Comprehensive assessment of early reporting of emerging infectious diseases

by

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Abstract

Background

An international public health emergency has been declared by the World Health Organisation on 30th January 2020 after the outbreak of a novel coronavirus in China that was subsequently named COVID-19. Various pandemic preparedness indices and estimates from mathematical models are being used for predicting the disease spread and to inform decisions about the pandemic. However, the reliability of these tools has not been sufficiently measured. In this study, I aim to assess the early reporting of the basic reproduction number (R_0) of COVID-19 and assess the efficacy of Global Health Security Index (GHSI) scores in predicting pandemic preparedness.

Methods

I conducted a systematic review and meta-analysis of articles published between 1st December 2019 and 30th September 2020 estimating basic reproduction number. I also conducted a sub-group analysis by country, continent, study duration and method, whether mean or median was reported for reproduction numbers, the month of publication, and whether the study was conducted in Wuhan, Hubei including Wuhan or outside Hubei in China. GHSI scores for 2019 were obtained from the publicly available data from the GHSI website. Poisson regression, logistic regression and survival analysis were used to assess the association of GHSI scores with case rate, death rate and vaccination coverage and rate adjusting for socio-developmental index, universal health coverage, life expectancy and total fertility rate of the country.

Results

Out of the 15714 articles screened, 81 articles were included in the meta-analysis and 76 articles were synthesised narratively. The result from the meta-analysis shows that in the absence of a deliberate intervention for COVID-19, the R_0 was estimated to be 2.66 with a 95% confidence interval (2.41–2.94). Additionally, I found that as the GHSI scores increased, the number of COVID-19 cases and death rates increased as well. In terms of vaccination, however, the countries with higher scores are more likely to quickly achieve desired vaccination coverage.

Conclusion

Global understanding of infectious disease outbreaks remains weak. This study shows that there is still much theoretical and practical work to be done before we can properly understand the dynamics of emerging infectious diseases. R_0 is a highly variable and unreliable measure of pandemic risk, subject to much uncertainty and vulnerable to the influence of modelling assumptions, data quality and data timeliness. Until we have a clearer understanding of and consensus on how to use infectious disease models for the pandemic response, we cannot hope to prepare for the next pandemic.

Keywords

Epidemics; infectious disease; covid19; basic reproduction number; GHSI score; vaccine; mortality; cases

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List of abbreviations

WHO	:	World Health Organization
WHA	:	World Health Assembly
IHR	:	International Health Regulations
PHEIC	:	Public Health Emergency of International Concern
IAEA	:	International Atomic Energy Agency
SARS	:	Severe Acute Respiratory Syndrome
R_0	:	Basic Reproduction Number
GHSI	:	Global Health Security Index
CI	:	Confidence Interval
CrI	:	Credible Interval
NHI	:	National Heart, Lung, and Blood Institute
UCI	:	Upper Confidence Interval
LCI	:	Lower Confidence Interval
SE	:	Standard Error
SD	:	Standard Deviation
REML	:	Restricted Maximum Likelihood Method
SDI	:	Socio-developmental Index
UHC	:	Universal Health Coverage
TFR	:	Total Fertility Rate

CHAPTER 1: Introduction

1.1 Background

The World Health Organization (WHO) has been involved in combating outbreaks since its inception in 1948. Over this time the World Health Assembly (WHA) has established increasingly formal mechanisms for global outbreak alert and response, culminating in the International Health Regulations (IHR).

1.1.1. The International Health Regulations

The IHR brings together 196 countries to collaborate on public health issues requiring international attention. IHR defines the rights and obligations of countries in dealing with public health emergencies and requires that they designate a National IHR Focal Point for communications with WHO. Detecting, assessing, and reporting of public health risks to the WHO must be built and strengthened by member states as soon as possible or within five years of the enforcement of the IHR.[1] The WHO will assist member states in strengthening and maintaining their public health capacities upon request. Beyond this role in strengthening pandemic response, the IHR also includes specific mechanisms for engaging countries in responding to a global pandemic, through the mechanism of public health emergencies.

1.1.2. Public Health Emergencies of International Concern

According to the international health regulations (IHR) of the WHO, a Public Health Emergency of International Concern (PHEIC) is defined as:

'An extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response'[2,3]

Public health emergencies of international concern (PHEIC) are of central importance to the operation of the IHR, and their declaration and management is key to protecting the global community from new pandemics. Timeliness, transparency, and scientific objectivity are essential elements of the process of defining a PHEIC, but the declaration of a PHEIC can have significant global costs, leading to closure of borders, restriction of basic civil freedoms, and mobilization of significant resources nationally and internationally. Ports, airports, and ground crossings are governed by the IHR measures for preventing the spread of disease internationally and to minimize unwarranted restrictions in travel and trade.

Travel restrictions that are likely to proceed from the declaration of a PHEIC can greatly limit the demand for tourism activities, affect family and personal life, interfere with free movement of labour and capital, and affect entire sectors of national economies. The most recent PHEIC, for COVID-19, has now been in effect for 34 months and in its early stages saw the complete collapse of global tourism, international travel, and freedom of movement. A report by the World Travel and Tourism Council showed that travel and tourism declined by 50.4% in 2020 with an overall decline in the global economy by 3.3%.[4] The decline in economy affected countries like Thailand and Vietnam more than countries like Japan.[5–9] In addition to raising public awareness, a PHEIC declaration can galvanize other member nations to mobilize funding and resources. However, the economic impact of trade and travel restrictions needs to

be considered seriously when declaring a PHEIC. As a result of the high economic and political consequences of declaring a PHEIC, the decision to do so is necessarily subject to strong political considerations, and as much as possible needs to be made in an objective, transparent and trustworthy way.

1.1.2.1. Public Health Emergencies under the IHR

The IHR was first adopted in 1969 by the World Health Assembly and has been amended three times. Following the 2002-2004 SARS outbreak, most recent amendments were made in 2005, including PHEIC declarations. Seven areas have been revised and improved over previous versions of the IHR (2005), notably: (1) An application scope that extends beyond diseases (2) Public health capacities should be developed at a minimum by each State Party (3) In the event of a PHEIC, member states have an obligation to notify WHO (4) Instances of public health events not reported by official sources can be considered by WHO after verification by State Parties (5) Guidelines for the WHO director general for determining a PHEIC and issuing recommendations (6) People and travellers' human rights protection (7) Facilitating communications between member states and WHO through establishment of WHO IHR contact points and National IHR focal points.[1]

The 2005 IHR was enforced binding 196 countries in June 2007 and was fully applied in 2009 in response to the swine flu pandemic of 2009. Since 2009, there have been seven PHEIC declarations including the recent novel coronavirus pandemic and the 2022 monkeypox

outbreak. All these declarations are for viral emerging infectious diseases and not for chemical and radioactive materials or bacterial diseases.

1.1.2.2. PHEIC assessment criteria

Measuring the severity of a disease outbreak is challenging due to differences in population health and services, lack of comparable data and non-standardised measurements.[10] Based on the decision instrument in Annex 2 of the IHR,[11] as shown in **Figure** 1.1, countries should assess each event according to four criteria: is the event 1) serious, 2) unexpected or unusual, 3) has a risk of spreading internationally and 4) has a risk of travel and trade restrictions in an international scale? If any two of the four criteria (I-IV) are met, the country should notify WHO of the event. These criteria are explained in detail in **Appendix A**, and are summarized here.

Criterion I: Is the public health impact of the event serious?

The answer to criterion I is 'Yes' if the number of cases or deaths of an event is large; or is likely to have a public health impact; or require assistance to control the event.

Criterion II: Is the event unusual or unexpected?

The answer to criterion II is 'Yes' if the event is unusual, such as when the cause is an unknown agent; or if it is an unexpected occurrence of disease that has been eliminated from the country.

Criterion III: Is there a significant risk of international spread?

The answer to criterion III is ‘Yes’ if there are similar events in other countries; or if the event is caused by environmental contamination or is in an area where there is dense international traffic with potential of cross border movement.

Criterion IV: Is there a significant risk of international restrictions?

The answer to criterion IV is ‘Yes’ if similar event has occurred in the past; or the suspected source is a water or food product; or it occurred during an international gathering; or if further information on the event is being asked by foreign officials.

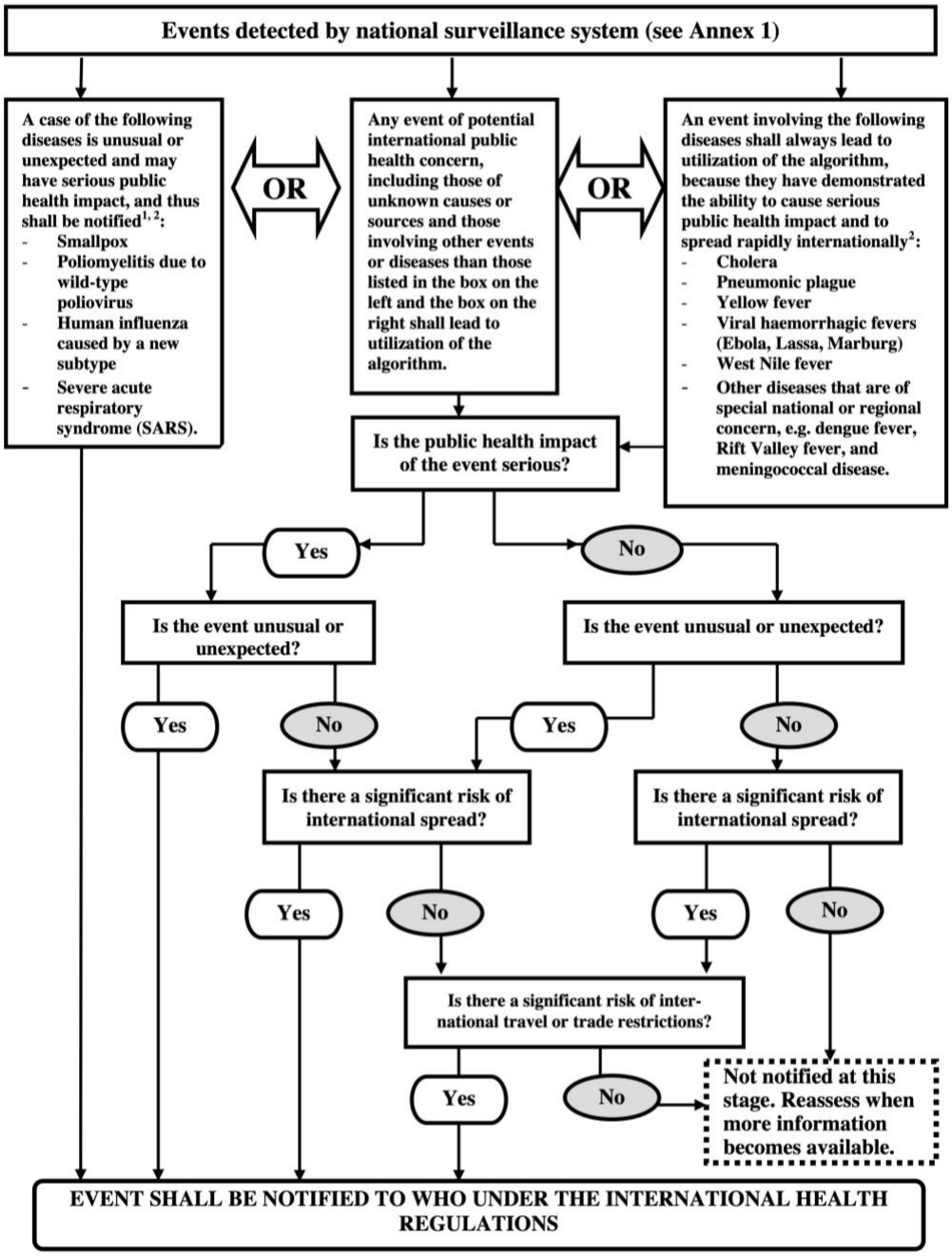


Figure 1.1 Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern, Annex 2. Source: WHO International Health Regulations (2005), www.who.int

The national IHR focal point from the member states should report a possible PHEIC to the WHO within 24 hours of assessment, however, informal reporting from a non-member state is also possible.[12] If deemed necessary, WHO will involve the International Atomic Energy Agency (IAEA). As per Article 9 in the IHR, the WHO may refer to other sources to gather further information as appropriate.[1] However, it needs to verify the obtained information with the State Party before taking any action based on the report.[1]

Severe Acute Respiratory Syndrome (SARS), wild type poliomyelitis, smallpox rand any new subtype of human influenza should always be notified to the WHO and are always a PHEIC even in the absence of a decision under the IHR.[1]

1.1.2.3. History of PHEIC declarations

Since the IHR were first introduced there have been seven PHEICs, which have been managed with varying degrees of success.

Swine flu (2009)

In March 2009, H_1N_1 virus was detected in Mexico. One month after the first emergence of H_1N_1, on 26th April 2009, WHO declared it a PHEIC, when it had spread across three countries.[13] The end of the H_1N_1 pandemic was announced by the WHO on 10th August 2010.[14] The swift response of the WHO to declare Swine flu a PHEIC was later criticised because of the perceived mildness of the disease as well decisions being influenced by the pharmaceutical industry.[15–17]

Poliovirus (2014)

With the spread of wild polio and vaccine-derived poliovirus in three countries–Afghanistan, Iraq and Equatorial Guinea from Pakistan, Syria and Cameroon respectively–particularly during the low virus transmission season (January–April/May), it was declared a PHEIC on 5th May 2014.[18] At the time of declaration, there were 68 reported cases of Wild Poliovirus , which is a very low number compared to the 417 cases in the previous year.[19] Amidst the ongoing cases in affected countries such as Afghanistan, it was determined on 20th June 2022 that the situation continues to constitute a PHEIC.[20]

Ebola- West Africa (2014)

Guinea and Liberia confirmed cases of Ebola in March 2014 and Sierra Leone in May 2014. Five months after the initial detection on 8th August 2014, when the virus spread to the United States and Europe, the WHO declared Ebola in West Africa a PHEIC.[21] There were 1711 cases when the declaration was made.[19] Given the high case fatality rate of 40%, the time taken to declare Ebola a PHEIC was criticised globally.[15,17,22,23] Guinea, Liberia, and Sierra Leone suffered economic disruptions and difficulties in humanitarian response due to travel restrictions during the Ebola epidemic from 2014-2016.[24–26] On 29th March 2016, the PHEIC status was lifted for Ebola in West Africa.

Zika virus (2016)

In March 2015, a cluster of microcephaly and Guillian-Barre syndrome was suspected to be linked to Zika virus.[27] The suspicion was confirmed in April of the same year.[29] In response to this situation, the WHO declared a PHEIC after one year on 1st February 2016.[28] During the time of declaration, there were 594 cases of microcephaly possibly related to Zika virus.[19] Slow political mobilisation let to the delay in declaration of Zika virus as a PHEIC.[17] Colombia, Suriname, El Salvador, Guatemala, Paraguay, and French Polynesia were some of the places that reported cases of Zika virus infection. The PHEIC declaration for Zika virus was the first declaration for a mosquito-borne disease and it was lifted on 18th November 2016.[30]

Kivu Ebola (2018-2020)

The first reported cases occurred in North Kivu province in the Democratic Republic of Congo at the end of July 2018.[31] During the three IHR meetings on October 2018, April 2019, and June 2019 the Kivu Ebola pandemic was not considered a PHEIC due to the low risk of international spread. However, by 11th June 2019, the number of related deaths had already reached 1405.[32] Goma, which is the capital of North Kivu, detected the first case of Ebola on 13th July 2019. Four days later, during the fourth IHR meeting on 17th July 2019, a PHEIC declaration was made by the WHO.[33] There were 2522 confirmed cases when the declaration was made.[19] WHO's delay and hesitancy in PHEIC declaration was highly criticised.[17,34–36] The declaration was lifted on 26th June 2020.[37]

COVID-19 (2020)

During December of 2019, a novel coronavirus was detected in China. It was later named COVID-19 by the WHO. COVID-19 is an infectious disease characterised by atypical pneumonia and is caused by SARS-CoV-2.[38] As COVID-19 became a global concern,[39,40] it was declared a PHEIC on 30th January 2020, during the second IHR meeting seven days after the first meeting of the Emergency Committee.[41] COVID-19 had already affected 19 countries globally with 7818 cases in five WHO regions on the day of the declaration.[42] COVID-19 was recognised as a pandemic on 11th March 2020. As of January 2022, more than 670 million people worldwide have been infected.[43] The WHO was criticised for the delay in declaration of COVID-19 as a PHEIC as the pandemic raised unprecedented challenges with its long-term consequences.[44–47] To date (24th January 2022), COVID-19 has spread to more than 190 countries and is still a PHEIC.

Monkeypox (2022)

An outbreak of monkeypox was confirmed in May 2022 in the United Kingdom.[48] After an inconclusive second IHR meeting on 21st July 2022,[49] the WHO declared Monkeypox a PHEIC on 23rd July 2022.[50] The PHEIC declaration of monkeypox virus raised concerns that an outbreak's perceived threat is largely determined by the wealth of the nation.[51–53] By the time monkeypox was declared a PHEIC it had already affected 17186 people, in 75 countries in all six WHO regions.

1.1.2.4. Notification and decision-making under the IHR

International experts in fields related to health emergencies, such as infectious disease epidemiology, vaccine development or virology serve as the IHR Emergency Committee. The WHO Director-General seeks technical advice related to PHEIC from the committee. The WHO Director General holds the responsibility to determine whether an event lies within this category. The Emergency Committee advises when determining a PHEIC in circumstances of inconsistencies. The epidemiological situation will be re-evaluated by the Emergency Committees at least every three months to determine if the event remains to be a PHEIC or any changes are to be made in the decisions and recommendations.

1.1.2.5. Subjective nature of the assessment criteria

Although the four assessment criteria set by the WHO are comprehensive and cover all aspects of an emergency, they are subjective and the WHO lacks an objective framework for declaring a PHEIC. The subjective nature of the definition of a PHEIC risks distrust of WHO's decision-making processes and lack of respect for subsequent guidance.[54] Regional and international dynamics, potential economic repercussions, together with a risk of political and social unrest, may play a role in delaying reporting of diseases of concern and/or declaration of a PHEIC, and may also lead to criticism of the decision by national governments or civil society organizations. In the absence of a strong epidemiological basis, it is difficult to make strong conclusions about criterion 1 for declaration of a PHEIC. Determination of the threat from a disease depends on the case fatality rate, infectiousness, and degree of health care burden of non-fatal cases of the disease, but these are often difficult to establish in the early stages of an

outbreak and there are no established standards for interpreting this information. There is a potential that any decision will be biased by political and economic concerns, or by the influence in particular of the country in which the outbreak was detected. Given the subjective nature of current decisions and the huge economic costs associated with declaring a PHEIC, it is possible that any decision might not be based purely on technical aspects of the emergency. Such influence may lead to a poorly timed or incorrect PHEIC declaration.

Past research on WHO's response to disease outbreaks has shown lack of confidence in the objectivity of its decisions. The World Health Organization has been criticised for lagging the global discussion when it should have acted as a world leader during outbreaks of emerging infectious diseases. Sudeepa Abeysinghe (2015) compared the WHO's quick response to H_1N_1 with its response to Ebola and how the institutional structures surrounding the global governance of infectious disease risk underpinned the action or inaction on both the diseases. [15] As the WHO's swift reaction to H_1N_1 was later criticised due to the perceived mildness of the event, the study suggested that WHO should create an objective means of measurement and management of disease outbreak as the scope of IHR is broad. Mart Eccleston-Turner (2020) highlighted the disconnection of PHEIC criteria and its interpretation by the Emergency Committee during the COVID-19 pandemic.[55] An editorial in *the Lancet* (2019) accused the WHO of favouring local protectiveness over global action.[54] A report by Mullen et al. showed that the emergency committee was inconsistent in applying the IHR criteria when making PHEIC decisions.[56,57] A 2018 study in the *American Journal of Public Health* found quicker WHO responses during PHEIC declarations in H_1N_1-2009, Ebola 2014, and Zika 2016, when

US citizens were infected.[58] Sometimes WHO does not say in the reporting if the criteria were met. The report of The Lancet Commission highlighted the delay in notification of COVID-19 during the initial outbreak as well as the slow and over-cautious response from the WHO.[47] The IHR measures fell short of ensuring a robust international response to the COVID-19 outbreak. The Lancet Commission[47] claimed that the WHO's decision was influenced by the ongoing tension between the USA and China, including the USA's May 2020 announcement of intention to withdraw from the WHO.[59,60]

This research will assess the scientific quality of the early reporting of the COVID-19 pandemic, with a focus on the estimation of infectiousness of the virus during the early stages of the pandemic. This will help determine the reliability of various parameters and tools widely used to estimate the disease spread and is intended to improve our understanding of the value of these tools in helping the WHO to make a timely, independent and objective PHEIC declaration. Improvements in the objectivity of these declarations will help with the prevention of the international spread of the infectious disease and support the response to affected countries. This will even help avoid and manage uncertainty in the decision-making process by easing risk identification and communication.

1.1.3. Objectives of this research

This research aims to assess the early reporting of the emerging infectious disease by using COVID-19 data. The specific objectives of this research are:

- To assess reliability of the published mathematical models estimating basic reproduction number (R_0) in predicting the COVID-19 pandemic

- To assess the effectiveness of Global Health Security Index (GHSI) Scores in predicting the epidemic
- To make recommendations for improvements in the relationship between policy decisions and the scientific information that supports them

CHAPTER 2: Systematic review

Reliability of early estimates of basic reproduction number of COVID-19: a systematic review and meta-analysis

2.1 Background

The World Health Organisation declared a public health emergency of international concern on 30th January 2020[61] after the outbreak of a novel coronavirus in China that was subsequently named COVID-19. Since that declaration there are more than 670 million confirmed cases and above 6.7 million deaths due to COVID-19 affecting more than 180 countries worldwide, and the rate of infection continues to rise.[43]

For infectious diseases like COVID-19, the basic reproduction number (R_0) is essential to understanding the disease transmissibility, preparing preventive measures such as social distancing and lockdowns, and evaluating the effectiveness of policy. The R_0 is often evaluated early in an emerging infectious disease outbreak to identify the pandemic potential of the disease,[62] while the effective reproduction number has been used extensively in some countries to assess the effectiveness of current interventions and the potential to control the epidemic.[63]

R_0 can be estimated using a variety of different methods, based on different forms of data and assumptions about population behaviour and risk. Moreover, early estimates of the R_0 may be based on limited and highly biased data, and estimates can change over time. Because of the vulnerability of these indices to estimaation differences and data quality, they have both been criticised as metrics for assessing either pandemicity or intervention effectiveness.[64]

Nonetheless their use has been widespread in the COVID-19 pandemic, both to make judgments about the effectiveness of highly controversial "herd immunity" strategies[65] and to assess the state of the pandemic at different time points and regions.[66] Many COVID-19 dashboards in many countries report this metric.[67,68]

Given these variations in types of reproduction number and methods used to estimate them and the important role this index played in policy assessments in many countries, it is essential to synthesise all existing evidence available to date and summarise the key findings. Previous reviews of the available estimates of R_0 included a small number of published articles, failed to take into account the different types of effect sizes reported in the study, or did not properly assess publication bias.[69,70] This study aimed to estimate the pooled R_0 for the COVID-19 outbreak from a full and comprehensive systematic review and meta-analysis of studies published early in the pandemic, and identify the impact of study-related factors such as methods, study location and study period on the estimated R_0.

2.2 Methods

The study was performed according to the protocol registered in PROSPERO (ID=CRD42021279514)[71] and PRISMA guidelines.

2.2.1. Database search and search strategy

All COVID-19-related studies with title and abstract published between 1st December 2019 and 30th September 2020 were screened. The search was performed in LitCovid, PubMed, MEDLINE, CINAHL, APA PsycInfo, EMBASE, the WHO COVID-19 database, the British Nursing Index, Coronavirus Research Database, Web of Science, CiNii, and the preprint

database arXiv. Finally, the reference list of the relevant articles was searched to find additional studies.

Electronic databases were searched using keywords such as ‘COVID-19’, ‘2019-nCoV’, ‘SARS-CoV-2’, ‘novel coronavirus’, ‘Basic reproduction number’, ‘Basic reproductive rate’ or ‘R0’, with no restriction of country/region and language but limited to human studies. The search strategies are presented below.

2.2.1.1. PubMed, LitCovid, MEDLINE (via PubMed)

	Keywords
#1	(((coronavirus*[Title/Abstract]) OR (coronavirus infection[Title/Abstract]) OR (coronavirus disease[Title/Abstract]) OR (coronavirus disease 2019[Title/Abstract]) OR (coronavirus disease-19[Title/Abstract]) OR (coronavirus disease 19[Title/Abstract]) OR (covid19[Title/Abstract]) OR (covid 19[Title/Abstract]) OR (covid-19[Title/Abstract]) OR (covid-19 pandemic[Title/Abstract]) OR (covid 19 pandemic[Title/Abstract]) OR (covid-19 virus infection[Title/Abstract]) OR (covid 19 virus infection[Title/Abstract]) OR (covid-19 virus disease[Title/Abstract]) OR (covid 2019[Title/Abstract]) OR (sars-cov-2[Title/Abstract]) OR (sars cov 2[Title/Abstract]) OR (severe acute respiratory syndrome coronavirus 2[Title/Abstract]) OR (severe acute respiratory syndrome coronavirus 2[Supplementary Concept]) OR (novel coronavirus 2019[Title/Abstract]) OR (2019 novel coronavirus disease[Title/Abstract]) OR (2019 novel coronavirus infection[Title/Abstract]) OR (2019-nCoV infection[Title/Abstract]) OR (2019-nCoV[Title/Abstract]) OR (2019nCov[Title/Abstract]) OR (2019 nCov[Title/Abstract]))
#2	((Basic Reproduction Number[Title/Abstract]) OR (Basic reproductive number[Title/Abstract]) OR (Morbidity[Title/Abstract]) OR (Mortality[Title/Abstract]) OR (Mortality rate[Title/Abstract]) OR (Case fatality rate[Title/Abstract]) OR (Incidence[Title/Abstract]) OR (Prevalence[Title/Abstract]) OR (Serial interval[Title/Abstract]) OR (Attack rate[Title/Abstract]) OR (Rate change[Title/Abstract]) OR (Percentage change[Title/Abstract]) OR (Percent

	change[Title/Abstract]) OR (Reduction rate[Title/Abstract]) OR (Absolute change[Title/Abstract]) OR (Reduction[Title/Abstract]) OR (Reduc*[Title/Abstract]) OR (Death[Title/Abstract]) OR (Excess death[Title/Abstract]) OR (Asymptomatic[Title/Abstract]) OR (Asymptomatic Infection[Title/Abstract]) OR (Asymptomatic Disease[Title/Abstract]) OR (Asymptomatic covid-19[Title/Abstract]) OR (Infection rate[Title/Abstract]) OR (Misreport*[Title/Abstract]) OR (Misreporting rate[Title/Abstract]) OR (Forecast*[Title/Abstract]) OR (Forecasting[Title/Abstract]) OR (Population Forecast[Title/Abstract]) OR (Prediction[Title/Abstract]) OR (trends[Title/Abstract]) OR (trend*[Title/Abstract]) OR (trend analysis[Title/Abstract]) OR (Lockdown[Title/Abstract]) OR (Lock down[Title/Abstract]) OR (travel ban[Title/Abstract]) OR (travel restriction[Title/Abstract]) OR (travel restrictions[Title/Abstract]) OR (quarantine[Title/Abstract]) OR (shut down[Title/Abstract]) OR (shutdown[Title/Abstract])))
#3	#1 AND #2 (human, 2019/12/1-2020/9/30) Search performed on: 15th October 2020 Total: 7949

2.2.1.2. MEDLINE Complete, CINAHL Plus with full text, APA PsychInfo (vis EBSCO host)

	Keywords
S1	AB coronavirus* OR AB "coronavirus infection" OR AB "coronavirus disease" OR AB "coronavirus disease 2019" OR AB "coronavirus disease-19" OR AB "coronavirus disease 19" OR AB covid19 OR AB "covid 19" OR AB "covid-19" OR AB "covid-19 pandemic" OR AB 2covid 19 pandemic" OR AB "covid-19 virus infection"
S2	AB "covid 19 virus infection" OR AB "covid-19 virus disease" OR AB "covid 2019" OR AB "sars-cov-2" OR AB "sars cov 2" OR AB "severe acute respiratory syndrome coronavirus 2" OR AB "novel coronavirus 2019" OR AB "2019 novel coronavirus disease" OR AB "2019 novel coronavirus infection" OR AB "2019-nCoV infection" OR AB "2019-nCoV" OR AB 2019nCov
S3	AB 2019 nCov
S4	AB S1 OR S2 OR S3
S5	AB "Basic Reproduction Number" OR AB "Basic reproductive number" OR AB Morbidity OR AB Mortality OR AB "Mortality rate" OR AB "Case fatality rate" OR AB Incidence OR AB Prevalence OR AB "Serial interval" OR AB "Attack rate" OR AB "Rate change" OR AB "Percentage change"
S6	AB "Percent change" OR AB "Reduction rate" OR AB "Absolute change" OR AB Reduction OR AB Reduc* OR AB Death OR AB "Excess death" OR AB Asymptomatic OR AB "Asymptomatic Infection2 OR AB "Asymptomatic Disease" OR AB "Asymptomatic covid 19" OR AB "Infection rate"
S7	AB S5 OR S6
S8	AB S4 AND S7
S9	AB S4 AND S7
	Limiters – Date of Publication: 20190101-20200930
	Narrow by Population: - human
	Search performed on: 16th October 2020
	Total: 258

2.2.1.3. EMBASE

	Keywords
#1	coronavirus*:ab,ti OR 'coronavirus infection':ab,ti OR 'coronavirus disease':ab,ti OR 'coronavirus disease 2019':ab,ti OR 'coronavirus disease-19':ab,ti OR 'coronavirus disease 19':ab,ti OR covid19:ab,ti OR 'covid 19':ab,ti OR 'covid-19 pandemic':ab,ti OR 'covid 19 pandemic':ab,ti OR 'covid-19 virus infection':ab,ti OR 'covid 19 virus infection':ab,ti OR 'covid-19 virus disease':ab,ti OR 'covid 2019':ab,ti OR 'sars-cov-2':ab,ti OR 'sars cov 2':ab,ti OR 'severe acute respiratory syndrome coronavirus 2':ab,ti OR 'novel coronavirus 2019':ab,ti OR '2019 novel coronavirus disease':ab,ti OR '2019 novel coronavirus infection':ab,ti OR '2019-ncov infection':ab,ti OR '2019-ncov':ab,ti OR '2019ncov':ab,ti OR '2019 ncov':ab,ti
#2	'basic reproduction number':ab,ti OR 'basic reproductive number':ab,ti OR morbidity:ab,ti OR mortality:ab,ti OR 'mortality rate':ab,ti OR 'case fatality rate':ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR 'serial interval':ab,ti OR 'attack rate':ab,ti OR 'rate change':ab,ti OR 'percentage change':ab,ti OR 'percent change':ab,ti OR 'reduction rate':ab,ti OR 'absolute change':ab,ti OR reduction:ab,ti OR reduc*:ab,ti OR death:ab,ti OR 'excess death':ab,ti OR asymptomatic:ab,ti OR 'asymptomatic infection':ab,ti OR 'asymptomatic disease':ab,ti OR 'asymptomatic covid 19':ab,ti OR 'infection rate':ab,ti OR misreport*:ab,ti OR 'misreporting rate':ab,ti OR forecast*:ab,ti OR forecasting:ab,ti OR 'population forecast':ab,ti OR prediction:ab,ti OR trends:ab,ti OR trend*:ab,ti OR 'trend analysis':ab,ti OR lockdown:ab,ti OR 'lock down':ab,ti OR 'travel ban':ab,ti OR 'travel restriction':ab,ti OR 'travel restrictions':ab,ti OR quarantine:ab,ti OR 'shut down':ab,ti OR shutdown:ab,ti
#3	#1 AND #2
#4	#1 AND #2 AND [humans]/lim AND [embase]/lim AND [2019-2020]/py Search performed on: 16th October 2020 Total: 10512

