geïnfecteerde persoon symptomen krijgt) en houdt dan enkele dagen aan waarna het minder wordt doordat het lichaam het virus opruimt. De **vooraf-kans** op een positieve PCR-test is dus het hoogst als een persoon 2 tot 10 dagen na infectie wordt bemonsterd.
- De kwaliteit van het afgenomen monster om te testen met de PCR-test; het meest sensitief is om zowel een monster te nemen van de keel (orofarynx) en uit de neus (nasofarynx of tenminste hoog in de neus). Mensen die monsters afnemen worden getraind om dit goed te doen. De **vooraf-kans** op een positieve PCR-test is dus het hoogst als een persoon op een juiste manier wordt bemonsterd.
- Of een persoon symptomen heeft of niet; bij iemand met symptomen die passen bij COVID-19 is de **vooraf-kans** op een positieve PCR-test hoger dan bij een persoon die geen klachten heeft; vooral in de eerste dagen na ontstaan van symptomen. Symptomatisch testen versus asymptomatisch testen.
- Of een persoon enkele dagen voor het testen een hoge waarschijnlijkheid van besmetting heeft of niet; iemand die dicht bij een COVID-19 patiënt is geweest heeft een veel hogere **vooraf-kans** om PCR-test positief te worden dan iemand die willekeurig van de straat wordt ‘geplukt’. Hoe langer een persoon dichtbij een COVID-19 patiënt is geweest hoe groter de **vooraf-kans** voor die persoon om PCR-test positief te worden. Screening met strikte casusdefinitie en bron en contactonderzoek versus algemene populatie screening.
- Hoe hoog de **prevalentie** is van circulatie van het virus; bij hoge prevalentie is de **vooraf-kans** dat bij een persoon het virus gedetecteerd wordt hoger dan bij een lage **prevalentie**. In het land kunnen er regionale verschillen in prevalentie zijn en daardoor dus ook verschillen in de **vooraf-kans** om PCR-test positief te worden.

Bovenstaande factoren bepalen de kans of een positieve PCR-test correct aangeeft of een geteste persoon het genetisch materiaal van het SARS-CoV-2 virus bij zich heeft en of een negatieve PCR-test correct aangeeft of de geteste persoon het genetisch materiaal van het SARS-CoV-2 virus niet bij zich heeft. Om daar vat op te krijgen worden een aantal grootheden gebruikt, **klinische sensitiviteit** en **klinische**

specificiteit en **positief voorspellende waarde** (PPV) en **negatief voorspellende waarde** (NPV) van de PCR-test en de afhankelijkheid van die grootheden van **prevalentie** en **vooraf-kans** om geïnfecteerd te zijn (13, 14).

De **klinische sensitiviteit** geeft de waarschijnlijkheid aan dat de PCR-test positief is als de geteste persoon COVID-19 heeft (% correct positief). Voor de SARS-CoV-2 PCR-test wordt deze op basis van analyse van veel publicaties geschat op **67 tot 98%** (2, 6, 7, 8, 9). Deze range is vooral het gevolg van de variatie in virusuitscheiding, type en juistheid van afgenomen monster en tijdstip van bemonstering bij een COVID-19 patiënt. Hier kan dus een **fout-negatief** resultaat voorkomen; in 2 tot 33**%** van personen met COVID-19.

De **klinische specificiteit** geeft de waarschijnlijkheid aan dat de PCR-test negatief is als de geteste persoon geen COVID-19 heeft (% correct negatief). Voor de SARS-CoV-2 PCR test wordt deze op basis van analyse van veel publicaties geschat op **96 tot 99.5%** (2, 6, 7, 8, 9). Deze range is vooral het gevolg van de analytische/technische specificiteit van de gebruikte PCR-testen. Hier kan dus een **fout-positief** resultaat voorkomen; in 0.5 tot 4% van personen zonder COVID-19.