2.2.1.4. COVID-19 database by the World Health Organization, LILACS (Americas), WPRIM (Western Pacific)

	Keywords
A	(tw:(coronavirus*)) OR (tw:("coronavirus infection")) OR (tw:("coronavirus disease")) OR (tw:("coronavirus disease 2019")) OR (tw:("coronavirus disease-19 ")) OR (tw:("coronavirus disease 19")) OR (tw:("covid19")) OR (tw:("covid 19")) OR (tw:("covid-19 pandemic")) OR (tw:("covid 19 pandemic")) OR (tw:("covid-19 virus infection")) OR (tw:("covid 19 virus infection")) OR (tw:("covid-19 virus disease")) OR (tw:("covid 2019")) OR (tw:("sars-cov-2")) OR (tw:("sars cov 2")) OR (tw:("severe acute respiratory syndrome coronavirus 2")) OR (tw:("novel coronavirus 2019")) OR (tw:("2019 novel coronavirus disease")) OR (tw:("2019 novel coronavirus infection")) OR (tw:("2019-nCoV infection")) OR (tw:("2019-nCoV")) OR (tw:(2019nCov)) OR (tw:("2019 nCov"))
B	(tw:("Basic Reproduction Number")) OR (tw:("Basic reproductive number")) OR (tw:(Morbidity)) OR (tw:(Mortality)) OR (tw:("Mortality rate")) OR (tw:("Case fatality rate")) OR (tw:(Incidence)) OR (tw:(Prevalence)) OR (tw:("Serial interval")) OR (tw:("Attack rate")) OR (tw:("Rate change")) OR (tw:("Percentage change")) OR (tw:("Percent change")) OR (tw:("Reduction rate")) OR (tw:("Absolute change")) OR (tw:("Reduction")) OR (tw:("Reduc*")) OR (tw:("Death")) OR (tw:("Excess death")) OR (tw:(Asymptomatic)) OR (tw:("Asymptomatic Infection")) OR (tw:("Asymptomatic Disease")) OR (tw:("Asymptomatic covid 19")) OR (tw:("Infection rate")) OR (tw:("Misreport*")) OR (tw:("Misreporting rate")) OR (tw:(Forecast*)) OR (tw:(Forecasting)) OR (tw:(Population Forecast)) OR (tw:(Prediction)) OR (tw:(trends)) OR (tw:(trend*)) OR (tw:("trend analysis")) OR (tw:(Lockdown)) OR (tw:("Lock down")) OR (tw:("travel ban")) OR (tw:("travel restriction")) OR (tw:("travel restrictions")) OR (tw:(quarantine)) OR (tw:("shut down")) OR (tw:(shutdown))
C	A AND B Search performed on: 18th October 2020 Total: 11

2.2.1.5. British Nursing Index, Coronavirus Research Database (via Proquest)

	Keywords
A	(ab(coronavirus*) OR ab("coronavirus infection") OR ab("coronavirus disease") OR ab("coronavirus disease 2019") OR ab("coronavirus disease-19 ") OR ab("coronavirus disease 19") OR ab("covid19") OR ab("covid 19") OR ab("covid-19") OR ab("covid-19 pandemic") OR ab("covid 19 pandemic") OR ab("covid-19 virus infection") OR ab("covid 19 virus infection") OR ab("covid-19 virus disease") OR ab("covid 2019") OR ab("sars-cov-2") OR ab("sars cov 2") OR ab("severe acute respiratory syndrome coronavirus 2") OR ab("novel coronavirus 2019") OR ab("2019 novel coronavirus disease"))
B	(ab("basic reproduction number") OR ab("basic reproductive rate") OR ab("morbidity") OR ab("Mortality") OR ab("mortality rate") OR ab("case fatality rate") OR ab("incidence") OR ab("prevalence") OR ab("Serial interval") OR ab("Attack rate") OR ab("rate change") OR ab("Percentage change") OR ab("Percent change") OR ab("Reduction rate") OR ab("Absolute change") OR ab(Reduction") OR ab(Reduc*") OR ab("Death") OR ab("Excess death") OR ab(Asymptomatic) OR ab("asymptomatic infections") OR ab("asymptomatic diseases") OR ab("Asymptomatic covid-19") OR ab("infection rate") OR Misreport* OR ab("Misreporting rate") OR ab(Forecast*) OR ab("Forecasting") OR ab("population forecast") OR ab(Prediction) OR ab("trends") OR ab(trend*) OR ab("trends analysis") OR ab(Lockdown) OR ab("Lock down") OR ab("travel ban") OR ab("travel restriction") OR ab("travel restrictions") OR ab(quarantine) OR ab("shut down") OR ab(shutdown))
C	A and B (2019-12-01 – 2020-09-30)(British Nursing Index) Search performed on: 16th October 2020 Total: 431

2.2.1.6. Web of science

	Keywords
#1	(TS=(coronavirus*) OR TS=(“coronavirus infection”) OR TS=(“coronavirus disease”) OR TS=(“coronavirus disease 2019”) OR TS= (“coronavirus disease-19 “) OR TS= (“coronavirus disease 19”) OR TS= (“covid19”) OR TS= (“covid 19”) OR TS= (“covid-19”) OR TS= (“covid-19 pandemic”) OR TS= (“covid 19 pandemic”) OR TS= (“covid-19 virus infection”) OR TS= (“covid 19 virus infection”) OR TS= (“covid-19 virus disease”) OR TS= (“covid 2019”) OR TS= (“sars-cov-2”) OR TS= (“sars cov 2”) OR TS=(“severe acute respiratory syndrome coronavirus 2”) OR TS= (“novel coronavirus 2019”) OR TS= (“2019 novel coronavirus disease”) OR TS= (“2019 novel coronavirus infection”) OR TS= (“2019-nCoV infection”) OR TS= (“2019-nCoV”) OR TS= (“2019nCov”) OR TS=(“2019 nCov”))
#2	(TS= (“Basic Reproduction Number”) OR TS=(“Basic reproductive number”) OR TS= (“Morbidity”) OR TS=(“Mortality”) OR TS= (“Mortality rate”) OR TS= (“Case fatality rate”) OR TS= (“Incidence”) OR TS=(“Prevalence”) OR TS= (“Serial interval”) OR TS= (“Attack rate”) OR TS= (“Rate change”) OR TS=(“Percentage change”) OR TS=(“Percent change”) OR TS=(“Reduction rate”) OR TS=(“Absolute change”) OR TS=(“Reduction”) OR TS= (“Reduc*”) OR TS= (“Death”) OR TS=(“Excess death”) OR TS=(Asymptomatic) OR TS=(“Asymptomatic Infection”) OR TS=(“Asymptomatic Disease”) OR TS=(“Asymptomatic covid 19”) OR TS=(“Infection rate”) OR TS=(“Misreport*”) OR TS=(“Misreporting rate”) OR TS=(Forecast*) OR TS= (Forecasting) OR TS= (“Population Forecast”) OR TS= (“Prediction”) OR TS=(“trends”) OR TS= (trend*) OR TS= (“trend analysis”) OR TS=(Lockdown) OR TS= (“Lock down”) OR TS= (“travel ban”) OR TS=(“travel restriction”) OR TS=(“travel restrictions”) OR TS=(“quarantine”) OR TS= (“shut down”) OR TS= (“shutdown”))
#3	#1 AND #2 (2019 to 2020) (Refined by: DOCUMENT TYPES: (ARTICLE OR EARLY ACCESS))
	Search performed on: 16th October 2020
	Total: 7111

2.2.1.7. aRxiv

	Keywords
A	"coronavirus*" OR "coronavirus infection" OR "covid 19" OR "coronavirus disease" OR "covid19" OR "covid 2019" OR "sars-cov-2"
B	"Basic Reproduction Number" OR "Basic reproductive number" OR "Morbidity" OR "Mortality" OR "Mortality rate" OR "Case fatality rate" OR "Incidence" OR "Prevalence" OR "Serial interval" OR "Attack rate" OR "Rate change" OR "Percentage change" OR "Percent change" OR "Reduction rate" OR "Absolute change" OR "Reduction" OR "Reduc*" OR "Death" OR "Excess death" OR "Asymptomatic" OR "Asymptomatic Infection" OR "Asymptomatic Disease" OR "Asymptomatic covid-19" OR "Infection rate" OR "Misreport*" OR "Misreporting rate" OR "Forecast*" OR "Forecasting" OR "Population Forecast" OR "Prediction" OR "trends" OR "trend*" OR "trend analysis" OR "Lockdown" OR "Lock down" OR "travel ban" OR "travel restriction" OR "travel restrictions" OR "quarantine" OR "shut down" OR "shutdown"
C	A AND B Search performed on: 16th October 2020 Total: 5

2.2.1.8. CiNii

	Keywords
A	(“coronavirus*” OR “coronavirus infection” OR “coronavirus disease” OR “coronavirus disease 2019” OR “coronavirus disease-19” OR “coronavirus disease 19” OR “covid19” OR “covid 19” OR “covid-19” OR “covid-19 pandemic” OR “covid 19 pandemic” OR “covid-19 virus infection” OR “covid 19 virus infection” OR “covid-19 virus disease” OR “covid 2019” OR “sars-cov-2” OR “sars cov 2” OR “severe acute respiratory syndrome coronavirus 2” OR “novel coronavirus 2019” OR “2019 novel coronavirus disease” OR “2019 novel coronavirus infection” OR “2019-nCoV infection” OR “2019-nCoV” OR “2019nCov” OR “2019 nCov”)
B	(“Basic Reproduction Number” OR “Basic reproductive number” OR “Morbidity” OR “Mortality” OR “Mortality rate” OR “Case fatality rate” OR “Incidence” OR “Prevalence” OR “Serial interval“ OR “Attack rate” OR “Rate change” OR “Percentage change” OR “Percent change” OR “Reduction rate” OR “Absolute change” OR “Reduction” OR “Reduc*” OR “Death” OR “Excess death” OR “Asymptomatic” OR “Asymptomatic Infection” OR “Asymptomatic Disease” OR “Asymptomatic covid-19” OR “Infection rate” OR “Misreport*” OR “Misreporting rate” OR “Forecast*” OR “Forecasting” OR “Population Forecast” OR “Prediction” OR “trends” OR “trend*” OR “trend analysis” OR “Lockdown” OR “Lock down” OR “travel ban” OR “travel restriction” OR “travel restrictions” OR “quarantine” OR “shut down” OR “shutdown”)
C	A AND B Search performed on: 16th October 2020 Total: 148

2.2.2. Study selection

Search results were combined, and duplicates were removed. Titles and abstracts were screened using Rayyan QCRI independently by two investigators. When eligibility could not be ascertained, inclusion was decided during full-text screening. Full-text screening was performed by two independent investigators and disagreements between investigators were resolved by consensus. Original articles reporting reproduction numbers after social interventions, opinion/correspondence, and reviews were also excluded. We limited our analysis to articles published before 30th September 2020 to limit the findings from data in the early phase of the pandemic when not many variants of COVID-19 had emerged. The variant of COVID-19 may affect the R_0 value. However, few new variants had emerged during the first year of the pandemic. The Beta variant of COVID-19 was first documented in the earliest samples in May 2020 in South Africa and the Alpha variant was identified in September 2020 in the United Kingdom. However, these variants were not designated as a Variant of Concern (VOC) until 18th December 2020, after the selection period for our study. Thus, as not many studies reported the COVID-19 variants in early 2020, we did not limit our analysis to any of the COVID-19 variants.

2.2.3. Data extraction and quality assessment

Two investigators independently extracted data from the included studies during full-text screening. A standardised data extraction form was prepared (**Appendix A**) to capture the following information and pilot tested. Title of the study, name of the authors, affiliated country

of the author, journal, date of publication, study period, study location, model used for estimating R_0, and the estimated value of R_0 with 95% confidence interval (CI) or credible interval (CrI) including other intervals were extracted from the selected articles. I used an assessment tool for case-series studies developed by the National Heart, Lung, and Blood Institute (NHI) to assess study quality.[72] Any disagreements were resolved by consensus or after discussing with the principal investigator.

2.2.4. Data analysis

I summarised the findings from the included studies using both narrative synthesis and meta-analysis. A narrative review was used for studies that did not report confidence or credible intervals or other forms of intervals for reproduction numbers as these could not be included in the meta-analysis. Ranges were converted into confidence intervals using appropriate formulae.

2.2.4.1. Conversion of effect sizes

Studies reported reproduction numbers with various interval estimates such as 90 or 95% confidence interval, 95% credible interval, 90% high density interval, mean±standard error, interquartile range, upper and lower quartile, maximum & minimum, and range. Standard error was calculated using appropriate formulae as below, which was then converted to 95% confidence interval to use comparable effect sizes in the meta-analysis.

Step 1: Calculating Standard Error

i. For 90 % Confidence or credible or high-density interval

$$SE = \frac{UCI - LCI}{2 * invnormal(0.95)}$$

ii. For 95% Confidence or credible interval

$$SE = \frac{UCI - LCI}{2 * invormal(0.975)}$$

iii. One study has credible interval but no mean value. Calculated mean value as:

$$SE = \frac{UCI - LCI}{2 * invnormal(0.95)}$$

$$R_0 = UCI - (invnormal(0.95) * SE)$$

iv. Two studies have SD but no interval. Calculated SE as:

$$SE = \frac{SD}{\sqrt{n}}$$

v. Interquartile range / lower and upper quartile: 3 studies

$$SD = \frac{UCI - LCI}{1.35}$$

$$SE = \frac{SD}{\sqrt{n}}$$

vi. Studies with Lower/Upper values or Minimum/Maximum or range

$$mean = \frac{(LCI + 2 * Median + UCI)}{4}$$

$$SD = \sqrt{\left(\frac{1}{12} * \left(\frac{(LCI - 2 * Median + UCI)^2}{4} + (UCI - LCI)^2\right)\right)}$$

$SE = \frac{SD}{\sqrt{n}}$ if n if given

$SE = SD$ if n is not given

vii. If $R_0 \pm$ XX, even if it is not mentioned whether the value after ± is SE or SD, it is assumed to be SE

viii. If R_0 ± SD, and sample size not available. SE = SD

Step 2: Calculating 95% confidence interval

After calculating standard error for all observations, 95% confidence interval (CI) of R_0 was calculated as:

95% Lower CI $= R_0 - 1.96 * SE$; 95% Upper CI $= R_0 + 1.96 * SE$

Studies with reproduction numbers and estimated confidence intervals were included in the meta-analysis. I first used fixed-effect meta-analysis to obtain the pooled reproduction numbers for studies that estimated multiple reproduction numbers for the same country based on different assumptions and methods. I later utilised this pooled estimate to calculate a summary estimate using a fixed-effect or random-effects meta-analysis based on heterogeneity across studies (I^2 statistics).[73] The I^2, τ^2, and Q value were used to examine the extent of heterogeneity between studies. I used the restricted maximum likelihood (REML) method in the case of the random-effects meta-analysis.[74] Log-transformed values of the effect sizes were used in the meta-analysis model and the results were transformed back to ensure that the pooled effect size was larger than zero (0). Pooled effect sizes along with a 95% confidence interval were presented. I assessed the possibility of publication bias through visual inspection of asymmetry in funnel and Doi plots, and the LFK index to measure asymmetry.[75] When evidence of publication bias was confirmed, I performed the trim-and-fill procedures to account for the possible publication bias.[76]

2.2.4.2. Sub-group and sensitivity analysis

I also conducted a sub-group analysis by country, continent, study duration and method, whether mean or median was reported for reproduction number, month of publication, and whether the study was conducted in Wuhan, Hubei including Wuhan or outside Hubei in China. Influence analysis was performed using leave-one-out analysis to detect which study influenced the pooled estimate of the meta-analysis most. Sensitivity analysis was conducted by leaving the most influential studies from the analysis, excluding studies with $R_0 < 1$

considering the increasing number of cases with the spread of the COVID-19 virus and excluding fair or low-quality studies. Version 14.2 of Stata software (Stata Corp, College Station, Texas, USA) was used to perform the analyses.

2.3 Results

A schematic representation of the process of selecting articles for this systematic review is shown in **Figure** 2.1**.** This study screened 15 714 articles after removing duplicates from 26 425 identified records. Abstract and title screening resulted in 773 articles with various outcomes. Upon full-text screening, I included 500 articles, out of which, 129 articles met the eligibility criteria, and I additionally included 22 articles from references of the included studies. Finally, 151 articles (**Appendix B**) estimating R_0 were included in this study. Seventy-six articles were synthesised narratively as they did not provide intervals or uncertainty estimates for R_0. Out of the 76 articles described narratively, six articles that provided interval estimates for some countries were included in the meta-analysis as well. Thus, a total of 81 articles were included in the meta-analysis. The included studies reported reproduction numbers for 73 countries.

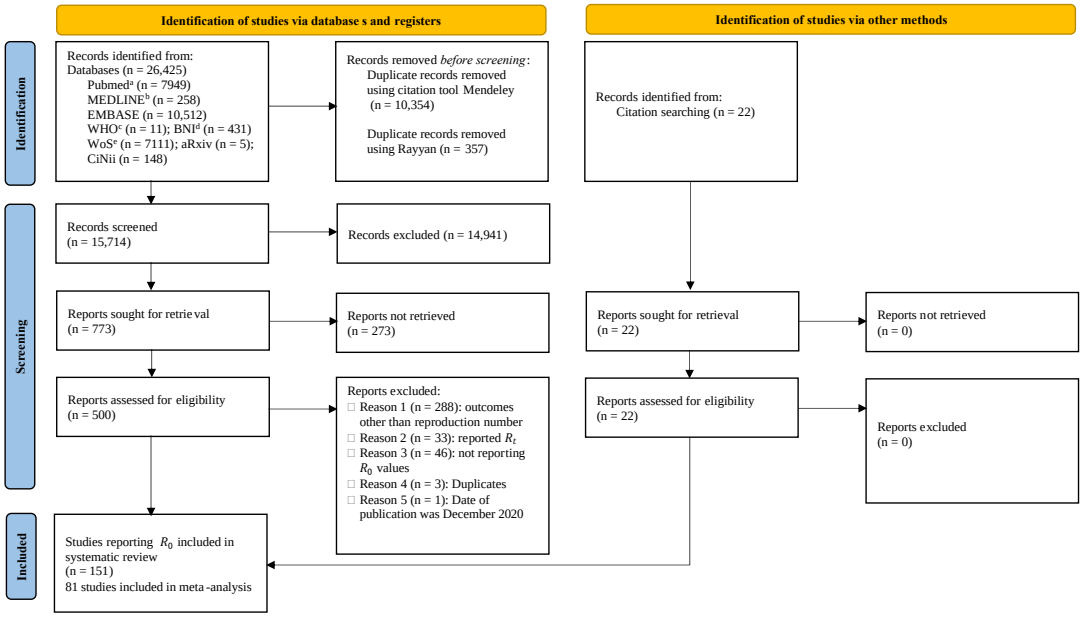


Figure 2.1. Selection of articles reporting basic reproduction number of COVID-19 published between 1st December 2019 and 31st September 2020 using PRISMA flow diagram 2020

The estimates of R_0 from the studies included in the meta-analysis ranged from 0.4 to 12.58. Details of the studies included in the meta-analysis can be obtained from **Table** 2.1. **Figure** 2.2 shows the forest plot with the distribution of R_0 values by study, with the overall pooled estimate. I estimated the pooled R_0 for COVID-19 to be 2.66 (95% CI, 2.41–2.94) using a random-effects model. This means that on average, a COVID-19-infected person transmits the infection to around two to three susceptible people. There was heterogeneity among studies ($I^2 = 100\%$, p-value <0.001, and $\tau^2 = 0.31$).

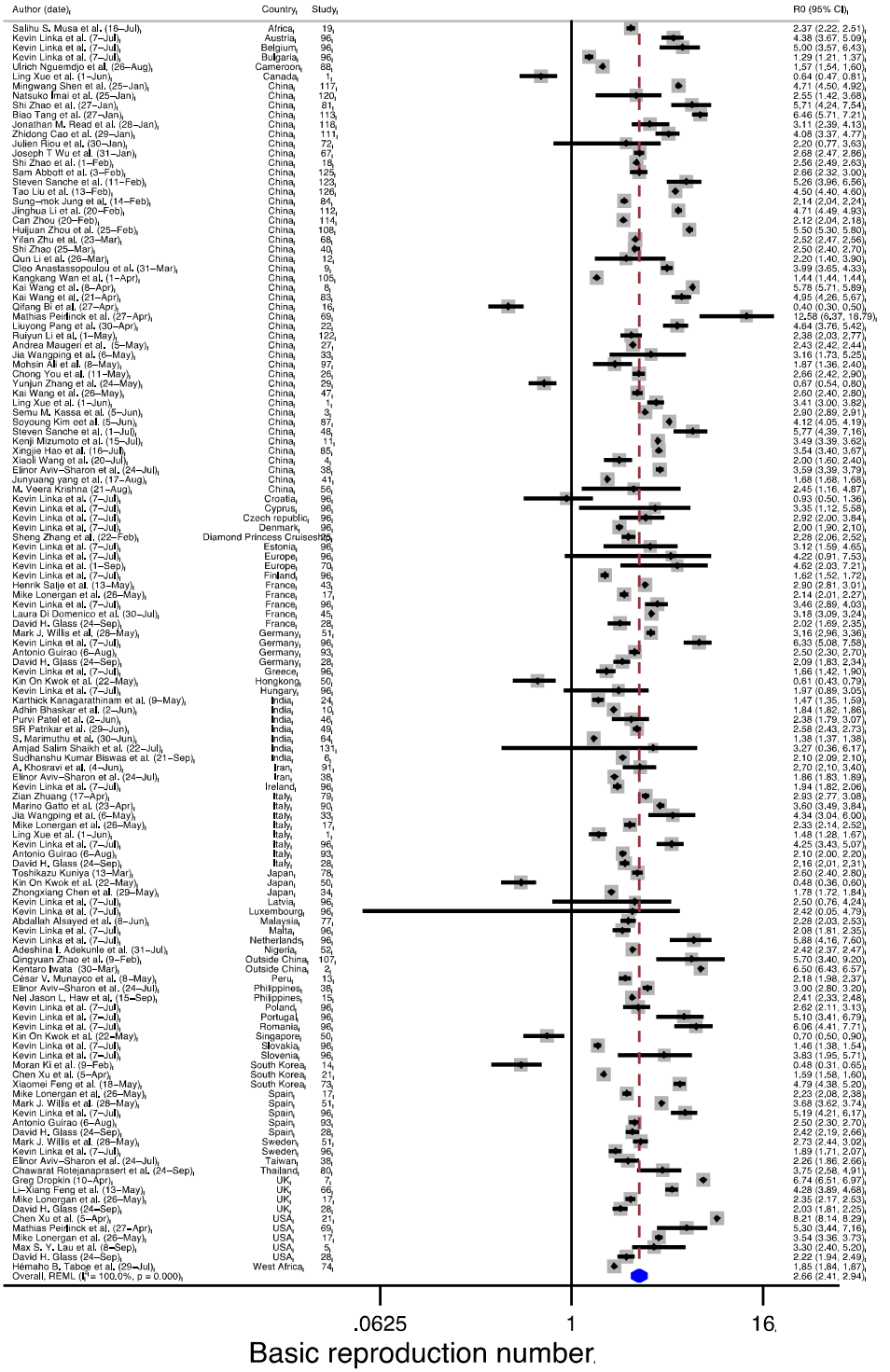


Figure 2.2. Pooled estimated of basic reproduction number values

Table 2.1. Details of the studies included in the meta-analysis

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
1	1	Ling Xue et al.	Canada	0.6	0.5	0.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
1	1	Ling Xue et al.	China	3.4	3.0	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
1	1	Ling Xue et al.	Italy	1.5	1.3	1.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
2	2	Kentaro Iwata	Outside China	6.5	5.6	7.2	Y	Y	N	Y	NA	Y	NR	Y	Y	6
3	3	Semu M. Kassa et al.	China	2.9	2.0	4.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
4	4	Xiaoli Wang et al.	China	2.0	1.6	2.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
5	5	Max S. Y. Lau et al.	USA	3.3	2.4	5.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
6	6	Sudhanshu Kumar Biswas et al.	India	2.1	2.0	2.2	Y	Y	Y	Y	NA	Y	Y	Y	N	7
7	7	Greg Dropkin	UK	5.8	5.1	7.0	Y	Y	Y	Y	Y	N	Y	Y	Y	8
7	7	Greg Dropkin	UK	6.7	6.4	7.0	Y	Y	Y	Y	Y	N	Y	Y	Y	8
7	7	Greg Dropkin	UK	6.7	5.6	9.6	Y	Y	Y	Y	Y	N	Y	Y	Y	8
7	7	Greg Dropkin	UK	6.9	6.5	7.4	Y	Y	Y	Y	Y	N	Y	Y	Y	8
8	8	Kai Wang et al.	China	5.8	5.7	5.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
9	9	Cleo Anastassopoulou et al.	China	3.1	2.5	3.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	6.1	5.0	7.2	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	3.4	2.9	3.9	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	4.6	3.6	5.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	4.8	3.4	6.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	7.1	5.8	8.4	Y	Y	Y	Y	NA	Y	N	Y	Y	7

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
9	9	Cleo Anastassopoulou et al.	China	5.1	4.3	6.0	Y	Y	Y	Y	NA	Y	N	Y	Y	7
9	9	Cleo Anastassopoulou et al.	China	3.2	2.4	4.0	Y	Y	Y	Y	NA	Y	N	Y	Y	7
10	10	Adhin Bhaskar et al.	India	1.9	1.1	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
11	11	Kenji Mizumoto et al.	China	3.5	3.4	3.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
12	12	Qun Li et al.	China	2.2	1.4	3.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
13	13	César V. Munayco et al.	Peru	2.3	2.0	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
13	13	César V. Munayco et al.	Peru	2.0	1.7	2.3	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
14	14	Moran Ki et al.	South Korea	0.5	0.3	0.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
14	14	Moran Ki et al.	South Korea	0.5	0.3	0.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
15	15	Nel Jason L. Haw et al.	Philippines	2.4	2.3	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
16	16	Qifang Bi et al.	China	0.4	0.3	0.5	Y	Y	Y	Y	NA	Y	Y	N	Y	7
17	17	Mike Lonergan et al.	USA	3.6	3.4	3.8	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	USA	3.2	2.7	3.7	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	UK	2.6	2.4	2.9	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	UK	2.1	1.8	2.3	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	Italy	3.7	3.1	4.4	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	Italy	2.2	2.0	2.4	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	France	2.0	1.8	2.1	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	France	2.7	2.4	3.0	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	Spain	3.2	2.4	4.1	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
17	17	Mike Lonergan et al.	Spain	2.2	2.1	2.4	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
18	18	Shi Zhao et al.	China	2.6	2.5	2.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
19	19	Salihu S. Musa et al.	Africa	2.4	2.2	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
20	21	Chen Xu et al.	South Korea	1.6	1.6	1.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
20	21	Chen Xu et al.	USA	8.2	8.1	8.3	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
21	22	Liuyong Pang et al.	China	4.6	3.8	5.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
22	24	Karthick Kanagarathinam et al.	India	1.5	1.4	1.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
23	25	Sheng Zhang et al.	Diamond Princess Cruiseship	2.3	2.1	2.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	1.9	0.9	3.3	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	6.8	5.1	8.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.7	2.0	3.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.2	1.6	3.0	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.7	2.1	3.6	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.4	1.8	3.2	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	7.8	4.1	12.8	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	4.5	3.2	6.0	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.4	1.8	3.1	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.8	1.6	4.4	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	3.4	1.5	6.0	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	1.7	0.6	3.3	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.1	1.5	2.8	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	2.7	1.0	4.6	Y	Y	Y	Y	NA	Y	N	Y	Y	7

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
24	26	Chong You et al.	China	2.8	1.0	4.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	6.2	3.9	8.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	3.0	1.4	5.3	Y	Y	Y	Y	NA	Y	N	Y	Y	7
24	26	Chong You et al.	China	3.6	2.6	5.2	Y	Y	Y	Y	NA	Y	N	Y	Y	7
25	27	Andrea Maugeri et al.	China	2.4	2.4	2.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
26	28	David H. Glass	France	2.0	1.7	2.4	Y	Y	Y	Y	Y	Y	N	Y	Y	8
26	28	David H. Glass	Germany	2.1	1.8	2.3	Y	Y	Y	Y	Y	Y	N	Y	Y	8
26	28	David H. Glass	Italy	2.2	2.0	2.3	Y	Y	Y	Y	Y	Y	N	Y	Y	8
26	28	David H. Glass	Spain	2.4	2.2	2.7	Y	Y	Y	Y	Y	Y	N	Y	Y	8
26	28	David H. Glass	UK	2.0	1.8	2.3	Y	Y	Y	Y	Y	Y	N	Y	Y	8
26	28	David H. Glass	USA	2.2	1.9	2.5	Y	Y	Y	Y	Y	Y	N	Y	Y	8
27	29	Yunjun Zhang et al.	China	0.7	0.5	0.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
27	29	Yunjun Zhang et al.	China	0.7	0.4	1.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
28	33	Jia Wangping et al.	China	3.2	1.7	5.3	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
28	33	Jia Wangping et al.	Italy	4.3	3.0	6.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
29	34	Zhongxiang Chen et al.	Japan	2.0	1.9	2.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
29	34	Zhongxiang Chen et al.	Japan	1.1	0.9	1.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
29	34	Zhongxiang Chen et al.	Japan	1.6	1.4	1.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
29	34	Zhongxiang Chen et al.	Japan	1.5	0.9	1.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
30	38	Elinor Aviv-Sharon et al.	China	3.6	3.4	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
30	38	Elinor Aviv-Sharon et al.	Iran	1.9	1.8	1.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
30	38	Elinor Aviv-Sharon et al.	Philippines	3.0	2.8	3.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
30	38	Elinor Aviv-Sharon et al.	Taiwan	2.3	1.9	2.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
31	40	Shi Zhao	China	2.5	2.4	2.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
32	41	Junyuang yang et al.	China	1.7	1.7	1.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
33	43	Henrik Salje et al.	France	2.9	2.8	3.0	Y	Y	Y	Y	NA	Y	CD	Y	Y	7
34	45	Laura Di Domenico et al.	France	3.2	3.1	3.2	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
35	46	Purvi Patel et al.	India	2.4	1.8	3.1	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
36	47	Kai Wang et al.	China	2.6	2.4	2.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
37	48	Steven Sanche et al.	China	5.8	4.4	7.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
37	48	Steven Sanche et al.	China	5.7	3.8	8.9	Y	Y	Y	Y	NA	Y	N	Y	Y	7
38	49	SR Patrikar et al.	India	2.6	2.3	3.0	Y	Y	Y	Y	Y	Y	NR	Y	Y	8
38	49	SR Patrikar et al.	India	2.5	2.2	2.8	Y	Y	Y	Y	Y	Y	NR	Y	Y	8
38	49	SR Patrikar et al.	India	2.6	2.3	3.0	Y	Y	Y	Y	Y	Y	NR	Y	Y	8
38	49	SR Patrikar et al.	India	2.6	2.3	2.9	Y	Y	Y	Y	Y	Y	NR	Y	Y	8
39	50	Kin On Kwok et al.	Hongkong	0.6	0.5	0.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
39	50	Kin On Kwok et al.	Japan	0.5	0.4	0.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
39	50	Kin On Kwok et al.	Singapore	0.7	0.6	0.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
40	51	Mark J. Willis et al.	Germany	3.2	3.1	3.3	Y	Y	Y	Y	NA	Y	Y	N	Y	7
40	51	Mark J. Willis et al.	Spain	3.7	3.7	3.7	Y	Y	Y	Y	NA	Y	Y	N	Y	7
40	51	Mark J. Willis et al.	Sweden	2.7	2.6	2.9	Y	Y	Y	Y	NA	Y	Y	N	Y	7
41	52	Adeshina I. Adekunle et al.	Nigeria	2.4	2.4	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
42	56	M. Veera Krishna	China	2.5	1.2	4.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
43	64	S. Marimuthu et al.	India	1.4	1.4	1.4	Y	Y	Y	Y	NA	Y	N	Y	Y	7

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
44	66	Li-Xiang Feng et al.	UK	4.3	3.9	4.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
45	67	Joseph T Wu et al.	China	2.7	2.5	2.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
46	68	Yifan Zhu et al.	China	2.5	2.4	2.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
46	68	Yifan Zhu et al.	China	2.5	2.5	2.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
47	69	Mathias Peirlinck et al.	China	12.6	9.4	15.8	Y	N	Y	Y	NA	Y	Y	Y	Y	7
47	69	Mathias Peirlinck et al.	USA	5.3	4.4	6.3	Y	N	Y	Y	NA	Y	Y	Y	Y	7
48	70	Kevin Linka et al.	Europe	4.6	3.3	5.9	Y	Y	Y	Y	NA	Y	Y	Y	N	7
49	72	Julien Riou et al.	China	2.2	1.4	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
50	73	Xiaomei Feng et al.	South Korea	4.8	4.4	5.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
51	74	Hémaho B. Taboe et al.	West Africa	1.9	1.8	1.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
52	77	Abdallah Alsayed et al.	Malaysia	2.3	2.2	2.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
53	78	Toshikazu Kuniya	Japan	2.6	2.4	2.8	Y	Y	O	Y	NA	Y	N	Y	Y	6
54	79	Zian Zhuang	Italy	3.3	3.0	3.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
54	79	Zian Zhuang	Italy	2.6	2.3	2.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
54	79	Zian Zhuang	South Korea	2.6	2.3	2.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
54	79	Zian Zhuang	South Korea	3.2	2.9	3.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
55	80	Chawarat Rotejanaprasert et al.	Thailand	3.8	2.2	5.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
55	80	Chawarat Rotejanaprasert et al.	Thailand	3.7	2.5	5.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
56	81	Shi Zhao et al.	China	5.7	4.2	7.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7
57	83	Kai Wang et al.	China	5.0	4.3	5.7	Y	Y	Y	Y	NA	Y	N	Y	Y	7
58	84	Sung-mok Jung et al.	China	3.2	2.7	3.7	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
58	84	Sung-mok Jung et al.	China	2.1	2.0	2.2	Y	Y	Y	Y	Y	Y	Y	Y	Y	9

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
59	85	Xingjie Hao et al.	China	3.5	3.4	3.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
60	87	Soyoung Kim eet al.	China	4.1	4.0	4.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
61	88	Ulrich Nguemdjo et al.	Cameroon	1.6	1.5	1.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
62	90	Marino Gatto et al.	Italy	3.6	3.5	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
63	91	A. Khosravi et al.	Iran	2.7	2.1	3.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
64	93	Antonio Guirao	Germany	2.5	2.3	2.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
64	93	Antonio Guirao	Italy	2.1	2.0	2.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
64	93	Antonio Guirao	Spain	2.5	2.3	2.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Austria	4.4	4.0	4.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Belgium	5.0	4.3	5.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Bulgaria	1.3	1.3	1.3	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Croatia	0.9	0.7	1.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Cyprus	3.4	2.2	4.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Czech republic	2.9	2.5	3.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Denmark	2.0	2.0	2.1	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Estonia	3.1	2.3	3.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Europe	4.2	2.5	5.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Finland	1.6	1.6	1.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	France	3.5	3.2	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Germany	6.3	5.7	7.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Greece	1.7	1.5	1.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Hungary	2.0	1.4	2.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
65	96	Kevin Linka et al.	Ireland	1.9	1.9	2.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Italy	4.3	3.8	4.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Latvia	2.5	1.6	3.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Lithuania	0.9	0.0	1.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Luxembourg	2.4	1.2	3.6	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Malta	2.1	1.9	2.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Netherlands	5.9	5.0	6.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Poland	2.6	2.4	2.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Portugal	5.1	4.2	6.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Romania	6.1	5.2	6.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Slovakia	1.5	1.4	1.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Slovenia	3.8	2.9	4.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Spain	5.2	4.7	5.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
65	96	Kevin Linka et al.	Sweden	1.9	1.8	2.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
66	97	Mohsin Ali et al.	China	1.9	1.4	2.4	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
67	105	Kangkang Wan et al.	China	1.4	1.4	1.5	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
68	107	Qingyuan Zhao et al.	Outside China	5.7	3.4	9.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
69	108	Huijuan Zhou et al.	China	5.5	5.3	5.8	Y	Y	CD	CD	Y	Y	Y	Y	Y	7
70	111	Zhidong Cao et al.	China	4.1	3.4	4.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
71	112	Jinghua Li et al.	China	5.5	5.2	5.9	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
71	112	Jinghua Li et al.	China	5.5	5.1	6.1	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
71	112	Jinghua Li et al.	China	6.0	5.0	7.0	Y	Y	Y	Y	NA	Y	Y	Y	Y	8

SN	Study	Author	Country	R_0	R_0 from	R_0 to	Quality Assessment*									
							1	2	3	4	5	6	7	8	9	TS
71	112	Jinghua Li et al.	China	1.7	1.1	2.3	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
71	112	Jinghua Li et al.	China	3.6	3.0	4.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
71	112	Jinghua Li et al.	China	4.4	3.6	5.1	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
72	113	Biao Tang et al.	China	6.4	1.7	10.0	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
72	113	Biao Tang et al.	China	6.5	5.7	7.2	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
73	114	Can Zhou	China	2.1	2.0	2.2	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
74	117	Mingwang Shen et al.	China	4.7	4.5	4.9	Y	Y	Y	Y	Y	Y	N	Y	Y	8
75	118	Jonathan M. Read et al.	China	3.1	2.4	4.1	Y	Y	Y	Y	Y	O	N	Y	Y	7
76	120	Natsuko Imai et al.	China	2.6	1.5	3.5	Y	Y	Y	Y	NA	Y	CD	Y	Y	7
77	122	Ruiyun Li et al.	China	2.4	2.0	2.8	Y	Y	Y	Y	NA	Y	N	Y	Y	7
78	123	Steven Sanche et al.	China	6.3	3.3	11.3	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
78	123	Steven Sanche et al.	China	4.9	3.3	7.2	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
78	123	Steven Sanche et al.	China	6.6	4.0	10.5	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
78	123	Steven Sanche et al.	China	4.7	2.8	7.6	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
79	125	Sam Abbott et al.	China		2.0	2.7	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
79	125	Sam Abbott et al.	China		2.8	3.8	Y	Y	Y	Y	NA	Y	Y	Y	Y	8
80	126	Tao Liu et al.	China	4.5	4.4	4.6	Y	Y	Y	N	Y	Y	Y	Y	Y	8
81	131	Amjad Salim Shaikh et al.	India	2.6	1.4	6.5	Y	Y	Y	Y	NA	Y	N	Y	Y	7

*Quality assessment- 1: Was the study question or objective clearly stated?; 2: Was the study population clearly and fully described, including a case definition?; 3: Were the cases consecutive?; 4: Were the subjects comparable?; 5: Was the intervention clearly described?; 6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?; 7: Was the length of follow-up adequate?; 8: Were the statistical methods well-described?; 9: Were the results well-described?; TS: Total score; CD: cannot determine; NA: not applicable; NR: not reported

The LFK index of 6.76 (**Figure** 2.3-**b**) showed strong evidence of small study-effect as indicated by the funnel plot (**Figure** 2.3-**a**) and Doi plot (**Figure** 2.3-**b**). The bias-adjusted results from trim-and-fill method in **Figure** 2.3-**c** showed an overall pool estimate of R_0 of 1.82 (95% CI, 1.74–1.91).

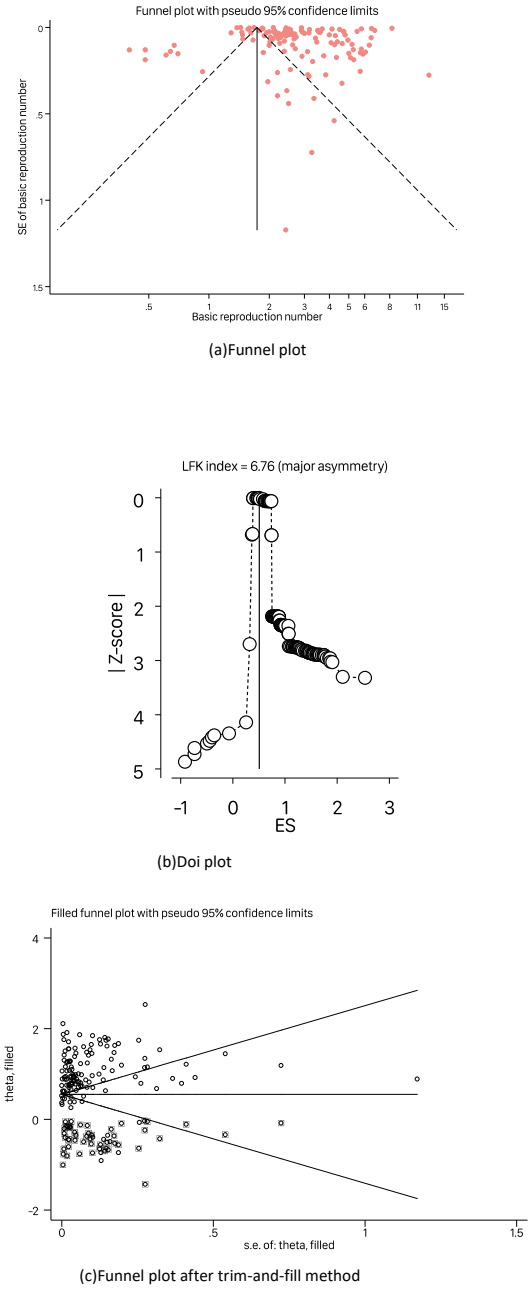


Figure 2.3. Funnel plot (a)before and (c)after trim-and-fill method, and (b)Doi plot for basic reproduction number values of all studies used to estimate the summary reproduction number of COVID-19

Sub-group analysis is reported in **Table** 2.2 and detailed figures are presented in **Figure** 2.4 – **Figure** 2.11. The pooled estimates for studies using the exponential growth model (R_0 = 3.06) and compartmental mathematical models (R_0 = 2.99) were higher than the pooled estimates obtained using the moment-generating function of the Lotka-Euler equation (R_0 = 2.47), logistic models (R_0 = 2.60), or other models (R_0 = 2.24). The overall R_0 was 2.64, and the pooled estimates were 2.74 for data duration of ≤ 2 weeks, 2.70 for 2 weeks to 1 month, 2.45 for 1–2 months, and 2.86 for > 2 months. This indicated that the estimates prepared in various stages of the epidemic with different periods of data availability were not very different from each other. The pooled estimate of R_0 using data collected up to January 2020 was relatively higher ($R_0 = 3.34$) compared to the estimates from subsequent months and was declining until March when more data were available. When COVID-19 started spreading rapidly to different countries, the pooled estimates were highest in studies published in January ($R_0 = 3.87$) while those published in August produced relatively lower estimates of 2.04.

Studies published using data in the USA found higher R_0 estimates of 4.09 than in India where the pooled R_0 was estimated to be 1.91. Similarly, studies from Europe reported higher estimates ($R_0 = 2.74$), while Africa's pooled R_0 was 1.94. Studies that reported mean R_0 had higher pooled estimates of 2.99 compared to studies reporting the median with pooled estimates of 2.39. In Wuhan, the pooled R_0 was higher in Wuhan, Hubei (including Wuhan) or overall in China (R_0~3.40) than outside Hubei in China ($R_0 = 1.50$).

Table 2.2. Sub-group analysis for basic reproduction number (R_0)

Characteristics	**Number of reporting**	**R_0 (95% CI)**	***P* value Heterogeneity**
Method considered	(*n* = 161)		<0.05
Exponential Growth Model	20	3.06 (2.32–4.03)	
Moment generating function of the Lotka-Euler equation	6	2.47 (2.13–2.86)	
Compartmental Model	87	2.99 (2.67–3.35)	
Logistic Model	4	2.60 (1.94–3.48)	
Others	44	2.24 (1.87–2.69)	
Duration of data	(*n* = 127)		<0.05
≤ 2 weeks	15	2.74 (2.26–3.31)	
2 weeks – 1 month	28	2.70 (2.11–3.46)	
1–2 months	53	2.45 (2.06–2.91)	
>2 months	31	2.86 (2.47–3.32)	
Last month of data	(*n* = 128)		<0.05
January	25	3.34 (2.89–3.87)	
February	14	2.23 (1.40–3.56)	
March	30	2.18 (1.73–2.76)	
April	13	2.72 (1.99–3.71)	
May	12	2.69 (2.40–3.01)	

Characteristics	**Number of reporting**	**R_0 (95% CI)**	***P* value Heterogeneity**
June	30	2.80 (2.31–3.39)	
July	4	2.60 (1.94–3.48)	
Month of publication	(*n* = 130)		<0.05
January	8	3.87 (2.97–5.03)	
February	11	2.90 (1.92–4.37)	
March	6	3.18 (2.28–4.45)	
April	11	3.37 (1.93–5.89)	
May	26	2.22 (1.74–2.85)	
June	11	2.12 (1.58–2.86)	
July	40	2.83 (2.43–3.28)	
August	6	2.04 (1.70–2.45)	
September	8	2.27 (2.12–2.43)	
Country	(*n* = 130)		<0.05
China	43	3.02 (2.55–3.59)	
Other	49	2.24 (1.87–2.68)	
USA	5	4.09 (2.60–6.43)	
Italy	8	2.69 (2.08–3.48)	
India	7	1.91 (1.56–2.33)	
France	5	2.68 (2.18–3.29)	

Characteristics	**Number of reporting**	**R_0 (95% CI)**	***P* value Heterogeneity**
UK	4	3.43 (1.99–5.91)	
Spain	5	3.02 (2.22–4.09)	
Germany	3	3.18 (1.99–5.08)	
Continent	(*n* = 126)		<0.05
Asia	66	2.54 (2.18–2.96)	
Europe	50	2.78 (2.46–3.15)	
North America	8	2.74 (1.62–4.64)	
Africa	2	1.94 (1.27–2.98)	
Type of central estimate	(*n* = 130)		<0.05
Mean	34	2.99 (2.43–3.68)	
Median	13	2.39 (1.91–2.98)	
Other	83	2.58 (2.28–2.92)	
Location in China	(*n* = 43)		<0.05
Wuhan	8	3.40 (2.61–4.44)	
Hubei including Wuhan	2	3.39 (2.48–4.64)	
Outside Hubei in China	6	1.50 (0.76–2.96)	
China overall	27	3.39 (2.84–4.04)	

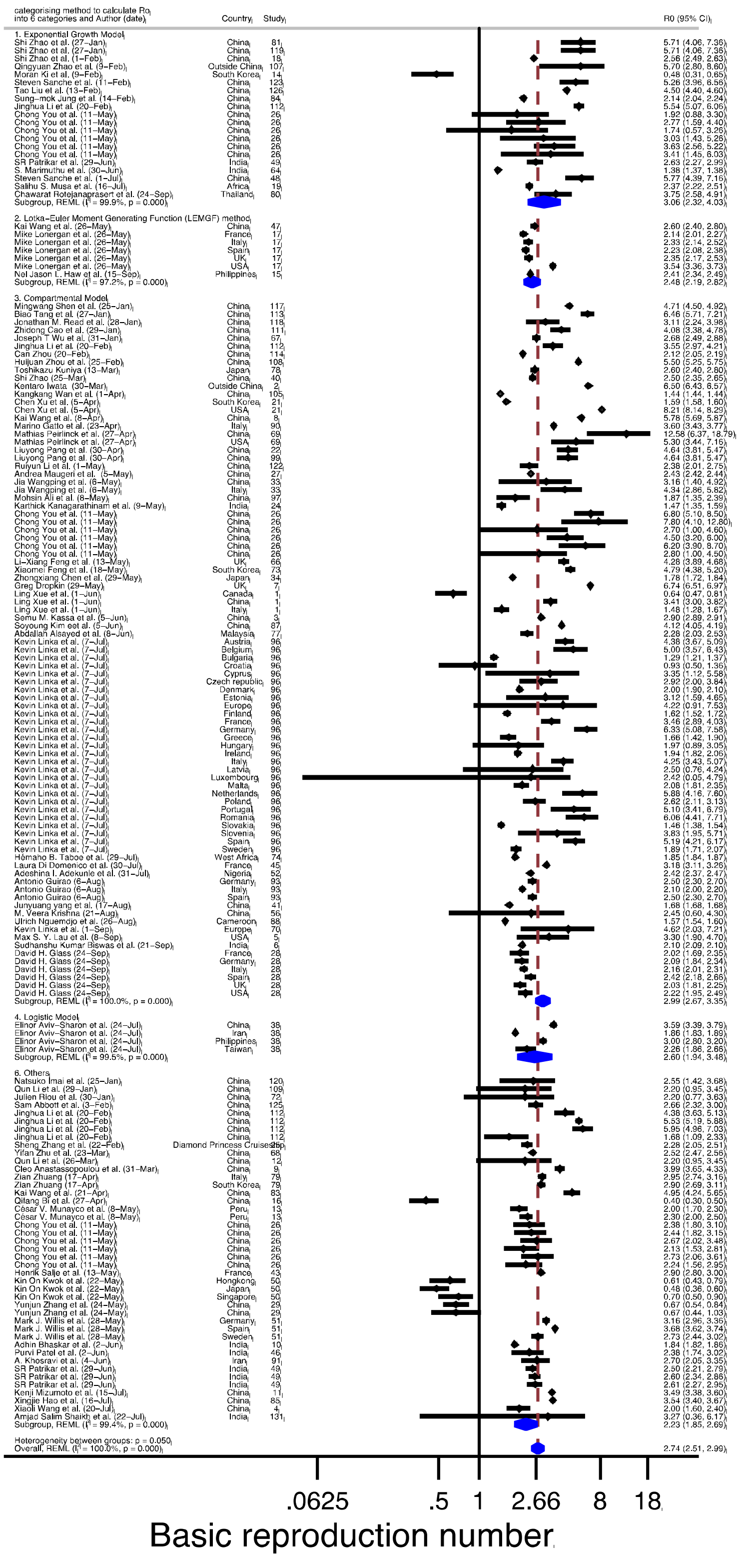


Figure 2.4. Sub-group analysis of basic reproduction number by method

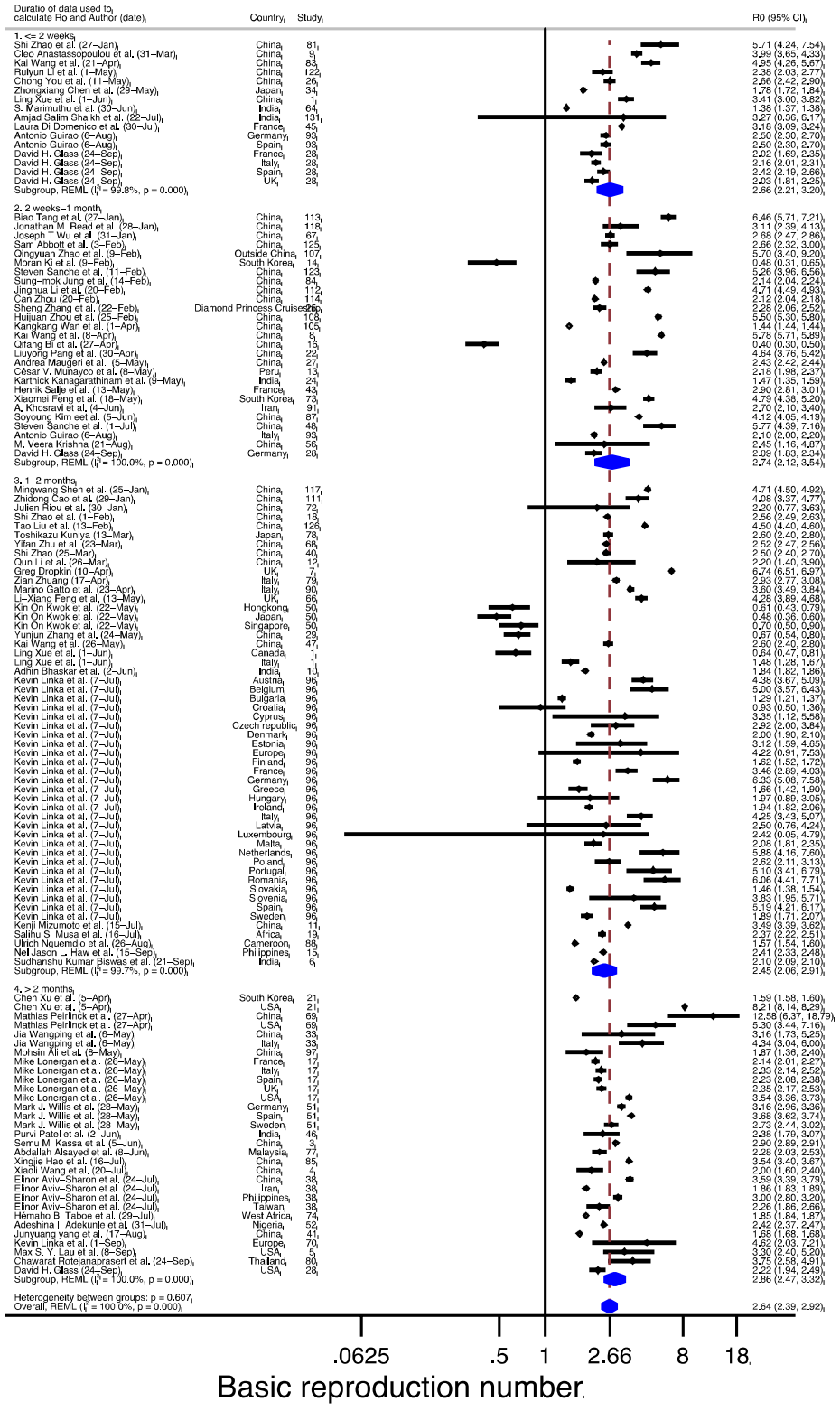


Figure 2.5. Sub-group analysis of basic reproduction number by duration of data

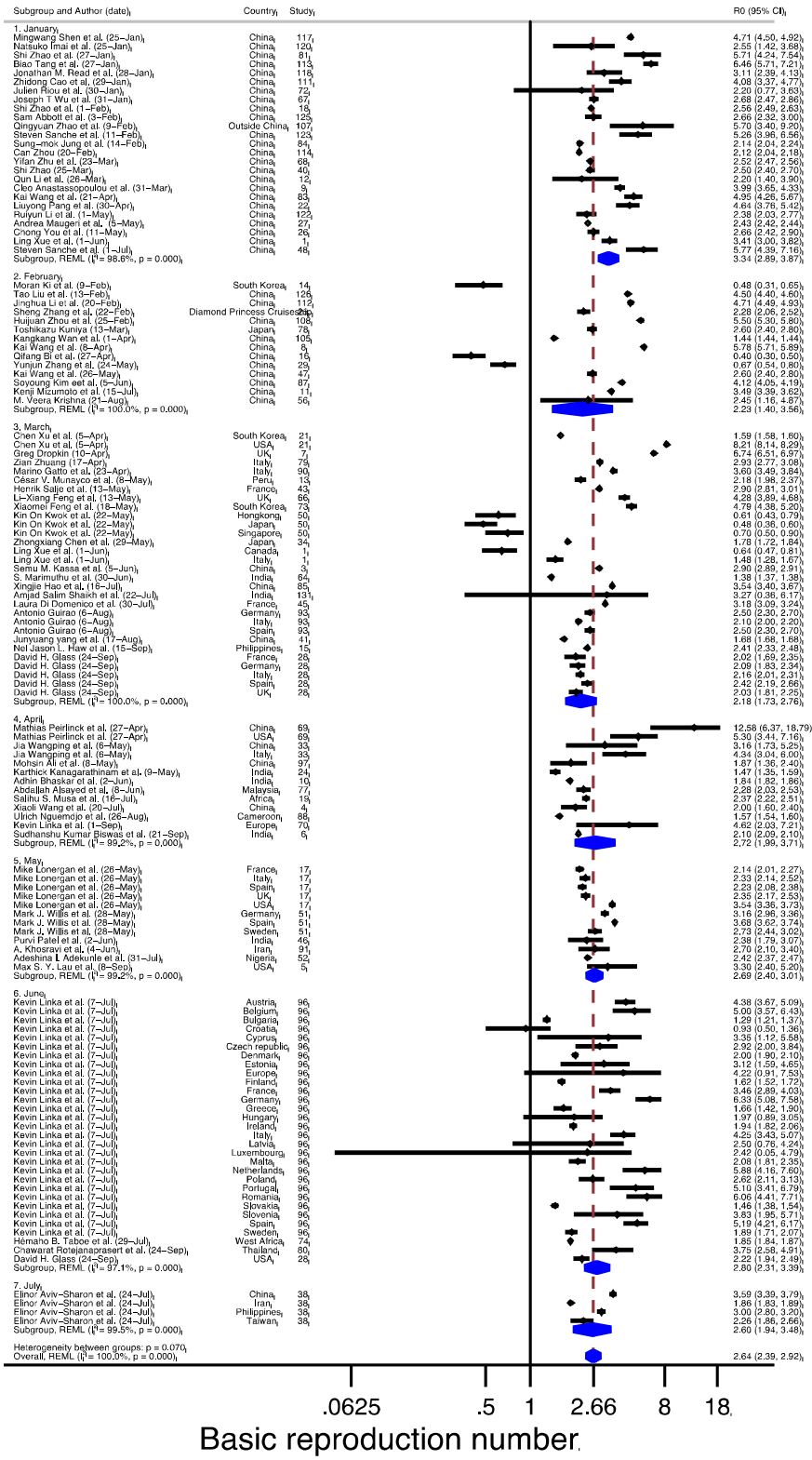


Figure 2.6. Sub-group analysis of basic reproduction number by last month of data

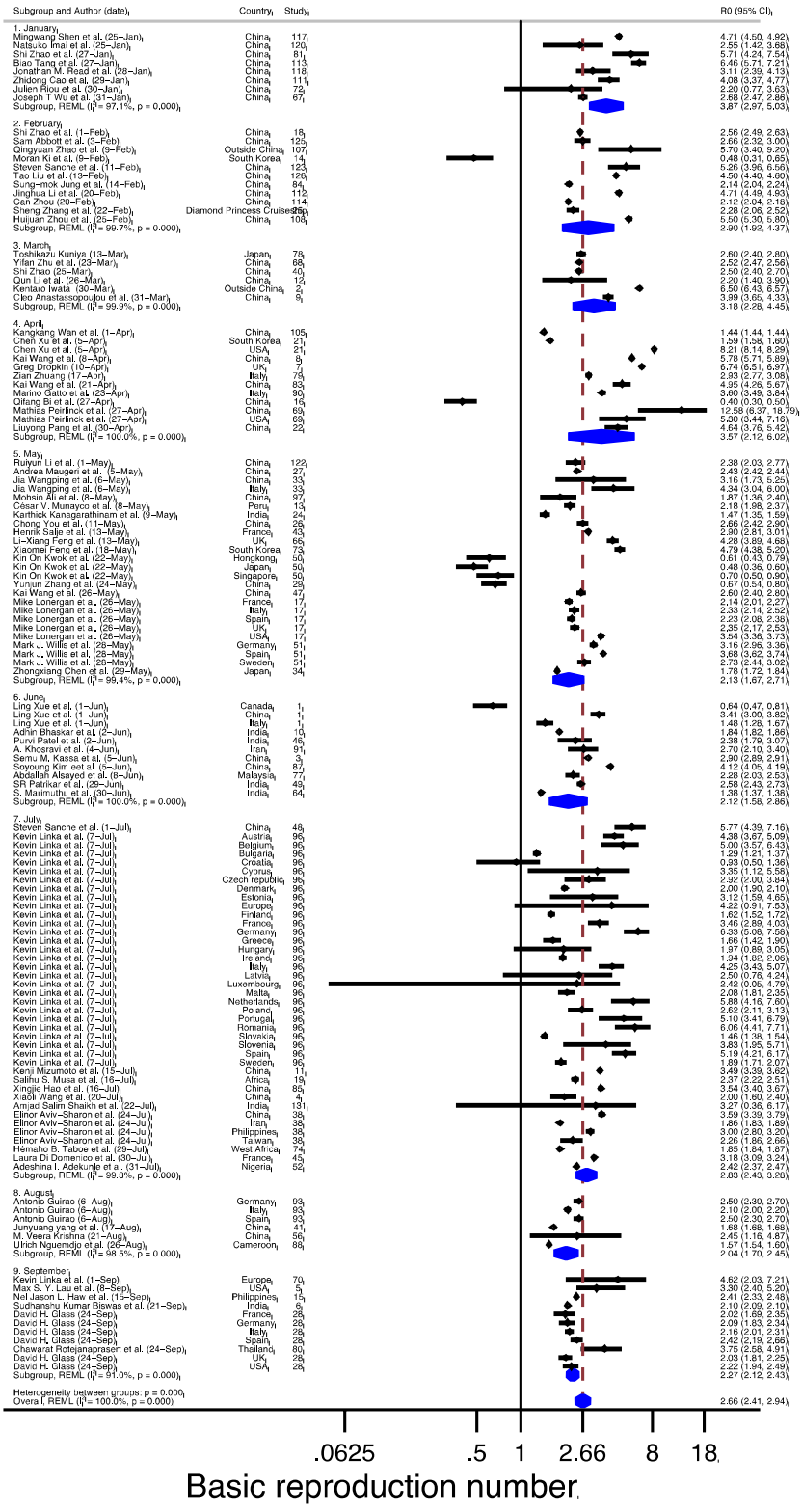


Figure 2.7. Sub-group analysis of basic reproduction number by month of publication