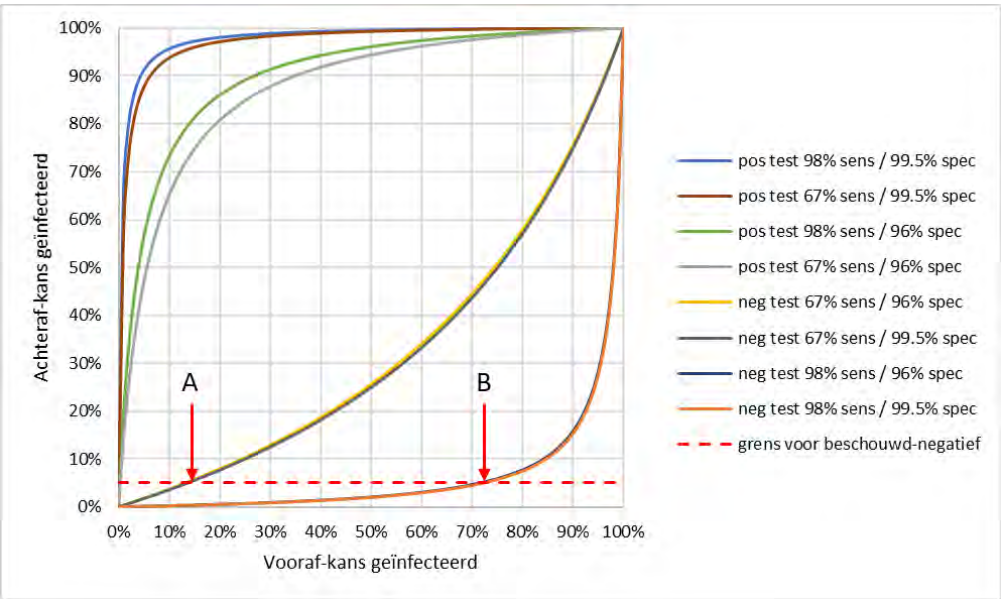
De **positief voorspellende waarde** (PPV) geeft de waarschijnlijkheid aan dat de geteste persoon COVID-19 heeft als de PCR-test positief is.

De **negatief voorspellende waarde** (NPV) geeft de waarschijnlijkheid aan dat de geteste persoon geen COVID-19 heeft als de PCR-test negatief is.

Zoals hierboven aangegeven is de **klinische sensitiviteit** en **klinische specificiteit** afhankelijk van de **vooraf-kans** dat een positieve PCR-test correct positief is en een negatieve PCR-test correct negatief. Omdat dit zo is wordt daarvan gebruik gemaakt om met hoogste zekerheid de personen te identificeren die COVID-19 hebben en bijdragen aan verspreiding. Daarom werd in het begin van de epidemie met een strenge casusdefinitie gewerkt van typische symptomen en mogelijk contact met COVID-19 positieve personen (o.a. reishistorie China). En is een voorwaarde om te laten testen het hebben van symptomen (10, 13). Het testen van personen zonder symptomen wordt nu toegevoegd aan het testbeleid. De **vooraf-kans** dat een positieve PCR-test correct positief is en een negatieve PCR-test correct negatief neemt daardoor af.

De samenhang tussen **vooraf-kans** en **achteraf-kans** om geïnfecteerd te zijn bij een positieve of negatieve PCR-test staat in figuur 1 (8, 9).

De buiging van de curves in figuur 1 voor positieve en negatieve test worden beïnvloed door de **klinische sensitiviteit** en **klinische specificiteit**. Bij een **klinische sensitiviteit** en **klinische specificiteit** van 50% is de **vooraf-kans** en **achteraf-kans** om geïnfecteerd zijn voor positief of negatief testen gelijk. Een hogere **klinische sensitiviteit** maakt dat vooral de curve voor negatieve test scherper naar rechtsonder doorbuigt. Een hogere **klinische specificiteit** maakt dat vooral de curve voor positieve test scherper naar linksboven uitbuigt.