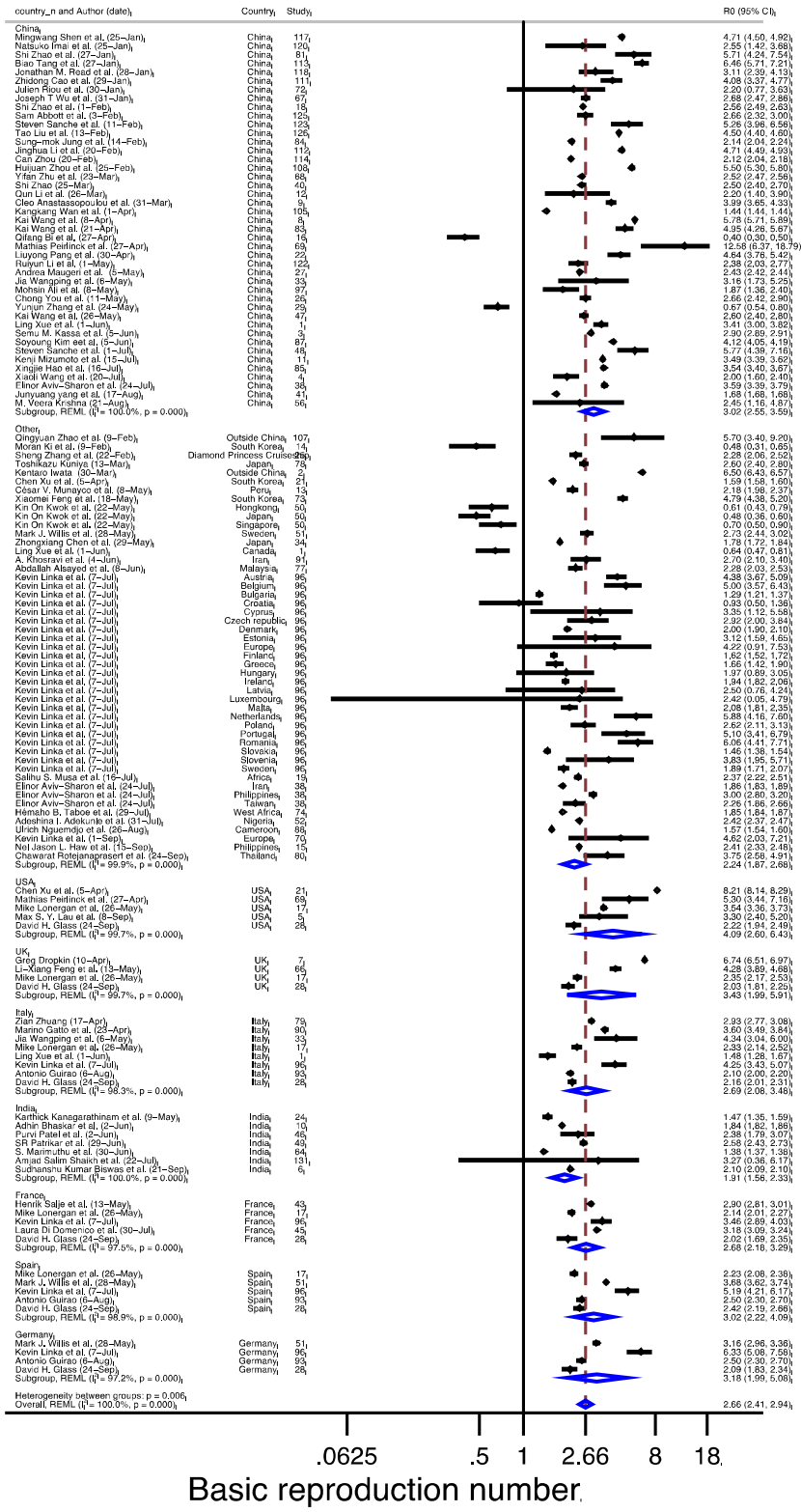


Figure 2.8. Sub-group analysis of basic reproduction number by country

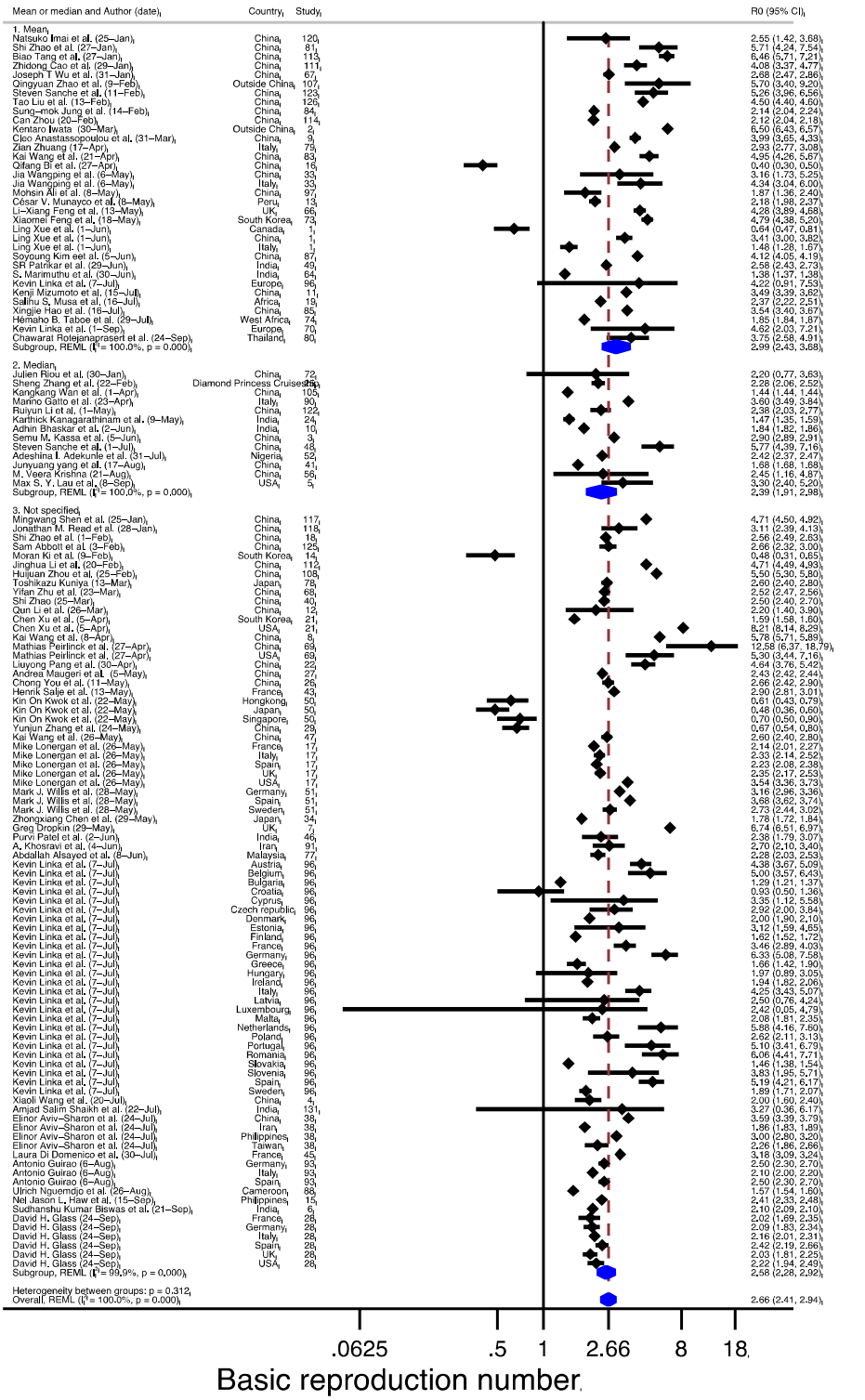
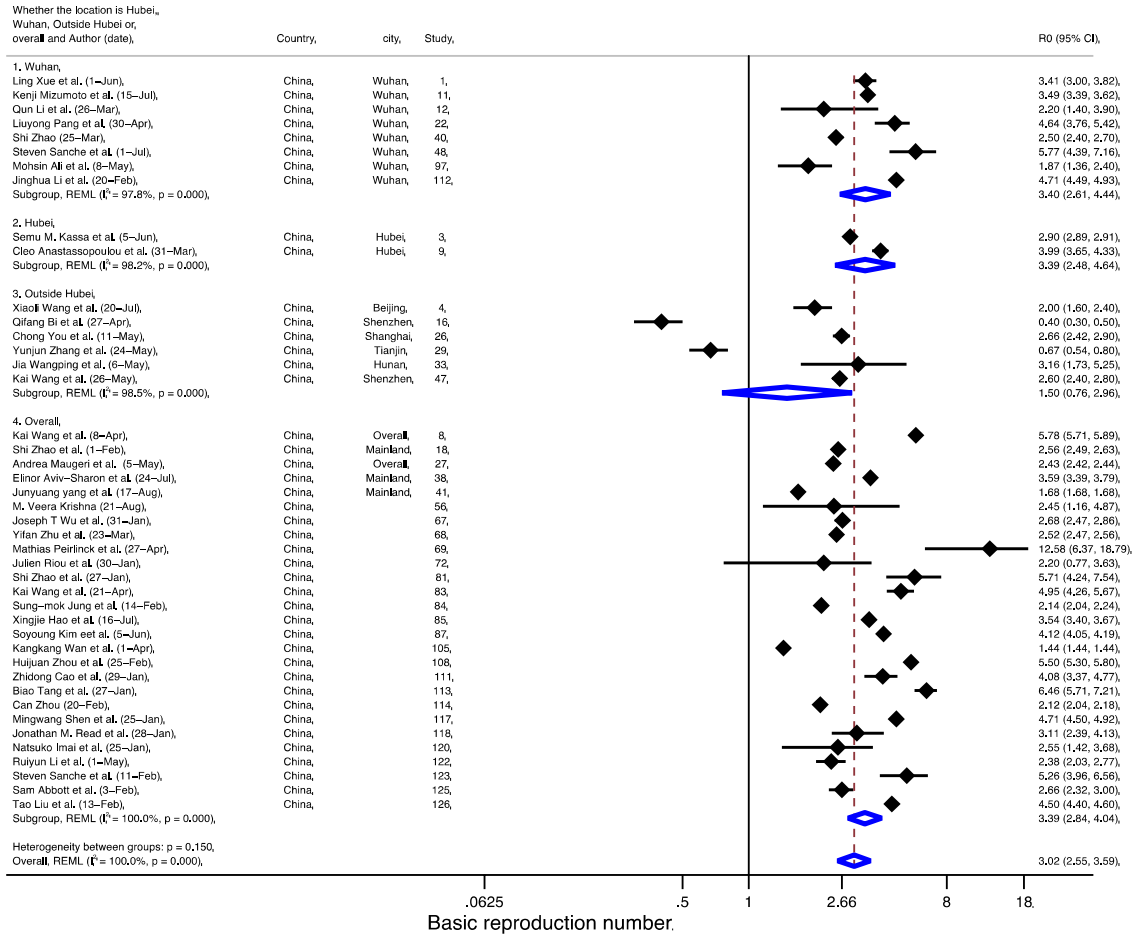


Figure 2.9. Sub-group analysis of basic reproduction number by type of central estimate



NOTE: Weights and between–subgroup heterogeneity test are from random–effects model.

Figure 2.10. Sub-group analysis of basic reproduction number by location in China

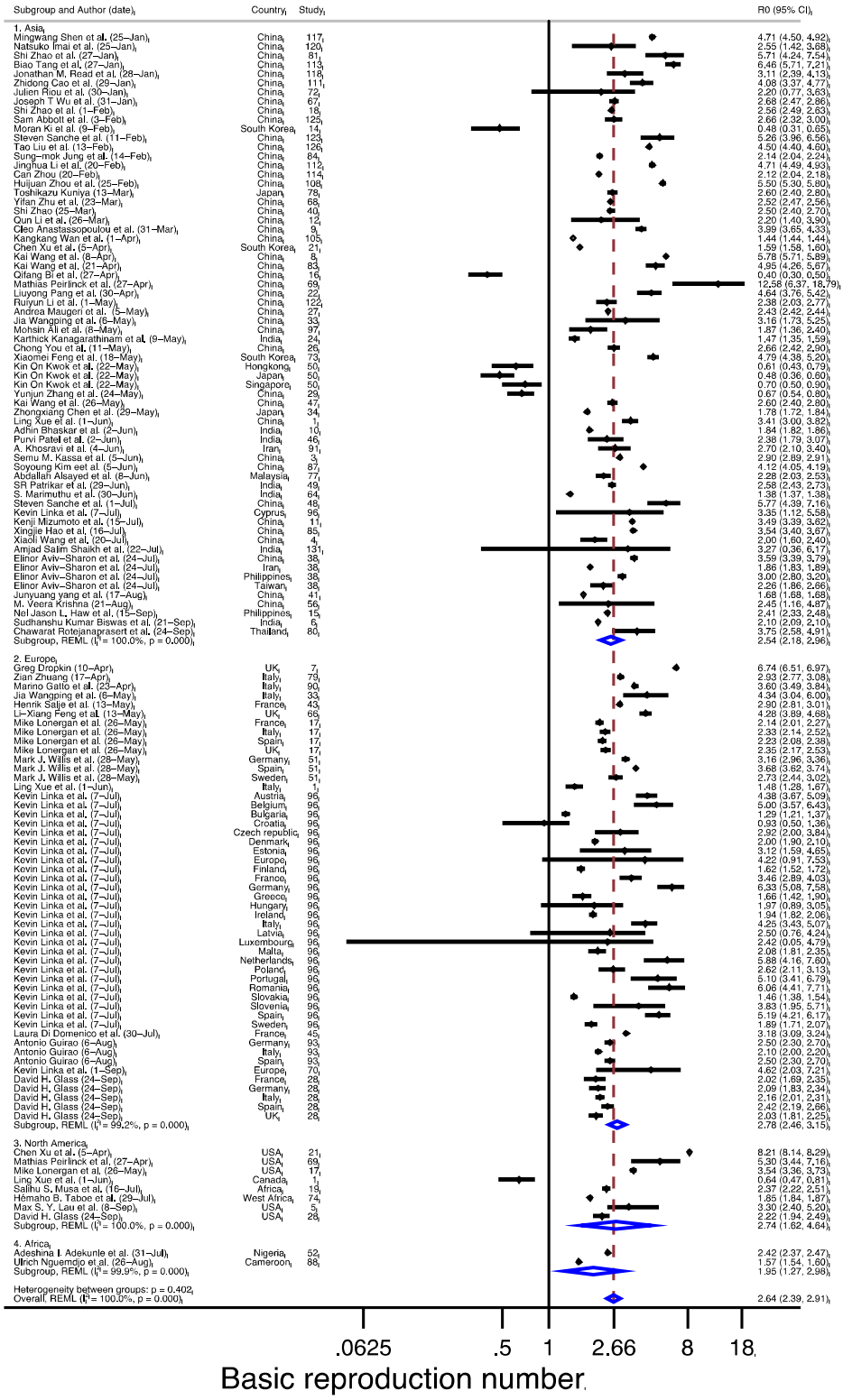


Figure 2.11. Sub-group analysis of basic reproduction number by continent

In sensitivity analysis conducted after excluding studies with R_0 <1, the pooled R_0 was estimated to be 2.92 (95% CI, 2.70–3.16) as shown in **Figure** 2.12. Similarly, an analysis of only good quality studies estimated the pooled reproduction number ($R_0 = 2.56$) very close to the overall estimate of 2.66 as shown in **Figure** 2.13. **Table** 2.3 shows the estimated R_0 after leave-one-out analysis ranged from 2.63 to 2.70. A study by Bi et al.[77] had the highest influence on the pooled estimate, but it increased the R_0 by only about 0.4. **Figure** 2.14 shows the scatterplot of the R_0 values of the 76 studies that were narratively synthesised. Detailed description can be obtained from **Table** 2.4. The estimated reproduction numbers from these studies are in line with the pooled R_0 estimated from this study, except a few studies that estimated extreme values of R_0.[78–80] An R_0 value of 14.8 was estimated in the Diamond Princess Cruise ship using data from 21st January to 19th February 2020.[79]

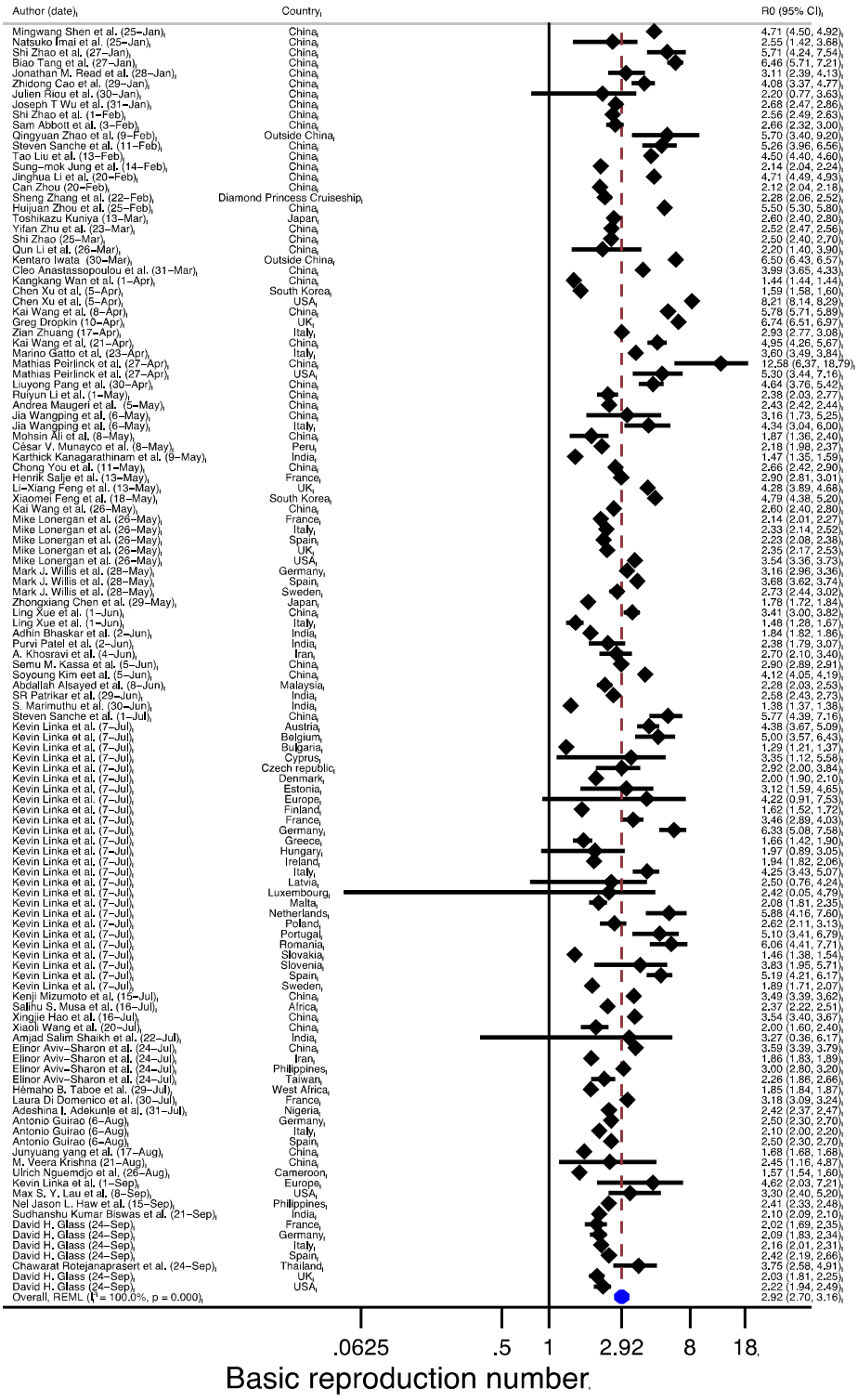


Figure 2.12. Sensitivity analysis of basic reproduction number excluding studies with $R_0 \leq 1$

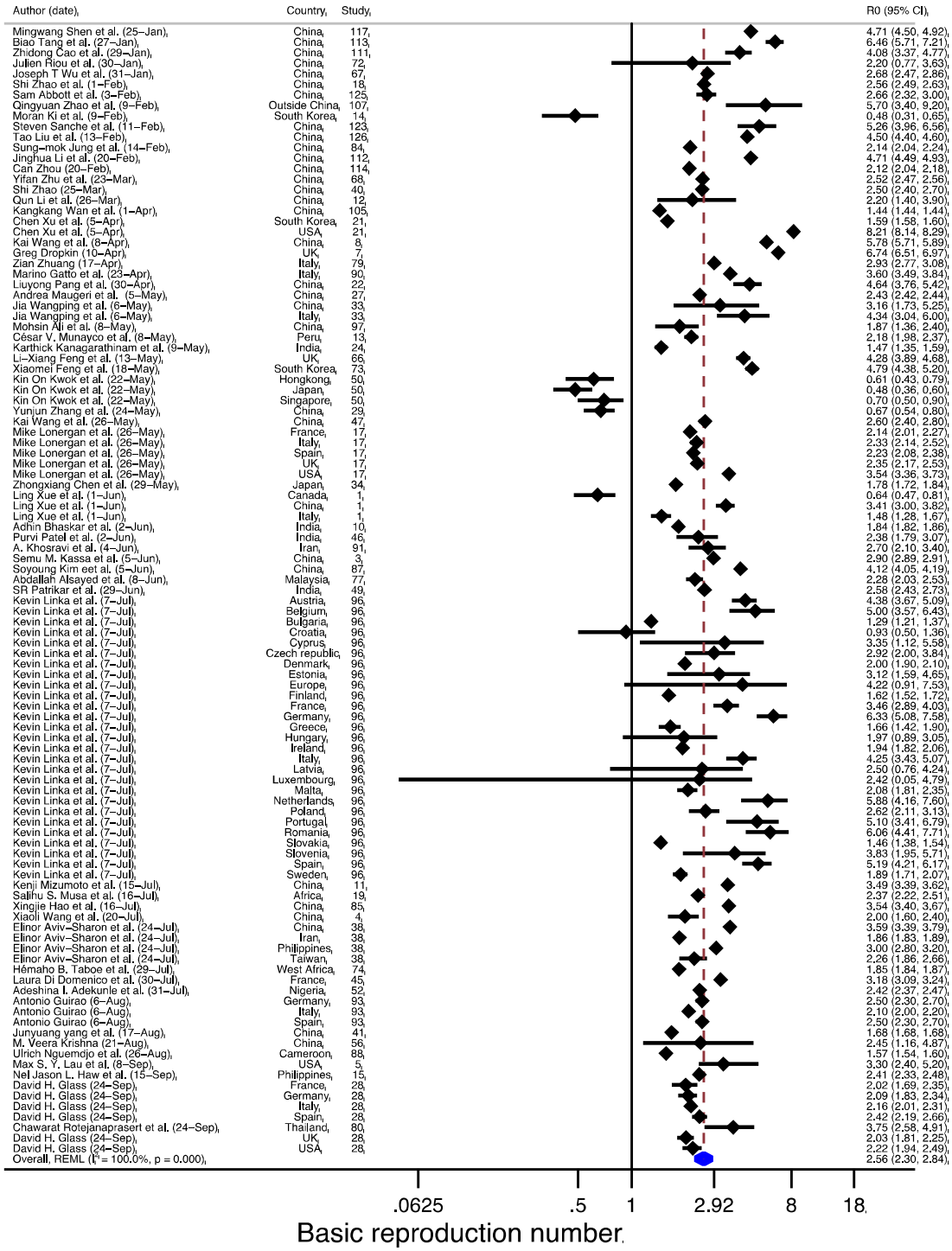


Figure 2.13. Sensitivity analysis of basic reproduction number excluding fair or low-quality studies

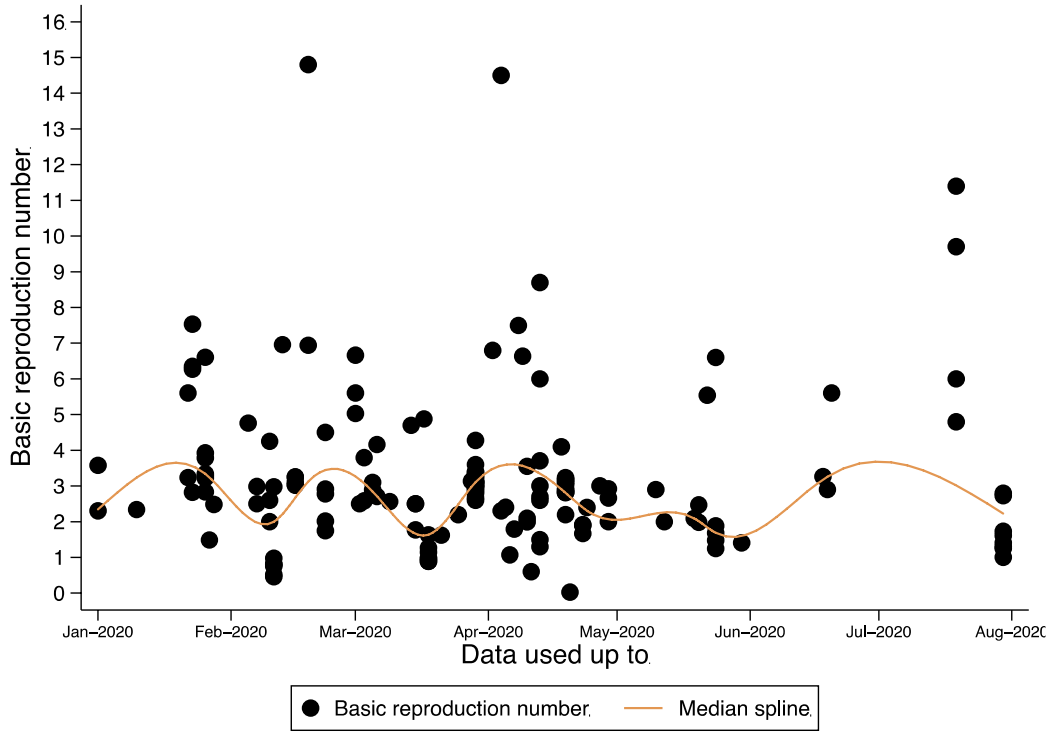


Figure 2.14. Timeline of the basic reproduction number (R_0) estimates for COVID-19 included in the narrative synthesis

Table 2.3. Result of influence analysis for basic reproduction number

Study no. omitted	Author	Estimate	95% CI
1	Ling Xue et al.	2.68	(2.42–2.95)
1	Ling Xue et al.	2.66	(2.41–2.94)
1	Ling Xue et al.	2.69	(2.44–2.97)
2	Kentaro Iwata	2.64	(2.40–2.92)
3	Semu M. Kassa et al.	2.66	(2.41–2.94)
4	Xiaoli Wang et al.	2.67	(2.42–2.95)
5	Max S. Y. Lau et al.	2.66	(2.41–2.94)
6	Sudhanshu Kumar Biswas et al.	2.67	(2.42–2.95)
7	Greg Dropkin	2.64	(2.40–2.92)
8	Kai Wang et al.	2.65	(2.40–2.92)
9	Cleo Anastassopoulou et al.	2.65	(2.40–2.93)
10	Adhin Bhaskar et al.	2.67	(2.42–2.95)
11	Kenji Mizumoto et al.	2.66	(2.41–2.93)
12	Qun Li et al.	2.67	(2.41–2.94)
13	César V. Munayco et al.	2.67	(2.41–2.95)
14	Moran Ki et al.	2.70	(2.45–2.97)
15	Nel Jason L. Haw et al.	2.67	(2.41–2.94)
16	Qifang Bi et al.	2.70	(2.46–2.97)
17	Mike Lonergan et al.	2.67	(2.41–2.94)
17	Mike Lonergan et al.	2.67	(2.41–2.94)
17	Mike Lonergan et al.	2.67	(2.41–2.95)
17	Mike Lonergan et al.	2.66	(2.41–2.93)
17	Mike Lonergan et al.	2.67	(2.42–2.95)
18	Shi Zhao et al.	2.66	(2.41–2.94)
19	Salihu S. Musa et al.	2.67	(2.41–2.94)
21	Chen Xu et al.	2.64	(2.39–2.91)
21	Chen Xu et al.	2.67	(2.42–2.95)

Study no. omitted	Author	Estimate	95% CI
22	Liuyong Pang et al.	2.65	(2.40–2.93)
24	Karthick Kanagarathinam et al.	2.68	(2.42–2.95)
25	Sheng Zhang et al.	2.67	(2.41–2.95)
26	Chong You et al.	2.66	(2.41–2.94)
27	Andrea Maugeri et al.	2.66	(2.41–2.94)
28	David H. Glass	2.67	(2.42–2.95)
28	David H. Glass	2.67	(2.41–2.95)
28	David H. Glass	2.67	(2.42–2.95)
28	David H. Glass	2.67	(2.41–2.95)
28	David H. Glass	2.67	(2.42–2.95)
28	David H. Glass	2.67	(2.41–2.94)
29	Yunjun Zhang et al.	2.69	(2.44–2.97)
33	Jia Wangping et al.	2.66	(2.41–2.94)
33	Jia Wangping et al.	2.65	(2.40–2.93)
34	Zhongxiang Chen et al.	2.67	(2.42–2.95)
38	Elinor Aviv-Sharon et al.	2.66	(2.41–2.93)
38	Elinor Aviv-Sharon et al.	2.66	(2.41–2.94)
38	Elinor Aviv-Sharon et al.	2.67	(2.42–2.95)
38	Elinor Aviv-Sharon et al.	2.67	(2.41–2.95)
40	Shi Zhao	2.66	(2.41–2.94)
41	Junyuang yang et al.	2.67	(2.42–2.95)
43	Henrik Salje et al.	2.66	(2.41–2.94)
45	Laura Di Domenico et al.	2.66	(2.41–2.94)
46	Purvi Patel et al.	2.67	(2.41–2.94)
47	Kai Wang et al.	2.66	(2.41–2.94)
48	Steven Sanche et al.	2.65	(2.40–2.92)
49	SR Patrikar et al.	2.66	(2.41–2.94)
50	Kin On Kwok et al.	2.69	(2.44–2.97)

Study no. omitted	Author	Estimate	95% CI
50	Kin On Kwok et al.	2.69	(2.44–2.97)
50	Kin On Kwok et al.	2.70	(2.45–2.97)
51	Mark J. Willis et al.	2.66	(2.41–2.94)
51	Mark J. Willis et al.	2.66	(2.41–2.94)
51	Mark J. Willis et al.	2.66	(2.40–2.93)
52	Adeshina I. Adekunle et al.	2.67	(2.41–2.94)
56	M. Veera Krishna	2.66	(2.41–2.94)
64	S. Marimuthu et al.	2.68	(2.43–2.96)
66	Li-Xiang Feng et al.	2.65	(2.40–2.93)
67	Joseph T Wu et al.	2.66	(2.41–2.94)
68	Yifan Zhu et al.	2.66	(2.41–2.94)
69	Mathias Peirlinck et al.	2.64	(2.39–2.90)
69	Mathias Peirlinck et al.	2.65	(2.40–2.92)
70	Kevin Linka et al.	2.65	(2.40–2.93)
72	Julien Riou et al.	2.67	(2.41–2.94)
73	Xiaomei Feng et al.	2.65	(2.40–2.93)
74	Hémaho B. Taboe et al.	2.67	(2.42–2.95)
77	Abdallah Alsayed et al.	2.67	(2.41–2.95)
78	Toshikazu Kuniya	2.66	(2.41–2.94)
79	Zian Zhuang	2.66	(2.41–2.94)
80	Chawarat Rotejanaprasert et al.	2.66	(2.40–2.93)
81	Shi Zhao et al.	2.65	(2.40–2.92)
83	Kai Wang et al.	2.65	(2.40–2.93)
84	Sung-mok Jung et al.	2.67	(2.42–2.95)
85	Xingjie Hao et al.	2.66	(2.41–2.93)
87	Soyoung Kim eet al.	2.65	(2.40–2.93)
88	Ulrich Nguemdjo et al.	2.67	(2.42–2.95)
90	Marino Gatto et al.	2.66	(2.41–2.93)

Study no. omitted	Author	Estimate	95% CI
91	A. Khosravi et al.	2.66	(2.41–2.94)
93	Antonio Guirao	2.66	(2.41–2.94)
93	Antonio Guirao	2.67	(2.42–2.95)
93	Antonio Guirao	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.64	(2.40–2.92)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.66	(2.41–2.93)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.65	(2.40–2.92)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.68	(2.43–2.96)
96	Kevin Linka et al.	2.65	(2.40–2.92)
96	Kevin Linka et al.	2.65	(2.40–2.92)
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.65	(2.40–2.93)
96	Kevin Linka et al.	2.65	(2.40–2.93)
96	Kevin Linka et al.	2.68	(2.43–2.96)
96	Kevin Linka et al.	2.65	(2.40–2.93)
96	Kevin Linka et al.	2.65	(2.40–2.93)
96	Kevin Linka et al.	2.66	(2.41–2.93)
96	Kevin Linka et al.	2.67	(2.42–2.95)

Study no. omitted	Author	Estimate	95% CI
96	Kevin Linka et al.	2.66	(2.41–2.94)
96	Kevin Linka et al.	2.67	(2.42–2.95)
96	Kevin Linka et al.	2.68	(2.42–2.95)
97	Mohsin Ali et al.	2.67	(2.42–2.95)
105	Kangkang Wan et al.	2.68	(2.42–2.95)
107	Qingyuan Zhao et al.	2.65	(2.40–2.92)
108	Huijuan Zhou et al.	2.65	(2.40–2.92)
111	Zhidong Cao et al.	2.65	(2.40–2.93)
112	Jinghua Li et al.	2.65	(2.40–2.93)
113	Biao Tang et al.	2.64	(2.40–2.92)
114	Can Zhou	2.67	(2.42–2.95)
117	Mingwang Shen et al.	2.65	(2.40–2.93)
118	Jonathan M. Read et al.	2.66	(2.41–2.94)
120	Natsuko Imai et al.	2.66	(2.41–2.94)
122	Ruiyun Li et al.	2.67	(2.41–2.94)
123	Steven Sanche et al.	2.65	(2.40–2.92)
125	Sam Abbott et al.	2.66	(2.41–2.94)
126	Tao Liu et al.	2.65	(2.40–2.93)
131	Amjad Salim Shaikh et al.	2.66	(2.41–2.94)
Combined		**2.66**	**2.41**

Table 2.4. Details of studies narratively synthesised

SN	Study	Author	Country	R_0	R_0 range
1	6	Sudhanshu Kumar Biswas et al.	India	2.4	–
2	9	Cleo Anastassopoulou et al.	China	2.0	–
2	9	Cleo Anastassopoulou et al.	China	2.6	–
3	20	Seo Yoon Chae et al.	USA	3.5	–
3	20	Seo Yoon Chae et al.	Germany	2.9	–
3	20	Seo Yoon Chae et al.	Canada	2.7	–
3	20	Seo Yoon Chae et al.	UK	2.6	–
3	20	Seo Yoon Chae et al.	Mexico	1.9	–
3	20	Seo Yoon Chae et al.	Iran	1.8	–
3	20	Seo Yoon Chae et al.	South Korea	2.2	–
3	20	Seo Yoon Chae et al.	Italy	2.2	–
3	20	Seo Yoon Chae et al.	China	2.7	–
3	20	Seo Yoon Chae et al.	Brazil	2.1	–
3	20	Seo Yoon Chae et al.	Spain	2.4	–
3	20	Seo Yoon Chae et al.	Japan	1.9	–
4	23	Md. Enamul Hoque	China	2.3	–
4	23	Md. Enamul Hoque	Turkey	14.5	–
5	30	Sungchan Kim et al.	South Korea	1.8	–
6	31	Longxiang Su et al.	China	1.8	–
6	31	Longxiang Su et al.	China	2.9	–
6	31	Longxiang Su et al.	China	2.8	–
6	31	Longxiang Su et al.	China	2.0	–
7	32	Jose Mario V Grzybowski et al.	Brazil	3.6	–
8	35	I Md Ady Wirawan et al.	Indonesia	2.0	–
9	36	Subhas Khajanchi et al.	India	1.7	–
9	36	Subhas Khajanchi et al.	India	1.9	–
9	36	Subhas Khajanchi et al.	India	1.5	–

SN	Study	Author	Country	R_0	R_0 range
9	36	Subhas Khajanchi et al.	India	1.2	–
10	37	Abdullah M. Almeshal et al.	Kuwait	2.2	–
11	39	Gabriel G. Katul et al.	Global	4.5	–
12	42	Luis Fernando Chaves et al.	Costa Rica	2.6	(0.2 – 5.0)
13	44	Conghui Xu et al.	USA	0.0	–
14	49	SR Patrikar et al.	India	1.9	–
14	49	SR Patrikar et al.	India	2.2	–
14	49	SR Patrikar et al.	India	1.8	–
14	49	SR Patrikar et al.	India	1.9	–
15	53	Tae Wuk Bae et al.	South Korea	2.6	–
15	53	Tae Wuk Bae et al.	South Korea	1.3	–
15	53	Tae Wuk Bae et al.	South Korea	3.7	–
15	53	Tae Wuk Bae et al.	South Korea	1.5	–
16	54	Muhammad Naveed et al.	NA	1.0	–
17	55	H. M. Yang et al.	Brazil	6.8	–
18	57	Shuo Jiang et al.	Italy	5.6	–
18	57	Shuo Jiang et al.	China		(3.0 – 3.3)
18	57	Shuo Jiang et al.	South Korea	5.0	–
18	57	Shuo Jiang et al.	China	6.7	–
19	58	Jingjing Tian et al.	China	3.0	–
20	59	Michael Irvine et al.	USA	2.5	–
21	60	Philip J Turk et al.	USA	1.8	–
22	61	Fernando Saldan˜a et al.	Mexico	2.5	–
23	63	Liping Wang et al.	China	2.7	–
24	65	Lara Goscé et al.	UK	2.6	–
25	70	Kevin Linka et al.	Austria	8.7	–
25	70	Kevin Linka et al.	Germany	6.0	–
25	70	Kevin Linka et al.	Denmark	2.7	–