Figuur 1. *Samenhang tussen* ***vooraf-kans*** *en* ***achteraf-kans*** *om geïnfecteerd te zijn bij een positieve (pos test) of negatieve (neg-test) PCR-test voor SARS-CoV-2.*
Noot: De kromme curves zijn voor de eerdere genoemde grenzen van de schattingen voor ***klinische sensitiviteit*** *en een* ***klinische specificiteit*** *van PCR-test. Het gebied onder de rode stippellijn geeft het gebied aan waarin het bijvoorbeeld veilig is om contact te hebben met anderen bij een negatief test resultaat omdat de kans dat je ondanks negatief PCR-test resultaat toch geïnfecteerd bent lager is dan 5%. De grens van dit gebied is afhankelijk van het geaccepteerde risico bij een* ***fout-negatief*** *resultaat.*

Met voorselectie voor hogere **vooraf-kans** om geïnfecteerd zijn neemt de **achteraf-kans** om inderdaad geïnfecteerd te zijn voor een positieve test sterker toe dan voor een negatieve test. Een hogere **vooraf-kans** resulteert dus in het adequater vinden van werkelijk geïnfecteerden.

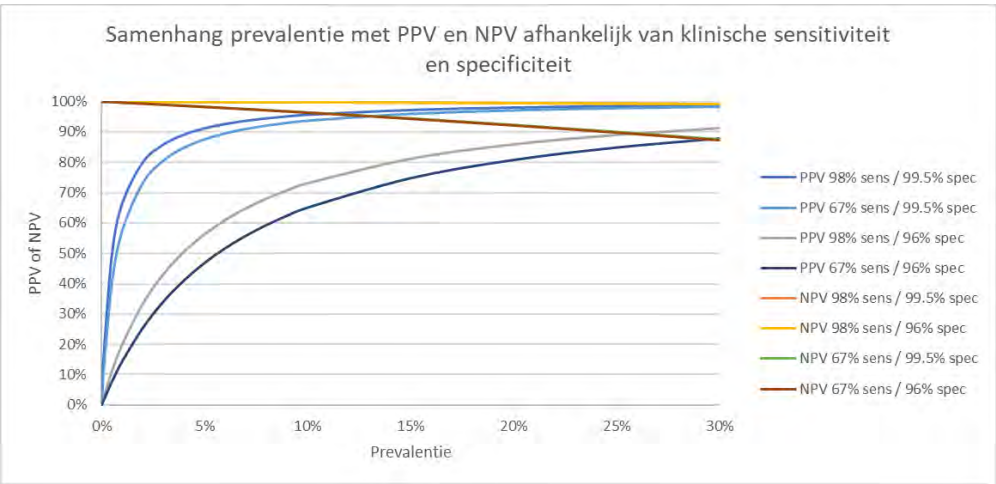
De samenhang tussen **vooraf-kans** en **achteraf-kans** om geïnfecteerd te zijn is voor positief testen dus vooral afhankelijk van de **klinische specificiteit**. Figuur 1 laat zien dat bij een **vooraf-kans** van 10% om geïnfecteerd te zijn en 99.5% specificiteit van de PCR-test de **achteraf-kans** om geïnfecteerd te zijn al circa 95% is, en de kans op **fout-positief** testen dus 5%. Hoe hoger de **vooraf-kans** om geïnfecteerd te zijn hoe lager de kans op **fout-positief** testen.

De samenhang tussen **vooraf-kans** en **achteraf-kans** om geïnfecteerd te zijn is voor negatief testen dus vooral afhankelijk van de **klinische sensitiviteit**. Bij hogere **klinische sensitiviteit** van de PCR-test wordt pas bij een hogere **vooraf-kans** op infectie een persoon niet geïnfecteerd beoordeeld (pijl B), dan bij een lagere **klinische sensitiviteit** van de PCR-test (pijl A). Bij een negatief resultaat van een PCR-test met lagere **klinische sensitiviteit** (curves voor 67% sens in figuur 1) wordt de drempel voor niet-geïnfecteerd beschouwd zijn overschreden als de vooraf-kans

om geïnfecteerd te zijn groter is dan circa 15%, en daardoor dus vrij gemakkelijk tot een **fout-negatief** resultaat kan leiden en toegenomen risico voor verspreiding bij contact met anderen. Bij een negatief resultaat van een PCR-test met hogere **klinische sensitiviteit** kan er een **vooraf-kans** zijn tot circa 72% om geïnfecteerd te zijn en het toch, uitgaande van de drempel van 5%, veilig is om contact te hebben met anderen. Omdat de kans op toch geïnfecteerd te zijn lager is dan 5% bij een negatieve testuitslag. Daarom is een PCR-test met hoge **klinische sensitiviteit** belangrijk om **fout-negatieve** uitslagen te voorkomen.

Figuur 1 laat ook zien waarom pogingen om de **vooraf-kans** om positief te testen te verkleinen ertoe doen, bijvoorbeeld door sociale afstand te nemen en mogelijk door maskers te dragen. Als de **vooraf-kans** om geïnfecteerd te zijn te hoog wordt (bijvoorbeeld boven de 50%; dus o.a. bij hoge **prevalentie**), verliest het testen zijn waarde omdat negatieve resultaten de kans op infectie niet voldoende kunnen verlagen om de drempel voor niet-geïnfecteerd beschouwd zijn te bereiken. Tenzij een PCR-test gebruikt wordt die hoog klinisch sensitief is; bij een 98% **klinische sensitiviteit** zoals eerder aangegeven schuift de **vooraf-kans** om de 5% **achteraf-kans** bij een negatief test resultaat te passeren op naar circa 72% **vooraf-kans**. Het is niet realistisch om uit te gaan van 98% **klinische sensitiviteit** van de PCR-test omdat de **klinische sensitiviteit** van te veel factoren afhankelijk is en daarom geschat wordt op tussen de 67 en 98%.

De samenhang van de **positief voorspellende waarde** (PPV) en **negatief voorspellende waarde** (NPV) van de PCR-test met **prevalentie** en **klinische sensitiviteit** en **klinische specificiteit** staat in figuur 2 weergegeven, ook hier weer gebaseerd op de grenzen van de eerder genoemde waarden uit de literatuur.



Figuur 2. *De samenhang van de* ***positief voorspellende waarde*** *(PPV) en* ***negatief voorspellende waarde*** *(NPV) van de PCR-test met* ***prevalentie*** *en* ***klinische sensitiviteit*** *en* ***klinische specificiteit****.*

Het is duidelijk uit figuur 2 dat vooral de **positief voorspellende waarde** van de PCR-test beïnvloed wordt door **prevalentie** tussen 0 en 30%. Dit is het sterkst merkbaar bij een lagere **klinische specificiteit** en niet zozeer bij een lagere **klinische sensitiviteit** van de PCR-test.

De invloed op de **negatief voorspellende waarde** van de PCR-test laat zich vooral gelden bij een lagere **klinische sensitiviteit** en niet zozeer bij een lagere **klinische specificiteit** van de PCR-test.

Prevalentie is dus ook een factor in de **vooraf-kans** om geïnfecteerd te zijn en dus of een persoon positief gaat testen voor COVID-19. Bij lage **prevalentie** is de **positief voorspellende waarde** van een PCR-test dus laag als de **vooraf-kans** of een persoon positief gaat testen voor COVID-19 niet beïnvloed wordt. De **positief voorspellende waarde** kan dus verhoogt worden door de **vooraf-kans** te verhogen, wat vooral nuttig is als de **prevalentie** laag is zoals uit de grafiek blijkt. Daarmee wordt automatisch ook de kans op **fout-positief** drastisch verlaagd. En daarmee het onterecht plaatsen van positief geteste personen in quarantaine. Van dit fenomeen is en wordt gebruik gemaakt door het toepassen van een **casus-definitie** waarin het hebben van specifieke symptomen (o.a. in screening) en blootstelling aan iemand met COVID-19 (o.a. in bron- en contactonderzoek) een rol spelen. Het toevoegen van testen van personen zonder symptomen en zonder direct contact met een COVID-19 patiënt verlaagd de **vooraf-kans** om geïnfecteerd te zijn drastisch en zal de prevalentie dus een grotere bijdrage geven aan de **positief voorspellende waarde** van de PCR-test; bij lage **prevalentie** zal dit dus resulteren in relatief meer **fout-positieven**.