SN	Study	Author	Country	R_0	R_0 range
25	70	Kevin Linka et al.	Malta	3.0	–
26	71	Soufiane Bentout et al.	Algeria	4.1	–
27	75	Z. Liu et al.	China	4.2	–
28	76	Ali Moussaoui et al.	Algeria	2.1	–
29	82	Tao Zhou et al.	China	3.2	–
29	82	Tao Zhou et al.	China	2.8	–
29	82	Tao Zhou et al.	China	3.8	–
29	82	Tao Zhou et al.	China	3.3	–
29	82	Tao Zhou et al.	China	3.3	–
29	82	Tao Zhou et al.	China	3.9	–
30	86	Shelby R. Buckman et l	USA	9.7	–
30	86	Shelby R. Buckman et l	China	4.8	–
30	86	Shelby R. Buckman et l	Brazil	11.4	–
30	86	Shelby R. Buckman et l	Italy	6.0	–
31	89	Rui Huang et al.	China		(4.8 – 5.8)
32	92	Marwan Al-Raeei	Russia	1.3	–
32	92	Marwan Al-Raeei	USA	1.6	–
32	92	Marwan Al-Raeei	Nigeria	1.0	–
32	92	Marwan Al-Raeei	India	1.3	–
32	92	Marwan Al-Raeei	Yemen	1.4	–
32	92	Marwan Al-Raeei	France	2.7	–
32	92	Marwan Al-Raeei	China	1.7	–
32	92	Marwan Al-Raeei	Syria	2.8	–
33	93	Antonio Guirao	Spain	2.2	–
33	93	Antonio Guirao	Spain	2.5	–
33	93	Antonio Guirao	Spain	2.5	–
34	94	Omar El Deeb et al.	Lebanon	5.6	–
35	95	Muhammad Altaf Khan et al.	China	6.6	–

SN	Study	Author	Country	R_0	R_0 range
36	98	Chentong Li et al.	China	3.8	–
37	100	Muhammad Dur-e-Ahmad et al.	South Korea	2.9	–
37	100	Muhammad Dur-e-Ahmad et al.	China	2.8	–
37	100	Muhammad Dur-e-Ahmad et al.	Iran	2.8	–
37	100	Muhammad Dur-e-Ahmad et al.	Italy	2.8	–
38	101	Konstantin S. Sharov	Europe	5.5	–
39	102	Rams´es H Mena et al.	Mexico	3.3	–
40	103	Feng Liu et al.	Japan	6.9	–
41	104	Haitao Song et al.	China	6.4	–
41	104	Haitao Song et al.	China	7.5	–
41	104	Haitao Song et al.	China	6.3	–
42	106	Jun Li	China	4.8	–
43	110	Yuxiao Bai et al.	China	1.5	–
44	115	Zhidong Cao et al.	China	3.2	–
45	116	B. Ivorra et al.	China	4.3	–
46	121	Hao Xiong et al.	China	3.0	–
47	124	Nian Shao et al.	China	3.3	–
47	124	Nian Shao et al.	China	3.2	–
47	124	Nian Shao et al.	China	3.0	–
47	124	Nian Shao et al.	China	3.1	–
47	124	Nian Shao et al.	China	3.0	–
48	126	Henrique Mohallem Paiva et al.	Spain	2.1	–
48	126	Henrique Mohallem Paiva et al.	France	2.0	–
48	126	Henrique Mohallem Paiva et al.	China	1.6	–
48	126	Henrique Mohallem Paiva et al.	Italy	2.0	–
48	126	Henrique Mohallem Paiva et al.	Germany	2.5	–
48	126	Henrique Mohallem Paiva et al.	USA	2.9	–
49	127	Sha He et al.	China	7.0	–

SN	Study	Author	Country	R_0	R_0 range
50	128	Zhenzhen Lu et al.	China	1.0	–
50	128	Zhenzhen Lu et al.	China	1.3	–
50	128	Zhenzhen Lu et al.	USA	1.1	–
50	128	Zhenzhen Lu et al.	Japan	1.6	–
50	128	Zhenzhen Lu et al.	China	0.9	–
				1336.	
50	128	Zhenzhen Lu et al.	Italy	8	–
50	128	Zhenzhen Lu et al.	China	0.9	–
50	128	Zhenzhen Lu et al.	China	1.0	–
51	129	Tian-Mu Chen et al.	China	2.3	–
51	129	Tian-Mu Chen et al.	China	3.6	–
52	130	Chayu Yang et al.	China	4.3	–
53	132	Zongo P et al.	France	4.9	–
54	133	Manotosh Mandal et al.	India		–
55	134	José M. Carcione et al.	Italy	3.0	–
56	135	Hanen Ben Hassen et al.	Morocco	2.9	–
56	135	Hanen Ben Hassen et al.	Tunisia	2.0	–
56	135	Hanen Ben Hassen et al.	Algeria	2.7	–
57	136	Mohsin Ali et al.	Pakistan	1.1	–
58	137	Youcef Belgaid et al.	Italy	3.1	–
59	138	W. E. Fitzgibbon et al.	Brazil	1.4	–
60	139	Yong Li	China	6.6	–
60	139	Yong Li	China	5.6	–
61	140	Chinwendu E. Madubueze et al	NA	1.5	–
61	140	Chinwendu E. Madubueze et al	NA	2.5	–
62	141	I. A. Lakman et al.	Russia	2.9	–
63	142	Salih Djilali et al.	Brazil	1.9	–
63	142	Salih Djilali et al.	South Africa	1.7	–

SN	Study	Author	Country	R_0	R_0 range
63	142	Salih Djilali et al.	Turkey	1.9	–
			Diamond Princess		
64	143	J Rocklöv et al.	Cruiseship	14.8	–
65	144	Cosimo Distante et al.	Italy		~2.2
65	144	Cosimo Distante et al.	Italy	3.0	–
65	144	Cosimo Distante et al.	Italy		(2.6 – 3.6)
65	144	Cosimo Distante et al.	Italy	3.1	–
65	144	Cosimo Distante et al.	Italy	3.1	–
65	144	Cosimo Distante et al.	Italy		(2.4 – 3.0)
65	144	Cosimo Distante et al.	Italy	3.1	–
65	144	Cosimo Distante et al.	Italy		(1.6 – 2.1)
65	144	Cosimo Distante et al.	Italy	3.0	–
65	144	Cosimo Distante et al.	Italy	3.1	–
65	144	Cosimo Distante et al.	Italy		(1.0 – 2.3)
65	144	Cosimo Distante et al.	Italy	3.0	–
65	144	Cosimo Distante et al.	Italy		(2.6 – 3.6)
65	144	Cosimo Distante et al.	Italy	2.7	–
65	144	Cosimo Distante et al.	Italy	3.4	–
65	144	Cosimo Distante et al.	Italy	3.3	–
65	144	Cosimo Distante et al.	Italy	3.0	–
65	144	Cosimo Distante et al.	Italy		(1.6 – 2.4)
65	144	Cosimo Distante et al.	Italy	3.0	–
65	144	Cosimo Distante et al.	Italy		(2.9 – 4.3)
65	144	Cosimo Distante et al.	Italy		(1.0 – 2.4)
65	144	Cosimo Distante et al.	Italy		(2.0 – 2.5)
65	144	Cosimo Distante et al.	Italy	2.9	–
65	144	Cosimo Distante et al.	Italy		(0.8 – 2.3)
65	144	Cosimo Distante et al.	Italy		(1.5 – 2.2)

SN	Study	Author	Country	R_0	R_0 range
65	144	Cosimo Distante et al.	Italy	3.6	–
65	144	Cosimo Distante et al.	Italy	3.4	–
65	144	Cosimo Distante et al.	Italy		(2.7 – 3.3)
65	144	Cosimo Distante et al.	Italy		(2.1 – 2.8)
65	144	Cosimo Distante et al.	Italy		(2.0 – 2.7)
65	144	Cosimo Distante et al.	Italy		(1.7 – 2.5)
65	144	Cosimo Distante et al.	Italy	3.2	–
65	144	Cosimo Distante et al.	Italy	3.1	–
65	144	Cosimo Distante et al.	Italy		(1.2 – 1.7)
65	144	Cosimo Distante et al.	Italy	2.8	–
65	144	Cosimo Distante et al.	Italy	2.6	–
65	144	Cosimo Distante et al.	Italy		(1.3 – 2.4)
65	144	Cosimo Distante et al.	Italy	3.3	–
65	144	Cosimo Distante et al.	Italy		(1.4 – 2.1)
65	144	Cosimo Distante et al.	Italy		(2.1 – 3.1)
65	144	Cosimo Distante et al.	Italy		(1.1 – 1.8)
65	144	Cosimo Distante et al.	Italy	2.8	–
65	144	Cosimo Distante et al.	Italy		(1.0 – 2.0)
66	145	Xinmiao Rong et al.	China	3.1	–
67	146	Ghada Nasr Radwan	Egypt	4.7	–
68	147	Joe Hilton et al.	Nepal	3.5	–
68	147	Joe Hilton et al.	Spain	2.0	–
68	147	Joe Hilton et al.	Belgium	2.0	–
68	147	Joe Hilton et al.	Italy	4.2	–
68	147	Joe Hilton et al.	Brazil	2.0	–
68	147	Joe Hilton et al.	Iraq	1.8	–
68	147	Joe Hilton et al.	China	2.4	–
68	147	Joe Hilton et al.	Iraq	3.6	–

SN	Study	Author	Country	R_0	R_0 range
68	147	Joe Hilton et al.	Canada	2.8	–
68	147	Joe Hilton et al.	Spain	2.8	–
68	147	Joe Hilton et al.	Austria	3.0	–
68	147	Joe Hilton et al.	Finland	3.6	–
68	147	Joe Hilton et al.	Canada	2.2	–
68	147	Joe Hilton et al.	Ethiopia	2.1	–
68	147	Joe Hilton et al.	Japan	4.1	–
68	147	Joe Hilton et al.	Japan	1.9	–
68	147	Joe Hilton et al.	Italy	2.4	–
68	147	Joe Hilton et al.	Egypt	1.4	–
68	147	Joe Hilton et al.	Austria	2.3	–
68	147	Joe Hilton et al.	Ethiopia	4.0	–
68	147	Joe Hilton et al.	Belgium	3.6	–
68	147	Joe Hilton et al.	Nepal	2.2	–
68	147	Joe Hilton et al.	Egypt	3.2	–
68	147	Joe Hilton et al.	China	2.4	–
68	147	Joe Hilton et al.	Brazil	2.8	–
68	147	Joe Hilton et al.	Finland	2.0	–
69	148	Patrick Bryant et al.	Austria	3.1	–
69	148	Patrick Bryant et al.	Germany	3.1	–
69	148	Patrick Bryant et al.	Denmark	3.0	–
69	148	Patrick Bryant et al.	Spain	3.2	–
69	148	Patrick Bryant et al.	Belgium	3.2	–
69	148	Patrick Bryant et al.	France	2.9	–
69	148	Patrick Bryant et al.	Norway	2.8	–
69	148	Patrick Bryant et al.	Italy	3.2	–
69	148	Patrick Bryant et al.	UK	2.8	–
69	148	Patrick Bryant et al.	Sweden	2.9	–

SN	Study	Author	Country	R_0	R_0 range
69	148	Patrick Bryant et al.	Switzerland	2.8	–
70	149	M. Liu et al.	China	2.3	–
70	149	M. Liu et al.	China	2.8	–
71	150	Elena Loli Piccolomini at al.	Italy	6.6	–
72	151	Haifa Ben Fredj et al.	Tunisia	7.5	–
73	152	Bernd Blasius	Countries worldwide and counties in the US	2.4	–
74	153	Muhammad Altaf Khan a et al.	China	2.5	–
75	154	Qiangsheng Huang et al.	China	0.5	–
75	154	Qiangsheng Huang et al.	China	1.0	–
75	154	Qiangsheng Huang et al.	China	0.5	–
75	154	Qiangsheng Huang et al.	China	0.8	–
75	154	Qiangsheng Huang et al.	China	0.8	–
75	154	Qiangsheng Huang et al.	China	0.8	–
76	155	Mohammed Al Zobbi et al.	South Korea	0.6	–

Table 2.5. Basic reproduction number (R_0) of various infectious diseases with proportion of studies reporting R_0 within the given threshold

Reproduction number threshold	Number (%)	Cumulative number (%)	Mean R_0	Range
Epidemic containment (R_0<1)	21 (6.2%)	21 (6.2%)	0.69	0.03–0.99
Influenza (1≥R_0<1.5) [81]	19 (5.6%)	40 (11.8%)	1.33	1.00–1.49
SARS-CoV (1.5≥R_0<4) [82]	231 (68.3%)	271 (80.2%)	2.61	1.50–3.99
HIV (4≥R_0<5) [83]	26 (7.7%)	297 (87.9%)	4.43	4.02–4.95
Smallpox (5≥ R_0<6) [84]	16 (4.7%)	313 (92.6%)	5.47	5.00–5.88
Rubella / Polio (6≥R_0<7) [85]	16 (4.7%)	329 (97.3%)	6.49	6.00–6.96
Chickenpox (7 ≥R_0<12) [86]	6 (1.8%)	335 (99.1%)	8.84	7.50–11.40
Measles (12≥R_0<18) [87]	3 (0.9%)	338 (100%)	13.96	12.58–14.80

2.4 Discussion

This study used meta-analysis to estimate the R_0 of COVID-19 using a systematic review of articles published between 1st December 2019 and 30th September 2020. I aggregated results published in these studies and synthesised estimates addressing the heterogeneity in different studies. When no deliberate intervention was taken for COVID-19, I estimated the R_0 to be 2.66 with 95% confidence interval (2.41–2.94), which is slightly higher than the estimates of 1.4 to 2.5 provided by the WHO.[88] Our estimates are similar to the R_0 of severe acute respiratory syndrome (R_0: 2.7; 95% CI: 2.2–3.7)[82] but greater than that of Middle East Respiratory Syndrome ($R_0 = 0.91$; 95% CI: 0.36–1.44).[89] Our sub-group analysis found very wide heterogeneity of estimates in our meta-analysis, with values ranging from 1.91 to 4.09. This shows the vulnerability of R_0 estimates to choices of modelling methods, data source, location, and timing. Of note, the test for asymmetry in our study indicated the possibility of a small-study effect meaning that studies with relatively large R_0 were more likely to be published. If the small-study effect observed in our study was due to publication bias, the true pooled R_0 will be 1.82, as estimated by the trim-and-fill method, which is relatively lower than our estimated R_0 (2.66). However, such a value is inconsistent with the behaviour of the virus in many countries.

Estimating a precise reproduction number is essential for determining the severity and size of any infectious disease and planning interventions to control its spread.[90] However, I found heterogeneity among included studies, which makes the use of the basic reproduction number

for basic epidemic planning difficult. The estimated reproduction number of studies included in the meta-analysis ranged from 0.4 to 12.58, orders of magnitude of difference. This heterogeneity was not ameliorated by choice of method, by longer periods of data collection, or by the national origin of the study. Even studies with data collected over periods of greater than 2 months had heterogeneity, and there was heterogeneity independent of the calculation method, nation of origin, or type of central estimate. I included studies from across the world and found wide variation in pooled estimates of R_0, which ranged from 1.91 in India to 4.09 in the USA. I also found high heterogeneity for estimates within countries, with estimates within single countries varying by orders of magnitude. I found estimated basic reproduction numbers below 1 in 6% of studies (**Table** 2.5), which is inconsistent with the rapid spread of the virus during that time period.

This high heterogeneity, which depends heavily on estimation method, data selection, and national characteristics presents a huge problem for risk assessment and data synthesis. National policymakers, emergency management committees, and the WHO need to be able to make judgments about the pandemic risk of a novel virus. But in order to do so, they must synthesise data on the transmissibility of the virus that is generated with a wide range of different models, has extreme variability, and gives radically different conclusions depending on which study is included in risk assessments and how data is pooled. The reproduction number of COVID-19 in a country is the average of R_0 in the sub-populations. Thus, even if the overall R_0 is low or even less than one, it is still necessary to implement strict measures to avert the consequences as the probability of disease transmission in specific sub-groups of a

population may still be high. Failure to take effective and adequate preventive measures may result in serious consequences. Given we found wide variation in estimation of R_0 between studies in the same country or using the same method, estimation of R_0 at sub-national level is unlikely to offer a reliable or useful tool for informing prevention policies.

I estimated that a COVID-19 infected individual can transmit the infection to two to three susceptible individuals if no control measure is applied. The pooled R_0 estimate of 2.66 estimated from this study is higher than the early WHO estimate of 1.4–2.5[88] and indicates a rapid spread of COVID-19. However, many governments and public health decision-makers acted based on lower estimates of R_0 that are inconsistent with the pooled study estimate found here, with disastrous consequences. For example, the UK Chief Medical Officer, Christ Whitty, announced a "herd immunity" threshold of 60% on national television in March 2020,[91] implying an assumed basic reproduction number of less than 2.5, but by this time only 31% of the published estimates in our study suggested a value in this range. In 2021 the US government set a target of 70% of adults vaccinated, also consistent with an R_0 value of less than 2.5,[92] even though less than 38% of the studies published to September 2020 found a value in this range. These decisions were inconsistent with the published evidence at that time and failed to take into account the full range of research findings on the infectiousness of the disease. However, with a wide range of published estimates even six months after the novel coronavirus was identified, and no consensus on the correct method for assessing this crucial number, it was very easy for governments to pick values consistent with their political priorities, and impossible to construct a coherent national or global vision for ending coronavirus-related

restrictions. The consequences of this have been particularly catastrophic in the USA but have also led to waves of sickness and death in some parts of Europe. The same inherent problems of heterogeneity by method, data source and timing likely also apply to estimates of the infectiousness of subsequent variants of the disease, such as Delta and Omicron, leading to further confusion and inconsistency in decision-making about the pandemic.

Estimation of the reproduction number depends on data sources, environmental factors, and model assumptions.[93] Our study shows that the competing influence of these factors can lead to a wide range of potential values of R_0 which make policy decisions difficult. Depending on the study group, data source and method used, the studies we reviewed concluded that the COVID-19 pandemic was disappearing; that the novel coronavirus was no more transmissible than seasonal influenza; that it was a dangerous virus with a pandemic potential twice that of seasonal influenza; or that it was more transmissible than smallpox. Policy responses to an infectious disease of this kind will vary enormously depending on the particular infectiousness regime policymakers believe they are dealing with, but the estimated R_0 values found within the published literature in 2020 cover such a wide range of regimes as to make policy decisions impossible. This renders this fundamental property of infectious diseases effectively useless for informing policy, and those nations which depended upon this value for determining when to relax restrictions have paid a high price.[64,94] I recommend that the basic reproduction number not be used as policy tools or to inform the public about the current state of pandemics, and that instead, policymakers rely on more precisely calculable measures with public health relevance such as hospital usage, deaths, doubling times, test numbers and positivity rates.

Furthermore, the infectious disease modelling and epidemiology community need to develop a consensus on the estimation and reporting of R_0, how they should be used in emerging infectious disease pandemics, and how they can be understood by laypeople and policymakers. During outbreaks of emerging infectious diseases such as Ebola,[95] SARS,[82] or other novel respiratory viruses[89] and hantaviruses,[96] it is common for outbreak analysts to rush early analyses of R_0 into publication, to inform national and global policymakers of the pandemic risk associated with the outbreak. This systematic review shows that these estimates are highly sensitive to assumptions, modelling methods and data, and cannot be relied upon to provide meaningful or comparable information about the nature of emerging pandemics. I therefore recommend that, in preparing for the next global pandemic or public health emergency of international concern, the WHO convene a working group to establish clear guidelines for the calculation, reporting and use of reproduction numbers, as well as information for policymakers, and the global health community should consider establishing a single, globally-agreed research group tasked with assessing outbreaks within a commonly-agreed framework endorsed by the WHO.

Global understanding of infectious disease outbreaks remains weak, and the novel coronavirus pandemic is the first rapidly spreading global pandemic since the 2018 Spanish influenza pandemic, which occurred at a time when sophisticated data analysis and disease modelling were not available. This study shows that there is still much theoretical and practical work to be done before we can properly understand the dynamics of emerging infectious diseases, and that R_0 offers a highly variable measure of pandemic risk, subject to much uncertainty and

vulnerable to the influence of modelling assumptions, data quality and data timeliness. Although infectious disease models and composite emergent indicators such as R_0 offer a tempting tool to simplify understanding of pandemics, they do not offer the clarity and precision needed to make decisions in a global pandemic. Until the epidemiological community has a clearer understanding of how to use these measures, they should be deprecated in favour of basic public health principles that offer a clear, simple framework for pandemic response. Until we have a clearer understanding of and consensus on how to use infectious disease models for pandemic response, we cannot hope to prepare for the next pandemic.

CHAPTER 3: Pandemic preparedness score

3.1 Background

The Global Health Security Index (GHSI) assesses the health security and public health preparedness capabilities across 195 countries.[97] It was developed by Johns Hopkins School of Public Health and was launched in October 2019, two months before the initial detection of the COVID-19 virus, and provides an annual evaluation of the readiness of 195 countries for epidemics and pandemics. Publicly available information is used to assess countries across six categories, 37 indicators, and 171 questions.

3.1.1 GHSI indicator categories

The GHSI scores countries based on the average of six indicator categories of *prevention*, *detection and reporting*, *rapid response*, *health system*, *compliance with international norms* and *risk environment*. Each indicator within the six categories contains up to seven underlying sub-indicators.

Figure 3.1. The indicator categories for global health security index. Source: GHSI report 2019, www.ghsindex.org

The 195 countries are ranked based on their scores across and within each of these categories. Although the GHSI measures readiness for a pandemic, very few countries were able to mitigate the spread of COVID-19 infection, and many countries failed miserably to prepare for or control the pandemic.[98] Given that the GHSI was prepared just months before the COVID-19 pandemic with the explicit purpose of assessing preparedness for a global pandemic, and ostensibly provides objective, numerical quantification of the degree to which every country is able to implement the international health regulations, it offers an excellent opportunity to assess how well the fundamental principles enshrined in the IHR actually prepare countries for a pandemic response. The findings from this study can be used to better prepare ourselves for other possible pandemics in the future.

This study will analyse the relationship between GHSI scores and incidence rate, mortality rate and vaccination rate during the COVID-19 pandemic. I aim to assess if countries with high GHSI scores did well in controlling the spread of the infection and mitigating the outbreak.
I also conduct a case study comparing the pandemic response in Japan and the USA with the goal of seeing whether pandemic response is primarily determined by objective elements of health system preparedness, or by the specific policies implemented during the pandemic, consistent with WHO best practice.

3.2 Methods

GHSI scores for 2019 were obtained from the publicly available data from the GHSI website. Data on COVID-19 cases, deaths and vaccination were obtained from the WHO coronavirus dashboard from 1st January to 31st December 2020.[43] For calculating rates, population data were obtained from the World Population Prospects.[99] Data on life expectancy, socio-developmental index (SDI), Universal Health Coverage (UHC) and total fertility rate (TFR) were obtained from the Global Health Data Exchange[97,100] and data on vaccine coverage were obtained from Our World in Data database.[101] All the data were merged by country name. GHSI scores were categorised as 'Low' for scores <= 60 and 'High' for scores > 60. I assessed the COVID-19 related case rate, death rate, vaccination rate and time taken for 64% vaccination coverage separately against GHSI scores for each country. Case rates are the total number of confirmed cases of COVID-19 per 1000 population, death rates are the total number of deaths attributed to COVID-19 per 1000 population and vaccination rates are the total number of people who received at least two doses of COVID-19 vaccination. The vaccination threshold was calculated to be 64% assuming the value of R_0 to be 2.7. The duration to achieve 64% vaccination coverage is the duration in months between 1st January 2021 and the date when 64% coverage was achieved. The calculated duration was then divided into two categories – duration of less than one year, or one year and more.

3.2.1 Statistical analysis

Poisson regression analysis with population offset was used to assess the association of GHSI scores separately with total cases, total deaths and total number of vaccinations. Poisson

regression analysis with population offset was used to estimate fitted lines in graphs depicting the relationship of GHSI scores with case rates and death rates. The fitted lines for vaccination rates were estimated using linear regression of natural log of vaccination proportion. A logistic regression analysis was used assessing the association between GHSI score and 64% vaccination coverage duration categorised into two groups. Linear regression analysis was used to estimate fitted lines for time taken to achieve 64% vaccination coverage by GHSI scores. Kaplan-Meier method was used for survival analysis and the cox-proportional hazard model confirmed the findings after adjusting for additional variables. For survival analysis, the GHSI scores were categorised as low for scores lower than or equal to 60 and high for scores above 60. All the analyses were adjusted for SDI index, UHC coverage, life expectancy and TFR of the country.

3.2.2 Case study

The epidemic curve of cases and deaths was examined separately for Japan and USA and the 7-day moving average was calculated. The time-varying reproduction number was estimated to analyse the spread of COVID-19 in USA and Japan during the early phase of the outbreak using the R package *EpiEstim*.[102] The assumed mean and standard deviation of the gamma distributed serial intervals are 7.8 days and 5.2 days respectively.[103]

3.3 Results

3.3.1 Comparison of GHSI scores and COVID-19 related outcome

Figure 3.2 is a scatterplot of GHSI score and case rate per 1000 for different countries. The blue and green dots represent UK and USA respectively. These countries have the top two highest GHSI scores. The red and the black dot represent Japan and New Zealand. These have low GHSI scores of around 55 to 60. Results show that as the GHSI scores increased, the number of COVID-19 case rates increased as well.

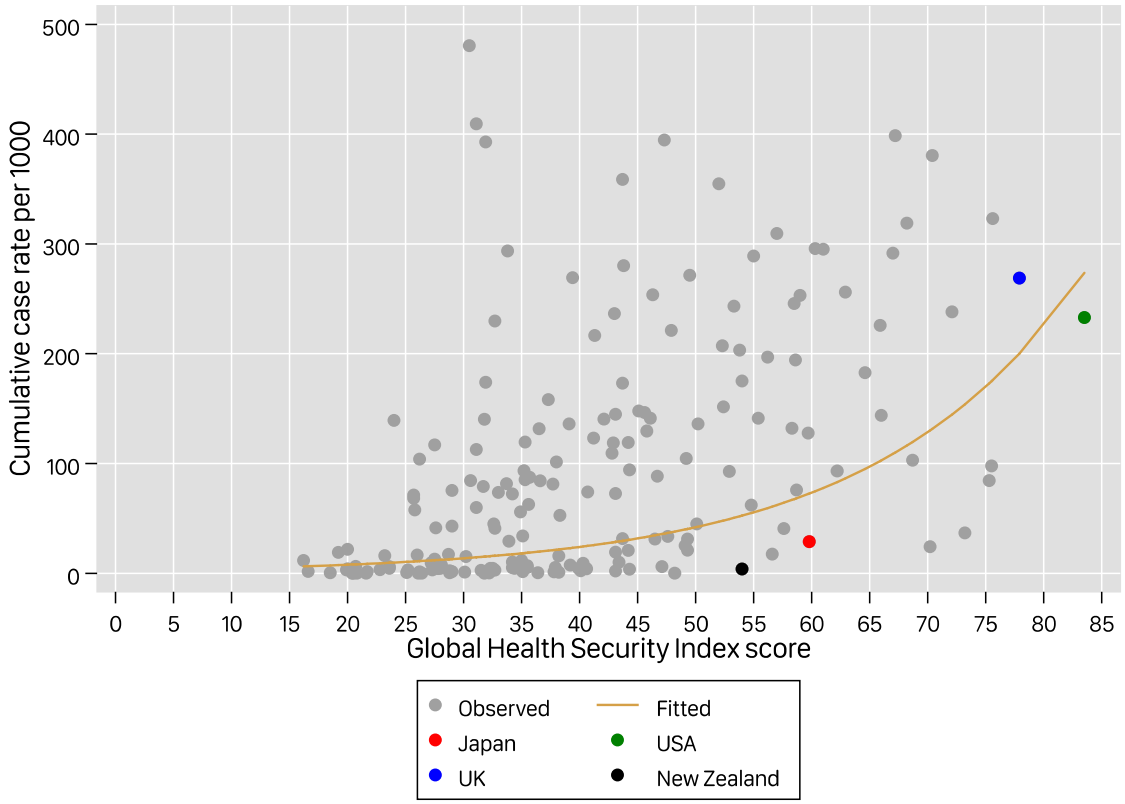


Figure 3.2. Cumulative case rate of COVID-19 by GHSI score for different countries

Figure 3.3 is a scatterplot of GHSI score and death rate per 1000 for different countries. Results show that as the GHSI scores increased, the COVID-19 death rate increased as well.

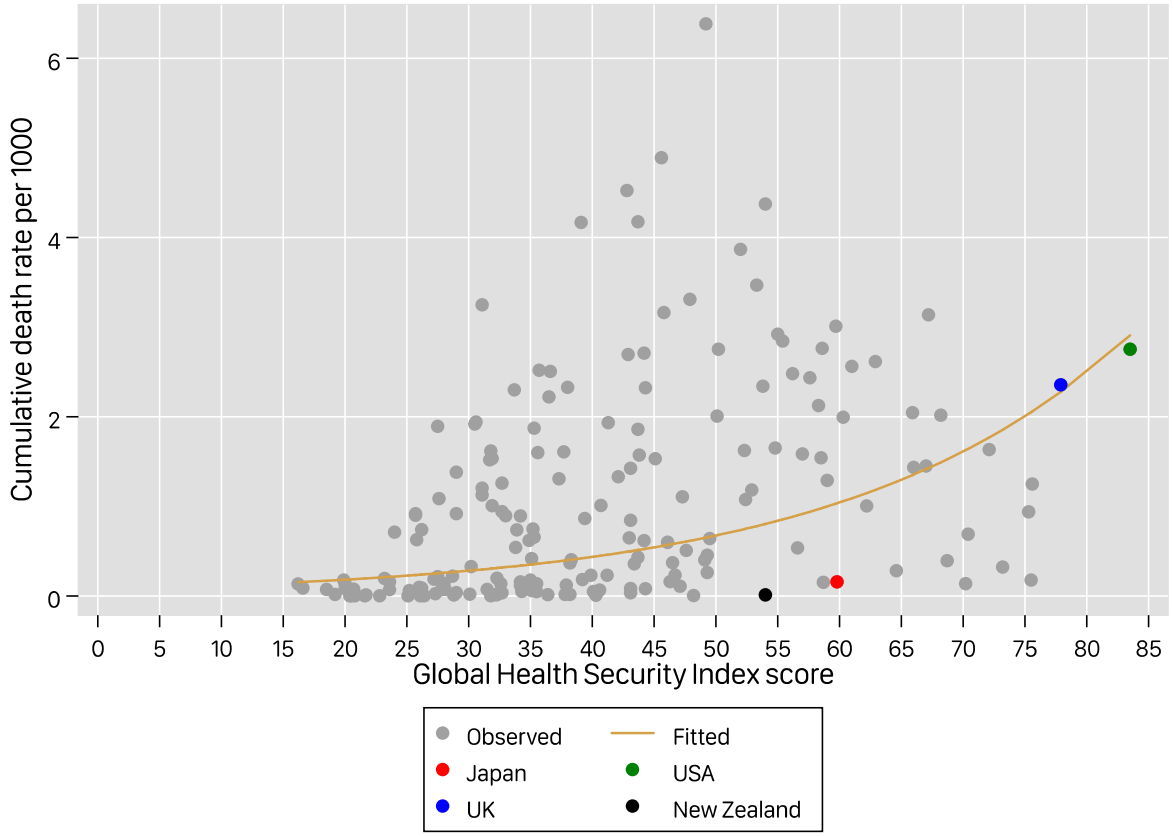


Figure 3.3. Cumulative death rate of COVID-19 by GHSI score for different countries

Figure 3.4 is a scatterplot of GHSI scores and vaccination rates for different countries. Result shows that as the GHSI scores increased, the vaccination rate of covid-19 increased as well.

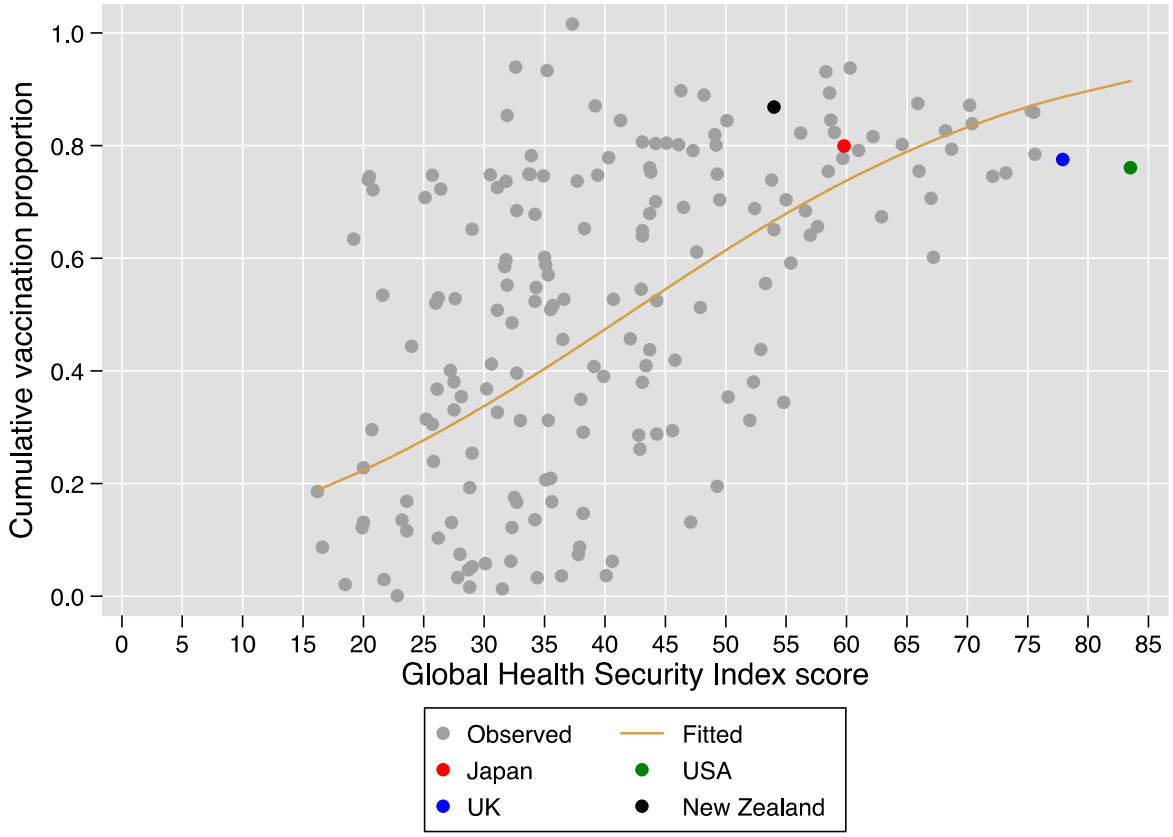


Figure 3.4. Cumulative vaccine rate of COVID-19 by GHSI score for different countries

Figure 3.5 is a scatterplot of GHSI score, and time taken for 64% of vaccination coverage for different countries. Results show that as the GHSI scores increased, the time taken to fully vaccinate 64% of the total population decreased.

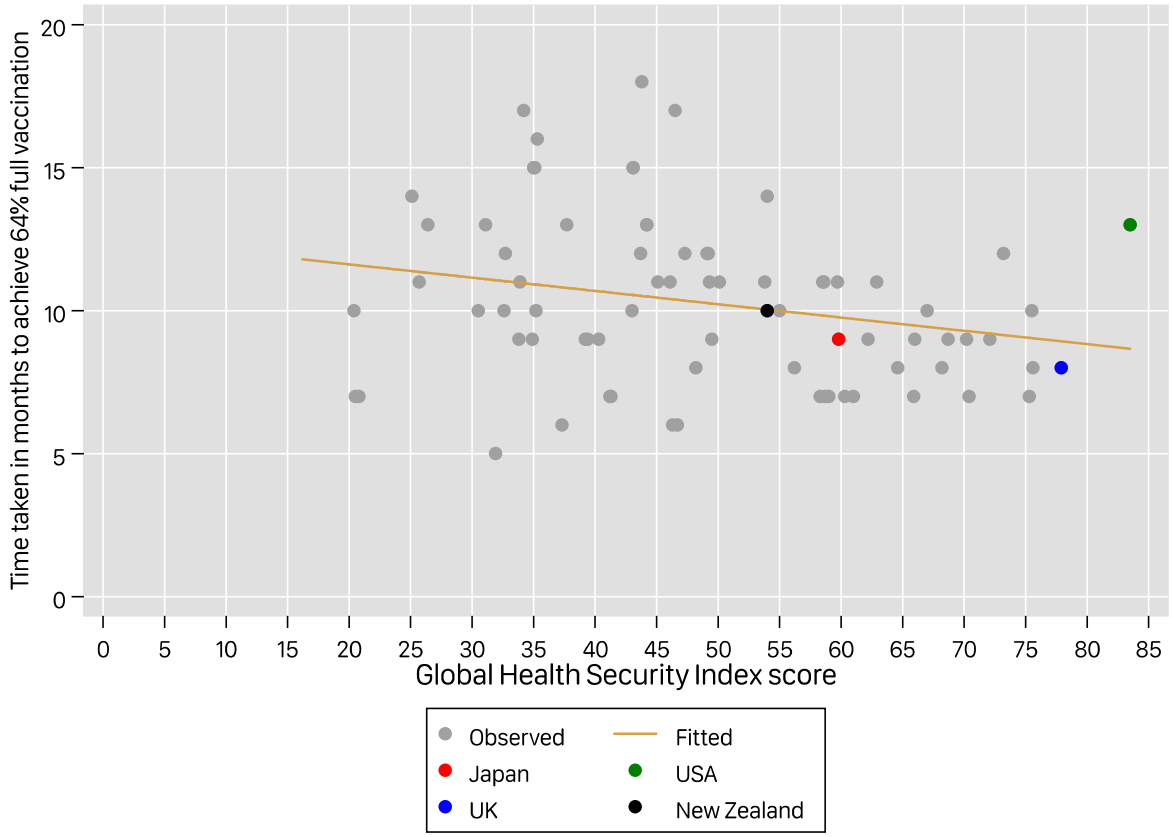


Figure 3.5. Vaccination coverage duration of COVID-19 by GHSI score for different countries

Table 3.1 shows the result of the Poisson regression analysis. The outcome here is COVID-19 cases. With a one-point increase in GHSI score, the COVID-19 case rate increased by 2% adjusting for covariates.

Table 3.1. Poisson regression analysis: Case rate of Covid-19

Variable	Incident rate ratio	Confidence Interval
Score	1.02	(1.02–1.02)
SDI	1.05	(1.05–1.05)
Life expectancy	0.94	(0.94–0.94)
Total Fertility Rate	1.05	(1.05–1.05)
Universal Health Coverage	1.02	(1.02–1.02)

Table 3.2 shows the result of the Poisson regression analysis for the death rate. With every one unit increase in GHSI score, the death rate increased by 3% adjusting for covariates.

Table 3.2. Poisson regression analysis: Death rate of Covid-19

Variable	Incident rate ratio	Confidence Interval
Score	1.03	(1.02–1.03)
SDI	1.03	(1.03–1.03)
Life expectancy	0.92	(0.92–0.92)
Total Fertility Rate	0.91	(0.91–0.91)
Universal Health Coverage	1.02	(1.02–1.02)

Table 3.3 shows the result of Poisson regression analysis of vaccination rate, and shows that with one point increase in GHSI score, the vaccination rate increases by 1% adjusting for covariates.

Table 3.3. Poisson regression analysis: Vaccine rate of Covid-19

Variable	Incident rate ratio	Confidence Interval
Score	1.01	(1.01–1.01)
SDI	0.99	(0.99–0.99)
Life expectancy	1.04	(1.04–1.04)
Total Fertility Rate	0.64	(0.64–0.64)
Universal Health Coverage	0.99	(0.99–0.99)

Table 3.4 shows the result of the Logistic regression analysis to achieve 64% vaccination coverage in less than one year or more. There is no statistically significant association between GHSI score and duration of vaccination coverage.

Table 3.4. Logistic regression analysis: Vaccine coverage duration of Covid-19

Variable	Odds Ratio	Confidence Interval
Score	1.02	(0.99–1.06)
SDI	1.03	(0.97–1.11)
Life expectancy	1.29	(0.99–1.68)
Total Fertility Rate	1.28	(0.50–3.26)
Universal Health Coverage	1.01	(0.93–1.09)

Table 3.5 and **Figure** 3.6 show the results of survival analysis of time to achieve 64% vaccination coverage. With one unit increase in GHSI scores, the hazard ratio for 64% vaccination coverage increases by 1%. The results are, however, not significant.

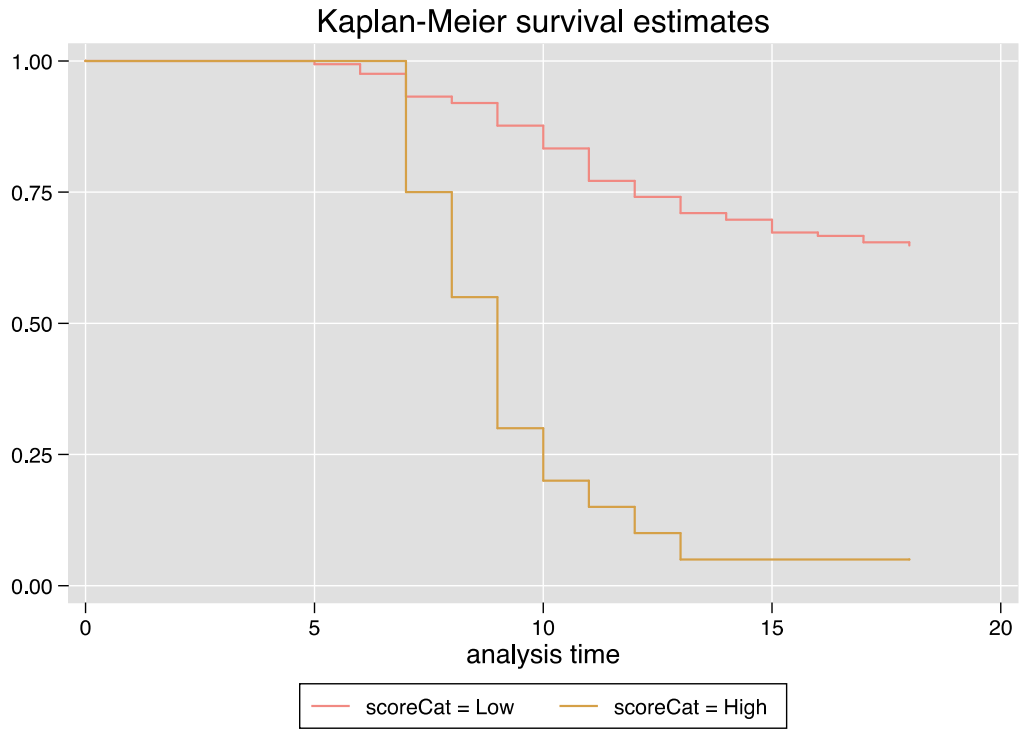


Figure 3.6. Kaplan-Meier curves for time taken for 64% of vaccine coverage separately by GHSI scores

Table 3.5 Cox-proportional hazards regression: Time taken to achieve 64% of vaccination coverage

Variable	Hazards Ratio	Confidence Interval
Score	1.01	(0.99–1.03)
SDI	0.97	(0.94–1.02)
Life expectancy	1.15	(0.99–1.32)
Total Fertility Rate	0.76	(0.45–1.30)
Universal Health Coverage	1.03	(0.99–1.08)

3.3.2 Case study of Japan and the USA

Both Japan and the USA are well-developed high-income countries, and the first case of COVID-19 was detected in these countries at around the same time. However, the GHSI ranks the USA as the most prepared country with the highest GHSI score of 83.5, while Japan is ranked as the 21st best prepared, with a score of 59.8. In these countries with such contrasting scores, this case study assesses if the USA did well in controlling the spread of the infection and mitigating the outbreak compared to Japan. To date, 17% of the Japanese population has been infected with COVID-19 while around one-third (30%) of the US population has been infected. The total number of deaths in Japan is around 45 thousand and in the USA it is over a million.

Control measures applied in Japan and USA

Both these countries have introduced various measures for controlling the spread of the outbreak. An anti-coronavirus task force was established in both countries during the early phase of the pandemic. Healthcare funding was increased, and the medical service system was reinforced. Various states and prefectures introduced travel restrictions, state of emergency and school closures at various time points. Mask mandates were divisive during the early phase of the pandemic in the USA. While the Trump led government did not seem supportive of the mask mandate, President Biden executed vigorous protocols mandating the use of face masks on federal properties. While Japan recommended the use of face masks, it never made it mandatory.[104] However, mask compliance in Japan was higher compared to the USA.[105,106] In both the countries, people were encouraged to maintain hand hygiene and other basic hygiene etiquette. People affected with coronavirus in both countries have been provided financial support[107,108] encouraging them to comply with the travel restriction measures and were encouraged to implement telework to the extent possible. Vaccination was started in both countries in late 2020. Both countries have implemented various strategies to mitigate the spread of infection.

Figure 3.7 shows the epidemic curve of cases in Japan and the USA from the beginning of 2020 to December 2020. It also depicts various major events and preventive steps at different time points. There were more than three waves of infection in both countries. In both countries, the daily cases reached a peak around December 2020. The graph shows that the number of cases increased in the USA after various major events, such as the Black Lives Matter protest in June 2020, and the presidential election in November 2020. Similarly, in Japan cases increased after the domestic travel campaign in July 2020, and around Christmas and new year of 2020/21.

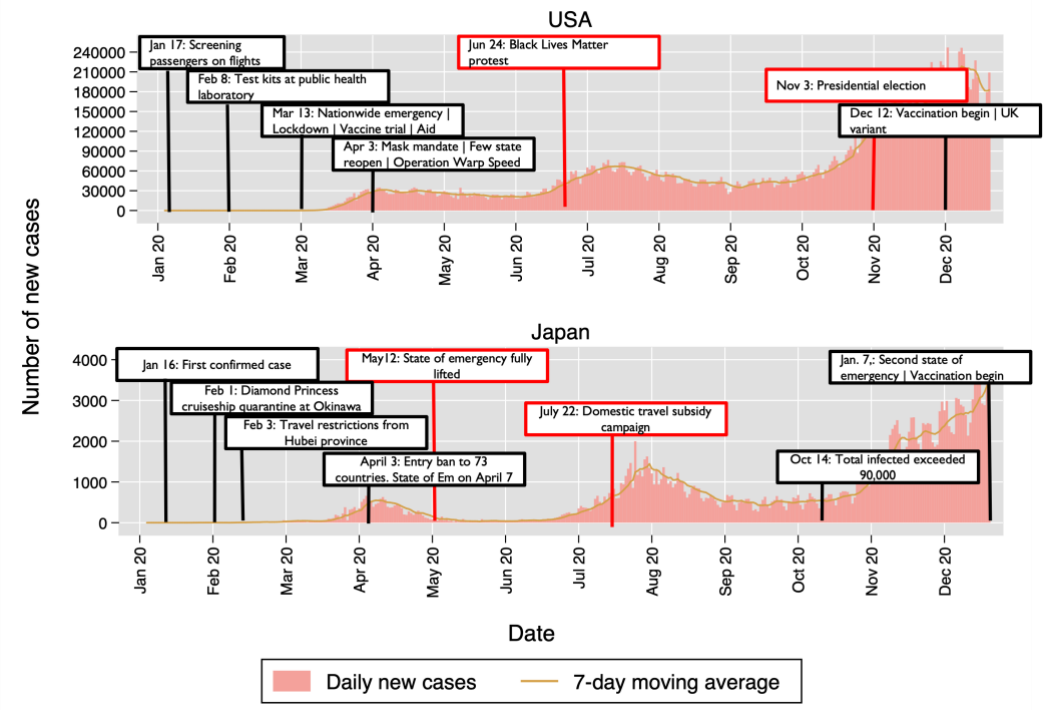


Figure 3.7. Epidemic curve of number of daily new cases and 7-day moving average. Note: The scales of the two graphs are different.

Differences in governance of these two countries led to different trajectories of COVID-19 cases and deaths in these two countries. The Japanese government adopted significant

responsibility for leading the country on important pandemic-related issues and requested voluntary closure of schools throughout the country in March 2020, initiated social distancing campaigns including a search for COVID-19 clusters and declared a national state of emergency in April.[109,110] Some of these measures may have contributed to the containment of the COVID-19 cases and deaths, leading the government to lift the state of emergency in early May. The policies in Japan absolutely contrast with that of the USA. Donald Trump on various occasions seemed to not be concerned of the situation and ignored or did not understand the urgency of the situation.[111] The major policy decision and resource allocation was primarily at state level, with significant variation between states. The USA was slow to act and educate the public to gain their trust on the importance of vaccination against COVID-19.[112] The centralized and coordinated response of the Japanese political leaders led to a good control over COVID-19, while the decentralised and fragmented response in the USA led to confusion and conflict, thus failing to mitigate the spread of COVID-19.

Figure 3.8 shows the epidemic curve of the number of daily COVID-19 deaths in the USA and Japan until 31st December 2020. The total number of daily deaths was as high as around 100 in Japan while in the USA it reached about 3400 deaths in a day.

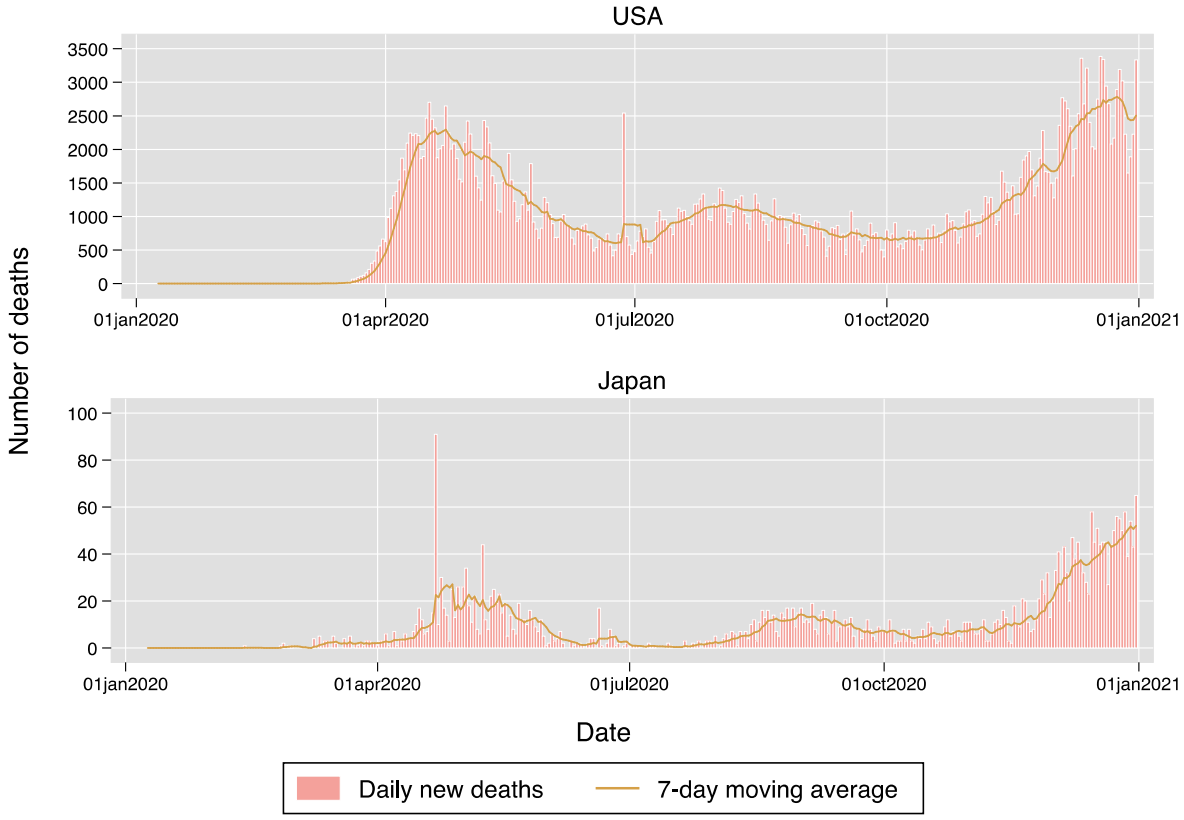


Figure 3.8. Epidemic curve of number of daily new deaths and 7-day moving average

Figure 3.9 shows the time-dependent reproduction numbers from the beginning of the infection until 31st December 2020. While the reproduction number was around 2-4 on average in Japan. During the first four months, the effective reproduction number was as high as six.

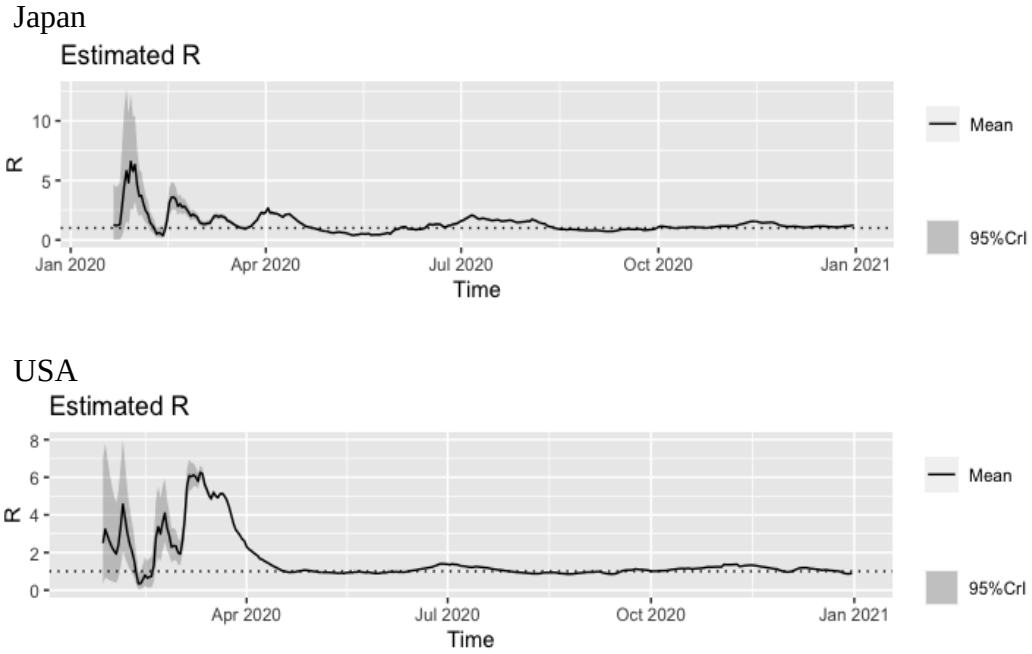


Figure 3.9. Time-dependent reproduction number before 31st December 2020

3.4 Discussion

Accurate pandemic preparedness metrics are essential for containing disease outbreaks. Despite this, GHSI indicators do not seem to be well correlated with the capacity of nations to prevent and combat epidemics. The countries with the highest GHSI scores are most impacted by COVID-19 in terms of total number of cases and deaths per million. The GHSI failed to predict COVID-19 cases and mortality in the first year of the pandemic. This study shows that

the GHSI indices could not accurately predict the case detection and mortality outcome in the early phase of the pandemic.

As the GHSI scores increased, COVID-19 cases and death rates increased as well. This shows that capability of pandemic preparedness reported in policy documents is not a reliable measure of the effectiveness of these policies in action. The effectiveness of long-term investments in health infrastructure is determined in a real outbreak, and the case study of Japan and the USA shows that the key determinants of the response are not these measures of health infrastructure investment or readiness, but the policies implemented at the time of the outbreak. COVID-19 performance indicators differed from GHSI rankings, suggesting that some countries may be underestimated and that individual national policy decisions and willingness to follow WHO recommendations on testing and isolation are more important than numerical measures of health system abundance such as how many hospital beds they have. In terms of vaccination, however, the countries with higher scores are more likely to quickly achieve desired vaccination coverage. In light of lessons learned from COVID-19, factors such as response time should be added to GHSI scoring tools in order to assess countries' true preparedness and vulnerability.[113]

Comprehensive approaches must be coordinated by governments and international organizations, to change the COVID-19 pandemic trajectory. Health infrastructure investments can mitigate infection risks within countries and reduce pandemic risks overall.[114] A well-structured capacity, however, will not suffice if it is not activated for political or socioeconomic

reasons. For mitigating public health emergencies, the major focus has been on resources and health systems, and not enough on political preparedness. The results suggest that preparedness is less important than following basic public health principles for the control of infectious diseases. Additionally, difficult public health measures require support from the community to be effectively implemented. Factors such as the universal health coverage of countries and the presence of a strong political leadership in times of crises are not sufficiently taken into account in the GHSI score rankings. Instead of adopting personal or collective responsibility, developed countries with high GHSI scores often resort to institutions with varied degrees of authority and responsibility to deal with health emergencies. GHSI indicators and weightings should be revised in the future based on lessons learned from COVID-19. Continual re-evaluation of the GHSI, including taking leadership factors into consideration, is essential, given the success of countries such as China, Vietnam, New Zealand, and South Korea. Further, future GHSI reports should take into account the country's response to past health threats.

CHAPTER 4: Discussion and conclusion

I conducted a systematic review and meta-analysis of studies published in the early phase of the COVID-19 pandemic assessing the estimated pooled R_0 of the disease. The findings from various studies were gathered and combined to provide a synthesis of estimates addressing the heterogeneity among the included studies. When no deliberate intervention was taken for COVID-19, I estimated the R_0 to be 2.66 with a 95% confidence interval (2.41–2.94). This means that on average, a COVID-19-infected person transmits the infection to around two to three susceptible people. Additionally, I conducted some analyses assessing the pandemic response of various countries to mitigate the COVID-19 pandemic. I assessed the COVID-19 cases, deaths, and vaccination status of countries with their pandemic preparedness GHSI scores. Results show that GHSI indicators do not seem to be well correlated with countries' ability to prevent and respond to epidemics given the higher number of COVID-19-related cases and deaths in countries with higher GHSI scores.

I screened 15714 articles related to COVID-19 published between 1st December 2019 and 30th September 2020 and included 151 studies. A total of 81 studies were included in the meta-analysis. Studies included in the meta-analysis reported R_0 estimates ranging from 0.4 to 12.58. We found a high heterogeneity of estimates indicating a vulnerability of R_0 estimates to choices of methods, data source, location, and timing. Sub-group analysis revealed that the pooled estimate of R_0 using data collected up to January 2020 was relatively higher ($R_0 = 3.34$) compared to the estimates from subsequent months and was declining until March when

more data were available. Additionally, the small study effect in the included studies indicated that the studies with relatively large R_0 were more likely to be published. The bias-adjusted estimate showed the pooled R_0 to be 1.82.

The results of the analysis of GHSI scores for different countries affected by COVID-19 showed that the countries most affected by COVID-19 in terms of deaths per million are those with the highest GHSI scores. COVID-19 cases and mortality were not well predicted by the GHSI scores in the first year of the pandemic. Countries like the UK and the USA had the highest GHSI scores yet failed to contain the COVID-19 cases or deaths. On the contrary, Japan and New Zealand had lower GHSI scores but still managed to control the spread of COVID-19 better than the UK and the USA. However, results show that vaccination rate increased with GHSI scores. The result from survival analysis showed that countries with higher GHSI scores too less time to achieve 64% vaccination coverage. Even in that case, Japan and New Zealand had higher cumulative vaccination proportion than the UK and USA. The case study of Japan and the USA showed that difference in policy measures during the early phase of the pandemic led to different trajectories of COVID-19 in these two countries. Results show that health preparedness indices in the GHSI were not predictive of cases detected and mortality outcomes until December 2020.

Despite its simple appearance, R_0's definition, calculation, and interpretation are complicated when it comes to assessing infectious disease transmission dynamics. It is evident that some misconceptions about R_0 have arisen as a result of its extensive use in the scientific literature.[93]

There are several challenges associated with estimating the basic reproductive number from available data, which has significant implications for interpreting the pandemic's course. Various biological, socio-behavioural, and environmental factors affect R_0 estimation.[93] Resulting reproduction numbers from various mathematical models may be biased in case the underlying assumptions are not met, such as in case of misspecification of general interval.[115] Due to the ease with which R_0 can be misrepresented, misinterpreted, and misused, this basic metric must be estimated, reported, and applied with great caution.[93] To estimate R_0 accurately and timely, most epidemiological data require statistical adjustments as the data itself may not always be ideal. Additionally, it is essential to understand the model inputs, structures, and interactions in order to interpret R_0 estimates derived from different models without distorting the metric's true meaning and value. Researchers and practitioners must take caution when applying and discussing R_0, since its value and relevancy depend on its correct use and interpretation.

When a new disease emerges, important decisions need to be made in a short time in the absence of quality evidence and amidst uncertainties. With the prevailing uncertainties, no single model can predict the disease or the effectiveness of intervention strategies in place. Similarly, one model may not necessarily be superior to another, but rather just provide a different perspective. The different model assumptions and simplification process in modelling make it difficult to assess the merits and limitations of a disease model. During the early stage, policymakers try to contain the disease through quarantine and isolation of infected cases. If this turns out to be unsuccessful, they face challenges to formulate effective intervention

strategies such as gathering and travel restrictions. However, there is a huge economic burden to society associated with such mass restrictions. Various epidemiological, infectious disease, and health policy analysis models for a long time are being used to guide policy decisions. It is effective for projecting short-term outcomes, but uncertainties compound as epidemic trajectories are predicted over a longer period. Objective measures of preparedness like the GHSI were just as incapable of predicting spread as objective measures of virus infectivity like, R_0. Decision rules from decision theorists provide theoretical constructs to account for uncertainty during decision-making process. Health protection must be balanced with preventing economic effects on society. Amidst the uncertainty, policymakers should continue to communicate their strategies and keep the public informed.

4.1 Policy recommendations about methods for assessing pandemic risk and pandemic preparedness

The issue of global health security is not simply one related to just health. Crises such as those caused by Ebola, Zika, or COVID-19 have the power to destroy economies and halt national progress. Globally, the COVID-19 pandemic is expected to cost $13.8 trillion by 2024. [116] As a result of this kind of economic devastation, the effects are more widespread than ever before. [117] All countries should be prepared for the next pandemic, and so, they should have a strong political engagement to enable multi-sectoral coordination. It is imperative to identify and make accessible the funding necessary to build a multi-resource capacity and implement pandemic preparedness and response activities. The establishment of an effective communication channel between sectors and stakeholders, as well as the creation of a pandemic

plan providing a framework for cross-border and national planning, is crucial. As part of planning activities, both national and subnational exercises and simulations should be conducted. In order to prevent diseases from spreading internationally, health systems in all countries should cooperate to detect and contain disease outbreaks. It is the responsibility of health systems in all countries to collaboratively work towards identifying and containing public health outbreaks before it spreads internationally. Only about one-third of countries around the world are currently capable of assessing, detecting, and responding to public health emergencies, despite a broader global agreement on IHR (2005).[1,118] Particularly, low- and middle-income are at risk due to these gaps in pandemic preparedness.

PHEICs are beneficial for funding and mobilization, but they also have a downside when it comes to their economic impact. There have been recent debates raising questions about the value of PHEIC declarations. It is necessary to review the 2005 regulations and the declaration in general in light of the controversy. In accordance with the WHO's emergency committee's recommendations, a new alert-level system needs to be developed.[119] It would allow the WHO to take quicker action when a PHEIC declaration is not required. Additionally, there is a need to standardize the emergency committee's reviews to specifically address whether an outbreak meets each core PHEIC criteria of IHR. Also, it is necessary to formulate guidelines for emergency committee members that allow them to interpret IHR criteria effectively. Disease outbreak response capabilities of the IHR and WHO will be strengthened by incorporating these recommendations in future emergency committee deliberations and PHEIC decision-making processes.

4.2 Conclusion

Different countries faced various challenges in the decision-making processes during the COVID-19 pandemic. Reliable information on effectiveness of disease containing measures and its impact on the population is essential for policymakers. Many countries have relied on expert opinions and result of modelling studies for making policy decisions. However, the prevailing uncertainty during the early spread of the disease outbreak imposes hindrance to formulate grounded predictions leading to misinterpretations and suboptimal decisions.

Despite our efforts, we still have a long way to go before we can fully understand the dynamics of emerging infectious diseases. Pandemic risk can vary greatly, depending on the quality, accuracy and timeliness of the data, and the assumptions made. A pandemic decision cannot be made with certainty and precision with infectious disease models and composite emergent indicators such as R_0, although it provides some basic information on the course of the pandemic. A clear and simple framework for pandemic response should be used instead of these measures until the epidemiological community understands how to measure and apply them. To be able to fully prepare ourselves for the next pandemic, there is a need to have a clearer understanding of and consensus on how to use infectious disease models for pandemic response. In turn, the mechanism by which scientific evidence is synthesized and incorporated into national and global decisions needs to be made clearer, more objective, and more comparable between nations. Until the global health and infectious disease community have a proper understanding of the governance measures required to properly incorporate scientific information into decision-making, the IHR will be of limited effectiveness, WHO decisions

will be subject to protest, distrust and delay, and there will be no global understanding of what is and is not a global health emergency. The world has failed to properly respond to COVID-19, and until more progress is made on these aspects of the interaction of science and decision-making, is vulnerable to the next emerging disease epidemic.