Het moge duidelijk zijn dat afhankelijk van het beoogde doel de kansen op **correct-positieve** en **correct-negatieve** PCR-test resultaten positief beïnvloed kunnen worden door de test-strategie. Helaas is het zo dat de één optimaal maken vaak resulteert in minder optimaal zijn van de ander. Het doel van de test-strategie bepaalt dan de balans.

Bronnen

<u>Literatuur</u>

1. Afzal A. Molecular diagnostic technologies for COVID-19: Limitations and challenges. J Adv Res. 2020 Nov;26:149-159. doi: 10.1016/j.jare.2020.08.002. Epub 2020 Aug 6. PMID: 32837738; PMCID: PMC7406419.
2. Bonten MJM. Covid-19: een fout-positieve PCR-testuitslag. Ned Tijdschr Geneeskd. 2020;164:C4670
3. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DG, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MP, Drosten C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill.

2020 Jan;25(3):2000045. doi: 10.2807/1560-7917.ES.2020.25.3.2000045. PMID: 31992387; PMCID: PMC6988269.
4. He J, Guo Y, Mao R, Zhang J. Proportion of asymptomatic coronavirus disease 2019: A systematic review and meta-analysis. J Med Virol. 2020 Jul 21:10.1002/jmv.26326. doi: 10.1002/jmv.26326. Epub ahead of print. PMID: 32691881; PMCID: PMC7404334.
5. Heneghan C, Brassey J, Jefferson T. COVID-19: What proportion are asymptomatic? The Centre for Evidence-Based Medicine. Evidence Service to support the COVID-19 response. April 6, 2020; https://www.cebm.net/covid-19/covid-19-what-proportion-are-asymptomatic/
6. Stites EC, Wilen CB. The Interpretation of SARS-CoV-2 Diagnostic Tests. Med (N Y). 2020 Aug 21. doi: 10.1016/j.medj.2020.08.001. Epub ahead of print. PMID: 32864639; PMCID: PMC7441939.
7. Surkova E, Nikolayevskyy V, Drobniewski F. False-positive COVID-19 results: hidden problems and costs. Lancet Respir Med. 2020 Sep 29:S2213-2600(20)30453-7. doi: 10.1016/S2213-2600(20)30453-7. Epub ahead of print. PMID: 33007240; PMCID: PMC7524437.
8. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. BMJ. 2020 May 12;369:m1808. doi: 10.1136/bmj.m1808. PMID: 32398230.
9. Woloshin S, Patel N, Kesselheim AS. False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications. N Engl J Med. 2020 Aug 6;383(6):e38. doi: 10.1056/NEJMp2015897. Epub 2020 Jun 5. PMID: 32502334.

RIVM en LCI webpagina's

10. RIVM. Testen op COVID-19. https://www.rivm.nl/coronavirus-covid-19/testen
11. RIVM. Toelichting PCR RIVM. https://www.rivm.nl/sites/default/files/2020-11/Toelichting%20PCR_RIVM.pdf
12. RIVM. Toelichting Ct-waarde. https://www.rivm.nl/sites/default/files/2020-11/Toelichting%20Ct-waarde_0.pdf
13. LCI-RIVM. COVID-19 richtlijn. https://lci.rivm.nl/richtlijnen/covid-19
14. LCI-RIVM. Aanvullende informatie diagnostiek COVID-19 Bijlage bij de LCI-richtlijn COVID-19 | Versie 12 november 2020; https://lci.rivm.nl/covid-19/bijlage/aanvullend

Berekeningen

Diagnostic test evaluation calculator. MedCalc® easy-to-use statistical software. https://www.medcalc.org/calc/diagnostic_test.php

Tenny S, Hoffman MR. Prevalence. [Updated 2020 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430867/