References

1. World Health Organization. International Health Regulations (2005) Third Edition. WHO Press. Published 2016. Accessed October 31, 2022. https://www.who.int/publications/i/item/9789241580496
2. WHO | IHR Procedures concerning public health emergencies of international concern (PHEIC). *WHO*. Published online 2017.
3. World Health Organization. Emergencies: International health regulations and emergency committees. Published December 19, 2019. Accessed October 26, 2022. https://www.who.int/news-room/questions-and-answers/item/emergencies-international-health-regulations-and-emergency-committees
4. UN World Tourism Organization. Tourism and COVID-19 – unprecedented economic impacts . UNWTO. Accessed October 31, 2022. https://www.unwto.org/tourism-and-covid-19-unprecedented-economic-impacts
5. Abe T. The Japanese Economy and the COVID-19 Pandemic. *Invest Econ*. 2021;80(316):56-68. doi:10.22201/FE.01851667P.2021.316.78431
6. Kanitha Kongrukgreatiyos. COVID-19 Crisis Lowers Thailand's Growth, Continued Support for the Poor Needed. The World Bank. Published July 15, 2021. Accessed November 15, 2022. https://www.worldbank.org/en/news/press-release/2021/07/15/covid-19-crisis-lowers-thailand-s-growth-continued-support-for-the-poor-needed

7. OECD. *OECD Economic Surveys-Greece 2020: The COVID-19 Shock Abruptly Interrupts Greece's Recovery*. OECD; 2020. doi:10.1787/B04B25DE-EN

8. Dominika Spyratou. *Greece Country Report: Impact of COVID-19 Crisis on Labour Market Integration | European Website on Integration*.; 2020. Accessed November 15, 2022. https://ec.europa.eu/migrant-integration/library-document/greece-country-report-impact-covid-19-crisis-labour-market-integration_en

9. Dyomina Y v., Mazitova MG. The COVID-19 pandemic and its impact on the Japanese economy. *Japanese Studies in Russia*. 2021;(3):57-75. doi:10.24412/2500-2872-2021-3-57-75

10. Vette K, Bareja C, Clark R, Lal A. Establishing thresholds and parameters for pandemic influenza severity assessment, Australia. *Bull World Health Organ*. 2018;96(8):558-567. doi:10.2471/BLT.18.211508

11. World Health Organization. Annex 2 of the International Health Regulations (2005). WHO Press. Published 2017. https://www.who.int/publications/m/item/annex-2-of-the-international-health-regulations-(2005)

12. Davies SE, Kamradt-Scott A, Rushton S. *Disease Diplomacy : International Norms and Global Health Security*. Johns Hopkins University Press; 2015. Accessed October 31, 2022. https://www.researchgate.net/publication/272087825_Disease_Diplomacy_International_norms_and_global_health_security

13. Hoffman SJ, Silverberg SL. Delays in Global Disease Outbreak Responses: Lessons from H1N1, Ebola, and Zika. *Am J Public Health*. 2018;108(3):329. doi:10.2105/AJPH.2017.304245

14. World Health Organization Europe. WHO Director-General declares H1N1 pandemic over. Published online August 10, 2010.

15. Abeysinghe S. Action and Inaction: Comparing the World Health Organization's Response to H1N1 and Ebola. *University of Edinburgh*. Published online 2015. Accessed November 15, 2022. https://www.ippapublicpolicy.org/file/paper/1433940917.pdf

16. Kamradt-Scott A. What Went Wrong? The World Health Organization from Swine Flu to Ebola. *Political Mistakes and Policy Failures in International Relations*. Published online February 16, 2017:215. doi:10.1007/978-3-319-68173-3_9

17. Hoffman SJ, Silverberg SL. Delays in Global Disease Outbreak Responses: Lessons from H1N1, Ebola, and Zika. *Am J Public Health*. 2018;108(3):333. doi:10.2105/AJPH.2017.304245

18. Pan American Health Organization. Polio declared public health emergency of international concern under International Health Regulations. World Health Organization. Published May 5, 2014. Accessed October 26, 2022. https://www3.paho.org/hq/index.php?option=com_content&view=article&id=9524:2014-polio-declared-public-health-emergency-international-concern&Itemid=0&lang=en#gsc.tab=0

19. Wilder-Smith A, Osman S. Public health emergencies of international concern: a historic overview. *J Travel Med*. 2020;27(8):taaaa227. doi:10.1093/JTM/TAAA227

20. World Health Organization. Statement of the Thirty-first Polio IHR Emergency Committee. Published March 11, 2022. Accessed October 26, 2022. https://www.who.int/news/item/11-03-2022-statement-of-the-thirty-first-polio-ihr-emergency-committee

21. World Health Organization. Statement on the 1st meeting of the IHR Emergency Committee on the 2014 Ebola outbreak in West Africa. Published August 8, 2014. Accessed October 26, 2022. https://www.who.int/news/item/08-08-2014-statement-on-the-1st-meeting-of-the-ihr-emergency-committee-on-the-2014-ebola-outbreak-in-west-africa

22. Gostin LO, Tomori O, Wibulpolprasert S, et al. Toward a Common Secure Future: Four Global Commissions in the Wake of Ebola. *PLoS Med*. 2016;13(5):e1002042. doi:10.1371/JOURNAL.PMED.1002042

23. Honigsbaum M. Between Securitisation and Neglect: Managing Ebola at the Borders of Global Health. *Med Hist*. 2017;61(2):270-294. doi:10.1017/MDH.2017.6

24. Herten-Crabb A, Moon S. *Outbreak-Related Travel Restrictions: Health & Economic Consequences*, *Briefing Note*. The Graduate Institute of International and Development Studies, Global Health Centre; 2017. Accessed October 29, 2022. https://repository.graduateinstitute.ch/record/295277

25. United Nations Economic Commission for Africa. Socio-economic impacts of Ebola on Africa, Addis Ababa. Published online 2015. Accessed October 29, 2022.

https://repository.uneca.org/bitstream/handle/10855/22723/b11540588.pdf?sequence=1

26. Moon S, Sridhar D, Pate MA, et al. Will Ebola change the game? Ten essential reforms before the next pandemic. The report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola. *Lancet*. 2015;386(10009):2204-2221. doi:10.1016/S0140-6736(15)00946-0

27. Pan American Health Organization. Timeline of Emergence of Zika virus in the Americas. Accessed October 26, 2022. https://www3.paho.org/hq/index.php?option=com_content&view=article&id=11959:timeline-of-emergence-of-zika-virus-in-the-americas&Itemid=0&lang=en#gsc.tab=0

28. World Health Organization. WHO Director-General summarizes the outcome of the Emergency Committee regarding clusters of microcephaly and Guillain-Barré syndrome. Published February 1, 2016. Accessed October 26, 2022. https://www.who.int/en/news-room/detail/01-02-2016-who-director-general-summarizes-the-outcome-of-the-emergency-committee-regarding-clusters-of-microcephaly-and-guillain-barr%c3%a9-syndrome

29. World Health Organization. Zika virus, microcephaly, and Guillain-Barre Syndrome situation report . Published April 7, 2016. Accessed October 26, 2022. https://apps.who.int/iris/bitstream/handle/10665/204961/zikasitrep_7Apr2016_eng.pdf?sequence=1

30. World Health Organization. Fifth meeting of the Emergency Committee under the International Health Regulations (2005) regarding microcephaly, other neurological

disorders and Zika virus. Published November 18, 2016. Accessed October 26, 2022. https://www.who.int/en/news-room/detail/18-11-2016-fifth-meeting-of-the-emergency-committee-under-the-international-health-regulations-(2005)-regarding-microcephaly-other-neurological-disorders-and-zika-virus

31. World Health Organization. Ebola Virus Disease: Democratic Republic of Congo-External Situation Report 01. Published online August 7, 2018.

32. Center for Infectious Disease Research and Policy. Ebola case counts spike again in DRC. University of Minnesota. Published June 17, 2019. Accessed October 26, 2022. https://www.cidrap.umn.edu/news-perspective/2019/06/ebola-case-counts-spike-again-drc

33. World Health Organization. Ebola outbreak in the Democratic Republic of the Congo declared a Public Health Emergency of International Concern. Published July 17, 2019. Accessed October 26, 2022. https://www.who.int/news-room/detail/17-07-2019-ebola-outbreak-in-the-democratic-republic-of-the-congo-declared-a-public-health-emergency-of-international-concern

34. Tomori O, Durrheim D, Gostin L, Kavanagh MM. Ebola in North Kivu, DR Congo - is it an undeclared public health emergency of international concern (PHEIC)? *Travel Med Infect Dis*. 2019;29:1-3. doi:10.1016/J.TMAID.2019.05.006

35. Giesecke J, Bedford J, Enria D, et al. The truth about PHEICs. *The Lancet*. 2019;6736(19):31566-1. doi:10.1016/S0140-6736(19)31566-1

36. The Lancet. The politics of PHEIC. *The Lancet*. 2019;393(10190):2470. doi:10.1016/S0140-6736(19)31406-0

37. World Health Organization. Final Statement on the 8th meeting of the International Health Regulations (2005). Published June 26, 2020. Accessed October 26, 2022. https://www.who.int/news-room/detail/26-06-2020-final-statement-on-the-8th-meeting-of-the-international-health-regulations

38. Sharma A, Tiwari S, Deb MK, Marty JL. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. *Int J Antimicrob Agents*. 2020;56(2). doi:10.1016/j.ijantimicag.2020.106054 LK - http://xz9wr2yb6e.search.serialssolutions.com/?sid=EMBASE&issn=18727913&id=doi:10.1016%2Fj.ijantimicag.2020.106054&atitle=Severe+acute+respiratory+syndrome+coronavirus-2+%28SARS-CoV-2%29%3A+a+global+pandemic+and+treatment+strategies&stitle=Int.+J.+Antimicrob.+Agents&title=International+Journal+of+Antimicrobial+Agents&volume=56&issue=2&spage=&epage=&aulast=Sharma&aufirst=Atul&auinit=A.&aufull=Sharma+A.&coden=IAAGE&isbn=&pages=-&date=2020&auinit1=A&auinitm=

39. WHO Director-General's opening remarks at the media briefing on COVID-19 - 3 March 2020. World Health Organization. Published 2020. Accessed March 13, 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---3-march-2020

40. Sohrabi C, Alsafi Z, O'Neill N, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International Journal of Surgery*. 2020;76:71-76. doi:10.1016/j.ijsu.2020.02.034 LK - http://xz9wr2yb6e.search.serialssolutions.com/?sid=EMBASE&issn=17439159&id=d

oi:10.1016%2Fj.ijsu.2020.02.034&atitle=World+Health+Organization+declares+global+emergency%3A+A+review+of+the+2019+novel+coronavirus+%28COVID-19%29&stitle=Int.+J.+Surg.&title=International+Journal+of+Surgery&volume=76&issue=&spage=71&epage=76&aulast=Sohrabi&aufirst=Catrin&auinit=C.&aufull=Sohrabi+C.&coden=&isbn=&pages=71-76&date=2020&auinit1=C&auinitm=

41. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Published January 30, 2020. Accessed October 26, 2022. https://web.archive.org/web/20210815071616/https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-%282005%29-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-%282019-ncov%29

42. World Health Organization. Novel coronavirus (2019-nCoV): Situation report-10. Published online January 30, 2020.

43. World Health Organization. WHO Coronavirus (COVID-19) Dashboard . Published November 18, 2021. Accessed November 21, 2021. https://covid19.who.int/

44. Boyd M, Wilson N. Failures with COVID-19 at the international level must not be repeated in an era facing global catastrophic biological risks. *Aust N Z J Public Health*. 2021;45(2):184. doi:10.1111/1753-6405.13082

45. The Editorial Board. How WHO Lost Its Way . The Wall Street Journal. Published May 15, 2020. Accessed November 16, 2022. https://www.wsj.com/articles/how-who-lost-its-way-11589583282

46. Ilja Richard Pavone. The COVID-19 Pandemic, the Failure of the Binary PHEIC Declaration System, and the Need for Reform. Havard law. Published December 7, 2022. Accessed November 16, 2022. https://blog.petrieflom.law.harvard.edu/2022/01/07/the-covid-19-pandemic-the-failure-of-the-binary-pheic-declaration-system-and-the-need-for-reform/

47. Sachs JD, Karim SSA, Aknin L, et al. The Lancet Commission on lessons for the future from the COVID-19 pandemic. *Lancet*. 2022;400(10359):1224-1280. doi:10.1016/S0140-6736(22)01585-9

48. World Health Orgainzation. Multi-country monkeypox outbreak in non-endemic countries. Published May 21, 2022. Accessed October 26, 2022. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385

49. World Health Organization. Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox. Published July 23, 2022. Accessed October 26, 2022. https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox

50. World Health Organization. WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern. Published July 23, 2022. Accessed October 26, 2022. https://web.archive.org/web/20220725054644/https://www.who.int/europe/news/item/

23-07-2022-who-director-general-declares-the-ongoing-monkeypox-outbreak-a-public-health-event-of-international-concern

51. Jeremy Youde. The Monkeypox Outbreak and the WHO's Existential Crisis. Think Global Health. Published August 10, 2022. Accessed November 16, 2022. https://www.thinkglobalhealth.org/article/monkeypox-outbreak-and-whos-existential-crisis

52. Gonsalves GS, Mayer K, Beyrer C. Déjà vu All Over Again? Emergent Monkeypox, Delayed Responses, and Stigmatized Populations. *J Urban Health*. 2022;99(4):606. doi:10.1007/S11524-022-00671-1

53. Taylor L. Monkeypox: What's behind WHO's decision not to declare a public health emergency? *BMJ*. 2022;377:o1604. doi:10.1136/BMJ.O1604

54. Giesecke J, STAG-IH. The truth about PHEICs. *Lancet*. Published online 2019. doi:10.1016/S0140-6736(19)31566-1

55. Mark Eccleston-Turner. COVID-19 Symposium: The Declaration of a Public Health Emergency of International Concern in International Law - Opinio Juris. Opinio Juris. Published 2020. Accessed May 17, 2020. http://opiniojuris.org/2020/03/31/covid-19-symposium-the-declaration-of-a-public-health-emergency-of-international-concern-in-international-law/

56. Lucia Mullen. An Analysis of IHR Emergency Committees and PHEIC Designations — Outbreak Observatory. Johns Hopkins Center for Health Security. Published June 25, 2020. Accessed November 2, 2022.

https://www.outbreakobservatory.org/outbreakthursday-1/6/25/2020/an-analysis-of-ihr-emergency-committees-and-pheic-designations

57. Mullen L, Mullen L, Potter C, et al. An analysis of International Health Regulations Emergency Committees and Public Health Emergency of International Concern Designations. *BMJ Glob Health*. 2020;5(6):e002502. doi:10.1136/BMJGH-2020-002502

58. Hoffman SJ, Silverberg SL. Delays in Global Disease Outbreak Responses: Lessons from H1N1, Ebola, and Zika. *Am J Public Health*. 2018;108(3):329. doi:10.2105/AJPH.2017.304245

59. The New York Times. Trump Administration Signals Formal Withdrawal From W.H.O. Published 2020. Accessed October 31, 2022. https://www.nytimes.com/2020/07/07/us/politics/coronavirus-trump-who.html

60. Jamey Keaten. Biden's US revives support for WHO, reversing Trump retreat. AP News. Published January 22, 2021. Accessed October 31, 2022. https://apnews.com/article/us-who-support-006ed181e016afa55d4cea30af236227

61. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;395(10223):497-506. doi:http://dx.doi.org/10.1016/S0140-6736(20)30183-5

62. Nishiura H. Correcting the Actual Reproduction Number: A Simple Method to Estimate R0 from Early Epidemic Growth Data. *Int J Environ Res Public Health*. 2010;7(1):302. doi:10.3390/IJERPH7010291

63. Sharma M, Mindermann S, Brauner JM, et al. How Robust are the Estimated Effects of Nonpharmaceutical Interventions against COVID-19? In: *34th Conference on Neural Information Processing Systems (NeurIPS 2020)*. ; 2020. Accessed February 2, 2022. https://github.com/epidemics/COVIDNPIs/tree/neurips.

64. Adam D. A guide to R - the pandemic's misunderstood metric. *Nature*. 2020;583(7816):346-348. doi:10.1038/D41586-020-02009-W

65. Gurdasani D, Drury J, Greenhalgh T, et al. Mass infection is not an option: we must do more to protect our young. *Lancet*. 2021;398(10297):297-298. doi:10.1016/S0140-6736(21)01589-0

66. UK Health Security Agency. The R value and growth rate. Government of the UK. Published May 15, 2020. Accessed January 26, 2022. https://www.gov.uk/guidance/the-r-value-and-growth-rate

67. Reproduction Live. Is Covid-19 multiplying or dying out in your region? Reproduction Live. Accessed March 12, 2022. https://reproduction.live/

68. Arroyo-Marioli F, Bullano F, Kucinskas S, Rondón-Moreno C. Tracking R of COVID-19: A new real-time estimation using the Kalman filter. Sartorius B, ed. *PLoS One*. 2021;16(1):e0244474. doi:10.1371/journal.pone.0244474

69. Yu CJ, Wang ZX, Xu Y, Hu MX, Chen K, Qin G. Assessment of basic reproductive number for COVID-19 at global level: A meta-analysis. *Medicine*. 2021;100(18):e25837. doi:10.1097/MD.0000000000025837

70. Billah MA, Miah MM, Khan MN. Reproductive number of coronavirus: A systematic review and meta-analysis based on global level evidence. Flacco ME, ed. *PLoS One*. 2020;15(11):e0242128. doi:10.1371/journal.pone.0242128

71. Dhungel B, Rahman MdS, Rahman MdM, et al. A systematic review and meta-analysis of the transmissibility and severity of COVID-19. *PROSPERO*. Published online September 27, 2021. Accessed January 26, 2022. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=279514

72. NIH. Study Quality Assessment Tools. National Heart Lung and Blood Institute. Published 2013. Accessed January 26, 2022. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

73. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560. doi:10.1136/BMJ.327.7414.557

74. Inthout J, Ioannidis JP, Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol*. 2014;14(1):25. doi:10.1186/1471-2288-14-25

75. Furuya-Kanamori L, Barendregt JJ, Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. *Int J Evid Based Healthc*. 2018;16(4):195-203. doi:10.1097/XEB.0000000000000141

76. Shi L, Lin L. The trim-and-fill method for publication bias: practical guidelines and recommendations based on a large database of meta-analyses. *Medicine*. 2019;98(23):e15987. doi:10.1097/MD.0000000000015987

77. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis*. 2020;20(8):911-919. doi:10.1016/S1473-3099(20)30287-5

78. Lu Z, Yu Y, Chen Y, et al. A fractional-order SEIHDR model for COVID-19 with inter-city networked coupling effects. *Nonlinear Dyn*. 2020;101(3):1717-1730. doi:10.1007/s11071-020-05848-4

79. Rocklöv J, Sjödin H, Wilder-Smith A. COVID-19 outbreak on the Diamond Princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures. *J Travel Med*. 2020;27(3). doi:10.1093/jtm/taaa030

80. Hoque ME. Estimation of the number of affected people due to the Covid-19 pandemic using susceptible, infected and recover model. *International Journal of Modern Physics C*. 2020;31(08):2050111. doi:10.1142/S0129183120501119

81. Chertow DS, Kindrachuk J. Influenza, Measles, SARS, MERS, and Smallpox. *Highly Infectious Diseases in Critical Care*. Published online 2020:69-96. doi:10.1007/978-3-030-33803-9_5

82. Riley S, Fraser C, Donnelly CA, et al. Transmission Dynamics of the Etiological Agent of SARS in Hong Kong: Impact of Public Health Interventions. *Science (1979)*. 2003;300(5627):1961-1966. doi:10.1126/science.1086478

83. National Emerging Special Pathogens Training & Education Center. Playing the Numbers Game: R0. NETEC. Published January 30, 2020. Accessed March 19, 2022. https://netec.org/2020/01/30/playing-the-numbers-game-r0/

84. Gani R, Leach S. Transmission potential of smallpox in contemporary populations. *Nature*. 2001;414(6865):748-751. doi:10.1038/414748a

85. Centers for Disease Control and Prevention; World Health Organization. History and epidemiology of global smallpox eradication: Day 1 Module 1 – Smallpox: disease, prevention, and intervention (training course) (Presentation). *Centers for Disease Control and Prevention*. 2014;cdc27929. Accessed March 19, 2022. https://stacks.cdc.gov/view/cdc/27929

86. Health Service Executive of Ireland. Chapter 23 Varicella-Zoster: Hospitalisation notifiable, outbreak notifiable . Published online 2022.

87. Guerra FM, Bolotin S, Lim G, et al. The basic reproduction number (R 0) of measles: a systematic review. *Lancet Infect Dis*. 2017;17(12):e420-e428. doi:10.1016/S1473-3099(17)30307-9

88. World Health Organisation. Statement on the meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus 2019 (n-CoV) on 23 January 2020. Published January 23, 2020. Accessed February 4, 2022. https://www.who.int/news/item/23-01-2020-statement-on-the-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)

89. Cauchemez S, Fraser C, van Kerkhove MD, et al. Middle East respiratory syndrome coronavirus: Quantification of the extent of the epidemic, surveillance biases, and transmissibility. *Lancet Infect Dis*. 2014;14(1):50-56. doi:10.1016/S1473-

3099(13)70304-9/ATTACHMENT/136D5230-D99F-47E0-A3EA-4364B5C8BB67/MMC1.PDF

90. Kwok KO, Tang A, Wei VWI, Park WH, Yeoh EK, Riley S. Epidemic Models of Contact Tracing: Systematic Review of Transmission Studies of Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome. *Comput Struct Biotechnol J*. 2019;17:186-194. doi:10.1016/J.CSBJ.2019.01.003

91. Secunder Kermani. Coronavirus: Whitty and Vallance faced "herd immunity" backlash, emails show. BBC News. Published September 23, 2020. Accessed January 26, 2022. https://www.bbc.com/news/uk-politics-54252272

92. Dan Diamond. U.S. to narrowly miss Biden's July 4 vaccination goal, White House says. The Washington Post. Published June 22, 2021. Accessed January 26, 2022. https://www.washingtonpost.com/health/2021/06/22/white-house-vaccination-goal/

93. Delamater PL, Street EJ, Leslie TF, Yang YT, Jacobsen KH. Complexity of the Basic Reproduction Number (R0). *Emerg Infect Dis*. 2019;25(1):1. doi:10.3201/EID2501.171901

94. Reuters. Bosnia reports sharp rise in coronavirus cases after relaxing lockdown. Published April 30, 2020. Accessed March 12, 2022. https://www.reuters.com/article/us-health-coronavirus-bosnia-cases-idUSKBN22B2DB

95. Lewnard JA, Ndeffo Mbah ML, Alfaro-Murillo JA, et al. Dynamics and control of Ebola virus transmission in Montserrado, Liberia: a mathematical modelling analysis. *Lancet Infect Dis*. 2014;14(12):1189-1195. doi:10.1016/S1473-3099(14)70995-8

96. Gedeon T, Bodelón C, Kuenzi A. Hantavirus Transmission in Sylvan and Peridomestic Environments. *Bull Math Biol*. 2010;72(3):541-564. doi:10.1007/s11538-009-9460-4

97. Bell JA, Nuzzo JB. Global Health Security Index: Advancing Collective Action and Accountability Amid Global Crisis. Published 2019. Accessed July 24, 2022. https://ghdx.healthdata.org/ihme_data

98. Atzrodt CL, Maknojia I, McCarthy RDP, et al. A Guide to COVID-19: a global pandemic caused by the novel coronavirus SARS-CoV-2. *FEBS J*. 2020;287(17):3633-3650. doi:10.1111/FEBS.15375

99. United Nations, Department of Economic and Social Affairs PD. World Population Prospects: Highlights (ST/ESA/SER.A/423). Published 2019. Accessed December 30, 2019. https://population.un.org/wpp/Graphs/DemographicProfiles/Pyramid/392

100. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Socio-Demographic Index (SDI) 1950–2019. *Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME)*. Published online 2020. Accessed July 24, 2022. https://ghdx.healthdata.org/

101. Roser M, Ritchie H and, Esteban OO. Coronavirus Disease (COVID-19) – Research and Statistics. *Our World in Data*. Published online 2020. Accessed March 13, 2020. https://ourworldindata.org/coronavirus

102. Cori MA. EpiEstim: A Package to Estimate Time Varying Reproduction Numbers from Epidemic Curves. *R package version 224*. Published online 2021. doi:10.1093/aje/kwt133

103. Ali ST, Wang L, Lau EHY, et al. Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions. *Science*. Published online 2020. doi:10.1126/science.abc9004

104. Osamu Tsukimori. With variants on the rise, Japan sticks to firm COVID-19 guidance | The Japan Times. *The Japan Times*. https://www.japantimes.co.jp/news/2021/07/06/national/variants-japan-coronavirus-guidance/. Published July 6, 2021. Accessed November 18, 2022.

105. Bir C, Widmar NO. Societal values and mask usage for COVID-19 control in the US. *Prev Med (Baltim)*. 2021;153:106784. doi:10.1016/J.YPMED.2021.106784

106. Lu JG, Jin P, English AS. Collectivism predicts mask use during COVID-19. *Proc Natl Acad Sci U S A*. 2021;118(23):e2021793118. doi:10.1073/PNAS.2021793118/SUPPL_FILE/PNAS.2021793118.SAPP.PDF

107. US Government Accountability Office. Millions of People May Still Be Eligible For COVID-19 Stimulus Payments, But Time Is Running Out | U.S. GAO. GAO. Published October 11, 2022. Accessed November 18, 2022. https://www.gao.gov/blog/millions-people-may-still-be-eligible-covid-19-stimulus-payments-time-running-out

108. Mainichi Japan. Editorial: Japan gov't decision for COVID-19 handouts comes late after much confusion - The Mainichi. *The Mainichi Newspapers*. https://mainichi.jp/english/articles/20200417/p2a/00m/0na/015000c. Published April 17, 2020. Accessed November 18, 2022.

109. Kyodo. All schools in Japan told to close until April over virus outbreak | The Japan Times. The Japan Times. Published February 27, 2020. Accessed November 18, 2022. https://www.japantimes.co.jp/news/2020/02/27/national/hokkaido-coronavirus-school/

110. Prime Minister's Office of Japan. Useful information on the novel coronavirus disease (COVID-19). Accessed November 18, 2022. https://japan.kantei.go.jp/ongoingtopics/coronavirus_info_e.html

111. Lloyd Doggett. Timeline of Trump's Coronavirus Responses | Congressman Lloyd Doggett. US Representative. Published March 2, 2022. Accessed November 18, 2022. https://doggett.house.gov/media/blog-post/timeline-trumps-coronavirus-responses

112. Elizabeth COhen, Dana Vigue. US government slow to act as anti-vaxxers spread lies on social media about coronavirus vaccine. CNN health. Published August 13, 2020. Accessed November 18, 2022. https://edition.cnn.com/2020/08/12/health/anti-vaxxers-covid-19/index.html

113. Ravi SJ, Warmbrod KL, Mullen L, et al. The value proposition of the Global Health Security Index. *BMJ Glob Health*. 2020;5(10):e0036488. doi:10.1136/BMJGH-2020-003648

114. World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus: interim guidance, 20 March 2020. Geneva, Switzerland: WHO. Published 2020. Accessed October 12, 2022. https://apps.who.int/iris/handle/10665/331506

115. Gostic KM, McGough L, Baskerville EB, et al. Practical considerations for measuring the effective reproductive number, Rt. *medRxiv [Preprint]*. Published online August 28, 2020. doi:10.1101/2020.06.18.20134858

116. Gita Gopinath, Jeremy Farrar, Richard Hatchett, Peter Sands, Ruchir Agarwal, Gerry Rice. Transcript of Global Strategy to Manage the Long-term Risks of COVID-19 Press Briefing. International Monetary Fund. Published April 5, 2022. Accessed November 2, 2022. https://www.imf.org/en/News/Articles/2022/04/06/tr040522-transcript-of-press-briefing-global-strategy-to-manage-the-long-term-risks-of-covid-19

117. Heymann DL, Chen L, Takemi K, et al. Global health security: The wider lessons from the west African Ebola virus disease epidemic. *The Lancet*. 2015;385(9980):1884-1901. doi:10.1016/S0140-6736(15)60858-3/ATTACHMENT/348F6BD6-2B41-4DE5-A4D4-DA3BC81E000D/MMC1.PDF

118. Centers for Disease Control and Prevention. International Health Regulations (IHR) . Division of Global Health Protection and Security. Accessed November 2, 2022. https://www.cdc.gov/globalhealth/healthprotection/ghs/ihr/index.html

119. World Health Organization. A Zero draft report of the Working Group on Strengthening WHO Preparedness and Response to Health Emergencies to the Seventy-fifth World Health Assembly. *Ninth meeting of the working group on strengthening WHO preparedness and response to health emergencies, Geneva*. Published online May 2022. Accessed November 3, 2022. https://apps.who.int/gb/wgpr/pdf_files/wgpr9/A_WGPR9_3-en.pdf

Appendices

Appendix A: PHEIC criteria as per the International Health regulations of the WHO

EXAMPLES FOR THE APPLICATION OF THE DECISION INSTRUMENT FOR THE ASSESSMENT AND NOTIFICATION OF EVENTS THAT MAY CONSTITUTE A PUBLIC HEALTH EMERGENCY OF INTERNATIONAL CONCERN

The examples appearing in this Annex are not binding and are for indicative guidance purposes to assist in the interpretation of the decision instrument criteria.

DOES THE EVENT MEET AT LEAST TWO OF THE FOLLOWING CRITERIA?

Is the public health impact of the event serious?	**I. Is the public health impact of the event serious?**
	1. *Is the number of cases and/or number of deaths for this type of event large for the given place, time or population?*
	2. *Has the event the potential to have a high public health impact?* THE FOLLOWING ARE EXAMPLES OF CIRCUMSTANCES THAT CONTRIBUTE TO HIGH PUBLIC HEALTH IMPACT: ✓ Event caused by a pathogen with high potential to cause epidemic (infectiousness of the agent, high case fatality, multiple transmission routes or healthy carrier). ✓ Indication of treatment failure (new or emerging antibiotic resistance, vaccine failure, antidote resistance or failure). ✓ Event represents a significant public health risk even if no or very few human cases have yet been identified. ✓ Cases reported among health staff. ✓ The population at risk is especially vulnerable (refugees, low level of immunization, children, elderly, low immunity, undernourished, etc.). ✓ Concomitant factors that may hinder or delay the public health response (natural catastrophes, armed conflicts, unfavourable weather conditions, multiple foci in the State Party). ✓ Event in an area with high population density. ✓ Spread of toxic, infectious or otherwise hazardous materials that may be occurring naturally or otherwise that has contaminated or has the potential to contaminate a population and/or a large geographical area.
	3. *Is external assistance needed to detect, investigate, respond and control the current event, or prevent new cases?* THE FOLLOWING ARE EXAMPLES OF WHEN ASSISTANCE MAY BE REQUIRED: ✓ Inadequate human, financial, material or technical resources – in particular: – insufficient laboratory or epidemiological capacity to investigate the event (equipment, personnel, financial resources); – insufficient antidotes, drugs and/or vaccine and/or protective equipment, decontamination equipment, or supportive equipment to cover estimated needs; – existing surveillance system is inadequate to detect new cases in a timely manner.
	IS THE PUBLIC HEALTH IMPACT OF THE EVENT SERIOUS? **Answer "yes" if you have answered "yes" to questions 1, 2 or 3 above.**

Is the event unusual or unexpected?	**II. Is the event unusual or unexpected?**
	4. *Is the event unusual?* THE FOLLOWING ARE EXAMPLES OF UNUSUAL EVENTS: ✓ The event is caused by an unknown agent or the source, vehicle, route of transmission is unusual or unknown. ✓ Evolution of cases more severe than expected (including morbidity or case-fatality) or with unusual symptoms. ✓ Occurrence of the event itself unusual for the area, season or population.
	5. *Is the event unexpected from a public health perspective?* THE FOLLOWING ARE EXAMPLES OF UNEXPECTED EVENTS: ✓ Event caused by a disease/agent that had already been eliminated or eradicated from the State Party or not previously reported.
	IS THE EVENT UNUSUAL OR UNEXPECTED? **Answer "yes" if you have answered "yes" to questions 4 or 5 above.**

Is there a significant risk of international spread?	**III. Is there a significant risk of international spread?**
	6. *Is there evidence of an epidemiological link to similar events in other States?*
	7. *Is there any factor that should alert us to the potential for cross border movement of the agent, vehicle or host?* THE FOLLOWING ARE EXAMPLES OF CIRCUMSTANCES THAT MAY PREDISPOSE TO INTERNATIONAL SPREAD: ✓ Where there is evidence of local spread, an index case (or other linked cases) with a history within the previous month of: – international travel (or time equivalent to the incubation period if the pathogen is known); – participation in an international gathering (pilgrimage, sports event, conference, etc.); – close contact with an international traveller or a highly mobile population. ✓ Event caused by an environmental contamination that has the potential to spread across international borders. ✓ Event in an area of intense international traffic with limited capacity for sanitary control or environmental detection or decontamination.
	IS THERE A SIGNIFICANT RISK OF INTERNATIONAL SPREAD? **Answer "yes" if you have answered "yes" to questions 6 or 7 above.**

Risk of international restrictions?	**IV. Is there a significant risk of international travel or trade restrictions?**
	8. *Have similar events in the past resulted in international restriction on trade and/or travel?*
	9. *Is the source suspected or known to be a food product, water or any other goods that might be contaminated that has been exported/imported to/from other States*?
	10. *Has the event occurred in association with an international gathering or in an area of intense international tourism?*
	11. *Has the event caused requests for more information by foreign officials or international media?*
	IS THERE A SIGNIFICANT RISK OF INTERNATIONAL TRADE OR TRAVEL RESTRICTIONS? **Answer "yes" if you have answered "yes" to questions 8, 9, 10 or 11 above.**

States Parties that answer "yes" to the question whether the event meets any two of the four criteria (I-IV) above, shall notify WHO under Article 6 of the International Health Regulations.

Appendix B: Data extraction form

Study ID (study number eg. 1, 2..)	

General information

Date form completed *(dd/mm/yyyy)*	
Name of person extracting data	
Notes:	

Study details

Study title	
DOI	
Journal	
Author	
Affiliation of author	
Date of publication *(year, month, date)*	

Characteristics of included studies

Methods

	Descriptions as stated in report/paper	Location in text or source *(pg & ¶/fig/table/other)*
Country		

City		
Data collected from date (year, month, date)		
Data collected until the date *(year, month, date)*		
Method used to calculate reproduction number		
Model used to calculate reproduction number		
Assumption of the model		
Sample size		
Notes:		

Outcome: Reproduction number

	Description	Location in text or source *(pg & ¶/fig/table/other)*
Type of reproduction number assessed		
Reproduction number		
Interval of reproduction number		
SD or SE (if mentioned)		

Type of interval (95% CI, 90% CI, max/min, Credible Interval)		
Type of central estimate *(mean, median)*		
Notes:		

Study quality assessment through National Institute of Health (NIH) quality assessment tool for case series studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	☐	☐	
2. Was the study population clearly and fully described, including a case definition?	☐	☐	
3. Were the cases consecutive?	☐	☐	
4. Were the subjects comparable?	☐	☐	
5. Was the intervention clearly described?	☐	☐	
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	☐	☐	
7. Was the length of follow-up adequate?	☐	☐	
8. Were the statistical methods well-described?	☐	☐	
9. Were the results well-described?	☐	☐	

Quality Rating (Good, Fair, or Poor)
Additional Comments (If POOR, please state why):

*CD, cannot determine; NA, not applicable; NR, not reported

Appendix C: References of the 151 articles included in the systematic review

1. Xue L, Jing S, Miller JC, et al. A data-driven network model for the emerging COVID-19 epidemics in Wuhan, Toronto, and Italy. Mathematical Biosciences. 2020;326.

2. Iwata K, Miyakoshi C. A Simulation on Potential Secondary Spread of Novel Coronavirus in an Exported Country Using a Stochastic Epidemic SEIR Model. Journal of Clinical Medicine. 2020;9(4):944.

3. Kassa SM, Njagarah JBH, Terefe YA. Analysis of the mitigation strategies for COVID-19: From mathematical modelling perspective. Chaos, Solitons & Fractals. 2020;138:109968.

4. Wang X, Pan Y, Zhang D, et al. Basic epidemiological parameter values from data of real-world in mega-cities: The characteristics of COVID-19 in Beijing, China. BMC Infectious Diseases. 2020;20(1).

5. Lau MSY, Grenfell B, Thomas M, Bryan M, Nelson K, Lopman B. Characterizing superspreading events and age-specific infectiousness of SARS-CoV-2 transmission in Georgia, USA. Proceedings of the National Academy of Sciences of the United States of America. 2020;117(36):22430-22435.

6. Biswas SK, Ghosh JK, Sarkar S, Ghosh U. COVID-19 pandemic in India: a mathematical model study. Nonlinear Dynamics. 2020;102(1):537-553.

7. Dropkin G. COVID-19 UK Lockdown Forecasts and R0. Frontiers in Public Health. 2020;8.

8. Wang K, Lu Z, Wang X, et al. Current trends, and future prediction of novel coronavirus disease (COVID-19) epidemic in China: a dynamical modeling analysis. Mathematical Biosciences and Engineering. 2020;17(4):3052-3061.

9. Anastassopoulou C, Russo L, Tsakris A, Siettos C. Data-based analysis, modelling and forecasting of the COVID-19 outbreak. PLoS ONE. 2020;15(3).

10. Bhaskar A, Ponnuraja C, Srinivasan R, Padmanaban S. Distribution and growth rate of COVID-19 outbreak in Tamil Nadu: A log-linear regression approach. Indian journal of public health. 2020;64(Supplement):S188-S191.

11. Mizumoto K, Kagaya K, Chowell G. Early epidemiological assessment of the transmission potential and virulence of coronavirus disease 2019 (COVID-19) in Wuhan City, China, January–February, 2020. BMC Medicine. 2020;18(1):217.

12. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. New England Journal of Medicine. 2020;382(13):1199-1207.

13. Munayco C v, Tariq A, Rothenberg R, et al. Early transmission dynamics of COVID-19 in a southern hemisphere setting: Lima-Peru: February 29th–March 30th, 2020. Infectious Disease Modelling. 2020;5:338-345.

14. Ki M. Epidemiologic characteristics of early cases with 2019 novel coronavirus (2019-nCoV) disease in Korea. Epidemiology and health. 2020;42:e2020007.

15. Haw NJL, Uy J, Sy KTL, Abrigo MRM. Epidemiological profile and transmission dynamics of COVID-19 in the Philippines. Epidemiology and infection. 2020;148:e204.

16. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. The Lancet Infectious Diseases. 2020;20(8):911-919.

17. Lonergan M, Chalmers JD. Estimates of the ongoing need for social distancing and control measures post-“lockdown” from trajectories of COVID-19 cases and mortality. European Respiratory Journal. 2020;56(1).

18. Zhao S, Musa SS, Lin Q, et al. Estimating the unreported number of novel coronavirus (2019-ncov) cases in China in the first half of January 2020: A data-driven modelling analysis of the early outbreak. Journal of Clinical Medicine. 2020;9(2).

19. Musa SS, Zhao S, Wang MH, Habib AG, Mustapha UT, He D. Estimation of exponential growth rate and basic reproduction number of the coronavirus disease 2019 (COVID-19) in Africa. Infect Dis Poverty. 2020;9(1):96.

20. Chae SY, Lee K, Lee HM, et al. Estimation of Infection Rate and Predictions of Disease Spreading Based on Initial Individuals Infected With COVID-19. Frontiers in Physics. 2020;8.

21. Xu C, Dong Y, Yu X, et al. Estimation of reproduction numbers of COVID-19 in typical countries and epidemic trends under different prevention and control scenarios. Frontiers of Medicine. 2020;14(5):613-622.

22. PANG L, LIU S, ZHANG X, TIAN T, ZHAO Z. Transmission dynamics and control strategies of covid-19 in Wuhan, China. Journal of Biological Systems. 2020;28(03):543-560.

23. Hoque ME. Estimation of the number of affected people due to the Covid-19 pandemic using susceptible, infected and recover model. International Journal of Modern Physics C. 2020;31(08):2050111.

24. Kanagarathinam K, Sekar K. Estimation of the reproduction number and early prediction of the COVID-19 outbreak in India using a statistical computing approach. Epidemiology and health. 2020;42:e2020028.

25. Zhang S, Diao M, Yu W, Pei L, Lin Z, Chen D. Estimation of the reproductive number of novel coronavirus (COVID-19) and the probable outbreak size on the Diamond Princess cruise ship: A data-driven analysis. International Journal of Infectious Diseases. 2020;93:201-204.

26. You C, Deng Y, Hu W, et al. Estimation of the time-varying reproduction number of COVID-19 outbreak in China. International journal of hygiene and environmental health. 2020;228:113555.

27. Maugeri A, Barchitta M, Battiato S, Agodi A. Estimation of unreported novel coronavirus (Sars-coV-2) infections from reported deaths: A susceptible–exposed–infectious–recovered–dead model. Journal of Clinical Medicine. 2020;9(5).

28. Glass DH. European and US lockdowns and second waves during the COVID-19 pandemic. Mathematical Biosciences. 2020;330.

29. Zhang Y, Li Y, Wang L, Li M, Zhou X. Evaluating transmission heterogeneity and super-spreading event of COVID-19 in a metropolis of China. International Journal of Environmental Research and Public Health. 2020;17(10).

30. Kim S, Jeong YD, Byun JH, et al. Evaluation of COVID-19 epidemic outbreak caused by temporal contact-increase in South Korea. International Journal of Infectious Diseases. 2020;96:454-457.

31. Su L, Hong N, Zhou X, et al. Evaluation of the Secondary Transmission Pattern and Epidemic Prediction of COVID-19 in the Four Metropolitan Areas of China. Frontiers in Medicine. 2020;7.

32. Grzybowski JM v., da Silva R v., Rafikov M. Expanded SEIRCQ Model Applied to COVID-19 Epidemic Control Strategy Design and Medical Infrastructure Planning. Mathematical Problems in Engineering. 2020;2020:1-15.

33. Wangping J, Ke H, Yang S, et al. Extended SIR Prediction of the Epidemics Trend of COVID-19 in Italy and Compared With Hunan, China. Frontiers in Medicine. 2020;7.

34. Chen Z, Yang J, Dai B. Forecast possible risk for COVID-19 epidemic dissemination under current control strategies in Japan. International Journal of Environmental Research and Public Health. 2020;17(11).

35. Wirawan A, Januraga PP. Forecasting COVID-19 Transmission and Healthcare Capacity in Bali, Indonesia. Journal of Preventive Medicine and Public Health. 2020;53(3):158-163.

36. Khajanchi S, Sarkar K. Forecasting the daily and cumulative number of cases for the COVID-19 pandemic in India. Chaos: An Interdisciplinary Journal of Nonlinear Science. 2020;30(7):071101.

37. Almeshal AM, Almazrouee AI, Alenizi MR, Alhajeri SN. Forecasting the Spread of COVID-19 in Kuwait Using Compartmental and Logistic Regression Models. Applied Sciences. 2020;10(10):3402.

38. Aviv-Sharon E, Aharoni A. Generalized logistic growth modeling of the COVID-19 pandemic in Asia. Infectious Disease Modelling. 2020;5:502-509.

39. Katul GG, Mrad A, Bonetti S, Manoli G, Parolari AJ. Global convergence of COVID-19 basic reproduction number and estimation from early-time SIR dynamics. PLoS ONE. 2020;15(9 September).

40. Zhao S, Stone L, Gao D, et al. Imitation dynamics in the mitigation of the novel coronavirus disease (COVID-19) outbreak in Wuhan, China from 2019 to 2020. Annals of Translational Medicine. 2020;8(7).

41. Yang J, Wang G, Zhang S, Xu F, Li X. Analysis of the age-structured epidemiological characteristics of SARS-COV-2 transmission in mainland China: An aggregated approach. Augeraud E, Banerjee M, Dhersin JS, et al., eds. Mathematical Modelling of Natural Phenomena. 2020;15:39.

42. Chaves LF, Hurtado LA, Rojas MR, Friberg MD, Rodríguez RM, Avila-Aguero ML. COVID-19 basic reproduction number and assessment of initial suppression policies in Costa Rica. Augeraud E, Banerjee M, Dhersin JS, et al., eds. Mathematical Modelling of Natural Phenomena. 2020;15:32.

43. Salje H, Kiem CT, Lefrancq N, et al. Estimating the burden of SARS-CoV-2 in France. Science. 2020;369(6500):208-211.

44. Xu C, Yu Y, Chen Y, Lu Z. Forecast analysis of the epidemics trend of COVID-19 in the USA by a generalized fractional-order SEIR model. Nonlinear Dynamics. 2020;101(3):1621-1634.

45. di Domenico L, Pullano G, Sabbatini CE, Boëlle PY, Colizza V. Impact of lockdown on COVID-19 epidemic in Île-de-France and possible exit strategies. BMC Medicine. 2020;18(1).

46. Patel P, Athotra A, Vaisakh TP, Dikid T, Jain SK. Impact of nonpharmacological interventions on COVID-19 transmission dynamics in India. Indian journal of public health. 2020;64(Supplement):S142-S146.

47. Wang K, Zhao S, Liao Y, et al. Estimating the serial interval of the novel coronavirus disease (COVID-19) based on the public surveillance data in Shenzhen, China, from 19 January to 22 February 2020. Transboundary and Emerging Diseases. Published online 2020.

48. 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. Emerging Infectious Diseases. 2020;26(7):1470-1477.

49. Patrikar SR, Kotwal A, Bhatti VK, et al. Incubation Period and Reproduction Number for Novel Coronavirus 2019 (COVID-19) Infections in India. Asia Pacific Journal of Public Health. 2020;32(8):458-460.

50. Kwok KO, Chan HHH, Huang Y, et al. Inferring super-spreading from transmission clusters of COVID-19 in Hong Kong, Japan, and Singapore. Journal of Hospital Infection. 2020;105(4):682-685.

51. Willis MJ, Díaz VHG, Prado-Rubio OA, von Stosch M. Insights into the dynamics and control of COVID-19 infection rates. Chaos, Solitons & Fractals. 2020;138:109937.

52. Adekunle AI, Adegboye OA, Gayawan E, McBryde ES. Is Nigeria really on top of COVID-19? Message from effective reproduction number. Epidemiology and Infection. Published online 2020.

53. Bae TW, Kwon KK, Kim KH. Mass Infection Analysis of COVID-19 Using the SEIRD Model in Daegu-Gyeongbuk of Korea from April to May, 2020. Journal of Korean medical science. 2020;35(34):e317.

54. Naveed M, Rafiq M, Raza A, et al. Mathematical Analysis of Novel Coronavirus (2019-nCov) Delay Pandemic Model. Computers, Materials & Continua. 2020;64(3):1401-1414.

55. Yang HM, Lombardi Junior LP, Castro FFM, Yang AC. Mathematical model describing CoViD-19 in São Paulo, Brazil - evaluating isolation as control mechanism and forecasting epidemiological scenarios of release. Epidemiology and infection. 2020;148:e155.

56. Veera Krishna M. Mathematical modelling on diffusion and control of COVID–19. Infectious Disease Modelling. 2020;5:588-597.

57. Jiang S, Li Q, Li C, et al. Mathematical models for devising the optimal SARS-CoV-2 strategy for eradication in China, South Korea, and Italy. Journal of Translational Medicine. 2020;18(1).

58. Tian J, Wu J, Bao Y, et al. Modeling analysis of COVID-19 based on morbidity data in Anhui, China. Mathematical Biosciences and Engineering. 2020;17(4):2842-2852.

59. Irvine M, Coombs D, Skarha J, et al. Modeling COVID-19 and Its Impacts on U.S. Immigration and Customs Enforcement (ICE) Detention Facilities, 2020. Journal of urban health : bulletin of the New York Academy of Medicine. 2020;97(4):439-447.

60. Turk PJ, Chou SH, Kowalkowski MA, et al. Modeling COVID-19 Latent Prevalence to Assess a Public Health Intervention at a State and Regional Scale: Retrospective Cohort Study. JMIR public health and surveillance. 2020;6(2):e19353.

61. Saldaña F, Flores-Arguedas H, Camacho-Gutiérrez JA, Barradas I. Modeling the transmission dynamics and the impact of the control interventions for the COVID-19 epidemic outbreak. Mathematical Biosciences and Engineering. 2020;17(4):4165-4183.

62. Wang L, Wang J, Zhao H, et al. Modelling and assessing the effects of medical resources on transmission of novel coronavirus (COVID-19) in Wuhan, China. Mathematical Biosciences and Engineering. 2020;17(4):2936-2949.

63. Marimuthu S, Joy M, Malavika B, et al. Modelling of reproduction number for COVID-19 in India and high incidence states. Clinical Epidemiology and Global Health. Published online 2020.

64. Goscé L, Phillips PA, Spinola P, Gupta DRK, Abubakar PI. Modelling SARS-COV2 Spread in London: Approaches to Lift the Lockdown. Journal of Infection. 2020;81(2):260-265.

65. Feng LX, Jing SL, Hu SK, Wang DF, Huo HF. Modelling the effects of media coverage and quarantine on the COVID-19 infections in the UK. Mathematical Biosciences and Engineering. 2020;17(4):3618-3636.

66. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. The Lancet. 2020;395(10225):689-697.

67. Zhu Y, Chen YQ. On a Statistical Transmission Model in Analysis of the Early Phase of COVID-19 Outbreak. Statistics in Biosciences. Published online 2020.

68. Peirlinck M, Linka K, Sahli Costabal F, Kuhl E. Outbreak dynamics of COVID-19 in China and the United States. Biomechanics and Modelling in Mechanobiology. Published online 2020.

69. Linka K, Peirlinck M, Sahli Costabal F, Kuhl E. Outbreak dynamics of COVID-19 in Europe and the effect of travel restrictions. Computer Methods in Biomechanics and Biomedical Engineering. 2020;23(11):710-717.

70. Bentout S, Chekroun A, Kuniya T. Parameter estimation and prediction for coronavirus disease outbreak 2019 (COVID-19) in Algeria. AIMS public health. Published online 2020.

71. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. Eurosurveillance. 2020;25(4).

72. Feng X, Chen J, Wang K, et al. Phase-adjusted estimation of the COVID-19 outbreak in South Korea under multi-source data and adjustment measures: a modelling study. Mathematical Biosciences and Engineering. 2020;17(4):3637-3648.

73. Taboe HB, Salako K v, Tison JM, Ngonghala CN, Glèlè Kakaï R. Predicting COVID-19 spread in the face of control measures in West Africa. Mathematical Biosciences. 2020;328.

74. Liu Z, Magal P, Seydi O, Webb G. Predicting the cumulative number of cases for the COVID-19 epidemic in China from early data. Mathematical Biosciences and Engineering. 2020;17(4):3040-3051.

75. Moussaoui A, Auger P. Prediction of confinement effects on the number of Covid-19 outbreak in Algeria. Augeraud E, Banerjee M, Dhersin JS, et al., eds. Mathematical Modelling of Natural Phenomena. 2020;15:37.

76. Alsayed A, Sadir H, Kamil R, Sari H. Prediction of epidemic peak and infected cases for COVID-19 disease in Malaysia, 2020. International Journal of Environmental Research and Public Health. 2020;17(11):1-15.

77. Kuniya T. Prediction of the Epidemic Peak of Coronavirus Disease in Japan, 2020. Journal of Clinical Medicine. 2020;9(3):789.

78. Zhuang Z, Zhao S, Lin Q, et al. Preliminary estimates of the reproduction number of the coronavirus disease (COVID-19) outbreak in Republic of Korea and Italy by 5 March 2020. International Journal of Infectious Diseases. 2020;95:308-310.

79. Rotejanaprasert C, Lawpoolsri S, Pan-Ngum W, Maude RJ. Preliminary estimation of temporal and spatiotemporal dynamic measures of COVID- 19 transmission in Thailand. PLoS ONE. 2020;15(9 September).

80. Zhao S, Lin Q, Ran J, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. International Journal of Infectious Diseases. 2020;92:214-217.

81. Zhou T, Liu Q, Yang Z, et al. Preliminary prediction of the basic reproduction number of the Wuhan novel coronavirus 2019-nCoV. Journal of Evidence-Based Medicine. 2020;13(1):3-7.

82. Wang K, Zhao S, Li H, et al. Real-time estimation of the reproduction number of the novel coronavirus disease (COVID-19) in China in 2020 based on incidence data. Annals of translational medicine. Published online 2020.

83. Jung SM, Akhmetzhanov AR, Hayashi K, et al. Real-time estimation of the risk of death from novel coronavirus (COVID-19) infection: Inference using exported cases. Journal of Clinical Medicine. 2020;9(2).

84. Hao X, Cheng S, Wu D, Wu T, Lin X, Wang C. Reconstruction of the full transmission dynamics of COVID-19 in Wuhan. Nature. 2020;584(7821):420-424.

85. Buckman SR, Glick R, Lansing KJ, Petrosky-Nadeau N, Seitelman LM. Replicating and projecting the path of COVID-19 with a model-implied reproduction number. Infectious Disease Modelling. 2020;5:635-651.

86. Kim S, Choi S, Ko Y, Ki M, Jung E. Risk estimation of the SARS-CoV-2 acute respiratory disease outbreak outside China. Theoretical biology & medical modelling. 2020;17(1):9.

87. Nguemdjo U, Meno F, Dongfack A, Ventelou B. Simulating the progression of the COVID-19 disease in Cameroon using SIR models. PLoS ONE. 2020;15(8 August 2020).

88. Huang R, Liu M, Ding Y. Spatial-temporal distribution of COVID-19 in China and its prediction: A data-driven modeling analysis. Journal of Infection in Developing Countries. 2020;14(3):246-253.

89. Gatto M, Bertuzzo E, Mari L, et al. Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures. Proceedings of the National Academy of Sciences of the United States of America. 2020;117(19):10484-10491.

90. Khosravi A, Chaman R, Rohani-Rasaf M, Zare F, Mehravaran S, Emamian MH. The basic reproduction number and prediction of the epidemic size of the novel coronavirus (COVID-19) in Shahroud, Iran. Epidemiology and Infection. Published online 2020.

91. Al-Raeei M. The basic reproduction number of the new coronavirus pandemic with mortality for India, the Syrian Arab Republic, the United States, Yemen, China, France, Nigeria, and Russia with different rate of cases. Clinical Epidemiology and Global Health. Published online 2020.

92. Guirao A. The Covid-19 outbreak in Spain. A simple dynamics model, some lessons, and a theoretical framework for control response. Infectious Disease Modelling. 2020;5:652-669.

93. el Deeb O, Jalloul M. The dynamics of COVID-19 spread: evidence from Lebanon. Mathematical Biosciences and Engineering. 2020;17(5):5618-5632.

94. Khan MA, Atangana A, Alzahrani E, Fatmawati. The dynamics of COVID-19 with quarantined and isolation. Advances in Difference Equations. 2020;2020(1):425.

95. Linka K, Peirlinck M, Kuhl E. The reproduction number of COVID-19 and its correlation with public health interventions. Computational Mechanics. 2020;66(4):1035-1050.

96. Ali M, Shah STH, Imran M, Khan A. The role of asymptomatic class, quarantine, and isolation in the transmission of COVID-19. Journal of Biological Dynamics. 2020;14(1):389-408.

97. Li C, Xu J, Liu J, Zhou Y. The within-host viral kinetics of SARS-CoV-2. Mathematical Biosciences and Engineering. 2020;17(4):2853-2861.

98. Dur-e-Ahmad M, Imran M. Transmission Dynamics Model of Coronavirus COVID-19 for the Outbreak in Most Affected Countries of the World. International Journal of Interactive Multimedia and Artificial Intelligence. 2020;6(2):4.

99. Sharov KS. Trends in adaptation of fifteen European countries population to SARS-CoV-2 in March–May 2020: Can Taiwanese experience be adopted? Journal of the Formosan Medical Association. Published online 2020.

100. Mena RH, Velasco-Hernandez JX, Mantilla-Beniers NB, et al. Using posterior predictive distributions to analyse epidemic models: COVID-19 in Mexico City. Physical biology. 2020;17(6):65001.

101. Liu F, Li X, Zhu G. Using the contact network model and Metropolis-Hastings sampling to reconstruct the COVID-19 spread on the “Diamond Princess.” Science Bulletin. 2020;65(15):1297-1305.

102. Song H, Li F, Jia Z, Jin Z, Liu S. Using traveller-derived cases in Henan Province to quantify the spread of COVID-19 in Wuhan, China. Nonlinear Dynamics. 2020;101(3):1821-1831.

103. Wan K, Chen J, Lu C, Dong L, Wu Z, Zhang L. When will the battle against novel coronavirus end in Wuhan: A SEIR modeling analysis. Journal of global health. 2020;10(1):11002.

104. Li J. A Robust Stochastic Method of Estimating the Transmission Potential of 2019-nCoV. arXiv. Published online February 7, 2020.

105. Zhao Q, Chen Y, Small DS. Analysis of the epidemic growth of the early 2019-nCoV outbreak using internationally confirmed cases. medRxiv. Published online February 9, 2020.

106. Zhou H, Xue C, Gao G, Lawless L, Xie L, Zhang KK. Characterizing the transmission and identifying the control strategy for COVID-19 through epidemiological modeling. medRxiv. Published online February 25, 2020.

107. Bai Y, Nie X, Wen C. Epidemic Prediction of 2019-nCoV in Hubei Province, and Comparison with SARS in Guangdong Province. SSRN pre print.

108. Cao Z, Zhang Q, Lu X, et al. Estimating the effective reproduction number of the 2019-nCoV in China. medRxiv. Published online January 29, 2020.

109. Li J, Wang Y, Gilmour S, et al. Estimation of the epidemic properties of the 2019 novel coronavirus: A mathematical modeling study. medRxiv. Published online February 20, 2020.

110. Tang B, Wang X, Li Q, et al. Estimation of the Transmission Risk of the 2019-nCoV and Its Implication for Public Health Interventions. Journal of Clinical Medicine. 2020;9(2).

111. Zhou C. Evaluating new evidence in the early dynamics of the novel coronavirus COVID-19 outbreak in Wuhan, China with real time domestic traffic and potential asymptomatic transmissions. medRxiv. Published online February 20, 2020.

112. Cao Z, Zhang Q, Lu X, et al. Incorporating Human Movement Data to Improve Epidemiological Estimates for 2019-nCoV. medRxiv. Published online February 9, 2020.

113. Ivorra B, Ferrández MR, Vela-Pérez M, Ramos AM. Mathematical modeling of the spread of the coronavirus disease 2019 (COVID-19) taking into account the undetected infections. The case of China. Communications in Nonlinear Science & Numerical Simulation. 2020;88:105303.

114. Shen M, Peng Z, Xiao Y, Zhang L. Modelling the epidemic trend of the 2019 novel coronavirus outbreak in China. bioRxiv. Published online January 25, 2020.

115. Read JM, Bridgen JRE, Cummings DAT, Ho A, Jewell CP. Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions. medRxiv. Published online January 28, 2020.

116. Imai N, Cori A, Dorigatti I, et al. Report 3: Transmissibility of 2019-NCoV.; 2020.

117. Xiong H, Yan H. Simulating the Infected Population and Spread Trend of 2019-nCov Under Different Policy by EIR Model. SSRN preprint. Published online February 8, 2020.

118. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science. 2020;368(6490):489-493.

119. Sanche S, Lin YT, Xu C, Romero-Severson E, Hengartner N, Ke R. The Novel Coronavirus, 2019-nCoV, is Highly Contagious and More Infectious Than Initially Estimated [Preprint]. medRxiv. Published online February 11, 2020.

120. Shao N, Cheng J, Chen W. The reproductive number R0 of COVID-19 based on estimate of a statistical time delay dynamical system [Preprint]. medRxiv. Published online February 20, 2020.

121. Abbott S, Hellewell J, Munday J, Funk S. The transmissibility of novel Coronavirus in the early stages of the 2019-20 outbreak in Wuhan: Exploring initial point-source exposure sizes and durations using scenario analysis. Wellcome Open Research 2020 5:17. 2020;5:17.

122. Paiva HM, Afonso RJM, de Oliveira IL, Garcia GF. A data-driven model to describe and forecast the dynamics of COVID-19 transmission. PLoS ONE. 2020;15(7 July).

123. He S, Tang S, Rong L. A discrete stochastic model of the COVID-19 outbreak: Forecast and control. Mathematical Biosciences and Engineering. 2020;17(4):2792-2804.

124. Lu Z, Yu Y, Chen Y, et al. A fractional-order SEIHDR model for COVID-19 with inter-city networked coupling effects. Nonlinear Dynamics. 2020;101(3):1717-1730.

125. Chen TM, Rui J, Wang QP, Zhao ZY, Cui JA, Yin L. A mathematical model for simulating the phase-based transmissibility of a novel coronavirus. Infectious Diseases of Poverty. 2020;9(1).

126. Yang CY, Wang J. A mathematical model for the novel coronavirus epidemic in Wuhan, China. Mathematical biosciences and engineering : MBE. 2020;17(3):2708-2724.

127. Shaikh AS, Shaikh IN, Nisar KS. A mathematical model of COVID-19 using fractional derivative: outbreak in India with dynamics of transmission and control. Advances in Difference Equations. 2020;2020(1):373.

128. Zongo P, Zorom M, Mophou G, Dorville R, Beaumont C. A model of COVID-19 transmission to understand the effectiveness of the containment measures: application to data from France. Epidemiology and infection. 2020;148:e221.

129. Mandal M, Jana S, Nandi SK, Khatua A, Adak S, Kar TK. A model based study on the dynamics of COVID-19: Prediction and control. Chaos, Solitons & Fractals. 2020;136:109889.

130. Carcione JM, Santos JE, Bagaini C, Ba J. A Simulation of a COVID-19 Epidemic Based on a Deterministic SEIR Model. Frontiers in Public Health. 2020;8.

131. ben Hassen H, Elaoud A, ben Salah N, Masmoudi A. A SIR-Poisson Model for COVID-19: Evolution and Transmission Inference in the Maghreb Central Regions. Arabian Journal for Science and Engineering. 2021;46(1):93-102.

132. Ali M, Imran M, Khan A. Analysis, and prediction of the COVID-19 outbreak in Pakistan. Journal of Biological Dynamics. 2020;14(1):730-747.

133. Belgaid Y, Helal M, Venturino E. Analysis of a Model for Coronavirus Spread. Mathematics. 2020;8(5):820.

134. Fitzgibbon WE, Morgan JJ, Webb GF, Wu Y. Analysis of a reaction–diffusion epidemic model with asymptomatic transmission. Journal of Biological Systems. 2020;28(03):561-587.

135. Li Y, Wang LW, Peng ZH, Shen HB. Basic reproduction number and predicted trends of coronavirus disease 2019 epidemic in the mainland of China. Infectious Diseases of Poverty. 2020;9(1):94.

136. Madubueze CE, Dachollom S, Onwubuya IO. Controlling the Spread of COVID-19: Optimal Control Analysis. Computational and mathematical methods in medicine. 2020;2020:6862516.

137. Lakman IA, Agapitov AA, Sadikova LF, et al. COVID 19 mathematical forecasting in the Russian Federation. Arterial'naya Gipertenziya (Arterial Hypertension). 2020;26(3):288-294.

138. Djilali S, Ghanbari B. Coronavirus pandemic: A predictive analysis of the peak outbreak epidemic in South Africa, Turkey, and Brazil. Chaos, Solitons & Fractals. 2020;138:109971.

139. Rocklöv J, Sjödin H, Wilder-Smith A. COVID-19 outbreak on the Diamond Princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures. Journal of Travel Medicine. 2020;27(3).

140. Distante C, Piscitelli P, Miani A. Covid-19 outbreak progression in italian regions: Approaching the peak by the end of march in northern Italy and first week of april in southern Italy. International Journal of Environmental Research and Public Health. 2020;17(9).

141. Rong X, Yang L, Chu H, Fan M. Effect of delay in diagnosis on transmission of COVID-19. Mathematical Biosciences and Engineering. 2020;17(3):2725-2740.

142. Radwan GN. Epidemiology of sars-cov-2 in Egypt. Eastern Mediterranean Health Journal. 2020;26(7):768-773.

143. Hilton J, Keeling MJ. Estimation of country-level basic reproductive ratios for novel coronavirus (sars-cov-2/ covid-19) using synthetic contact matrices. PLoS Computational Biology. 2020;16(7).

144. Bryant P, Elofsson A. Estimating the impact of mobility patterns on COVID-19 infection rates in 11 European countries. PeerJ. 2020;8:e9879.

145. Liu M, Ning J, Du Y, et al. Modelling the evolution trajectory of COVID-19 in Wuhan, China: experience and suggestions. Public Health. 2020;183:76.

146. Loli Piccolomini E, Zama F, Piccolomini EL, Zama F. Monitoring Italian COVID-19 spread by a forced SEIRD model. PloS one. 2020;15(8 August):e0237417.

147. Fredj H ben, Chérif F. Novel Corona virus disease infection in Tunisia: Mathematical model and the impact of the quarantine strategy. Chaos, Solitons & Fractals. 2020;138:109969.

148. Blasius B. Power-law distribution in the number of confirmed COVID-19 cases. Chaos: An Interdisciplinary Journal of Nonlinear Science. 2020;30(9):093123.

149. Khan MA, Atangana A. Modeling the dynamics of novel coronavirus (2019-nCov) with fractional derivative. Alexandria Engineering Journal. 2020;59(4):2379-2389.

150. Huang Q, Kang YS. Mathematical Modeling of COVID-19 Control and Prevention Based on Immigration Population Data in China: Model Development and Validation. JMIR public health and surveillance. 2020;6(2):e18638.

151. al Zobbi M, Alsinglawi B, Mubin O, Alnajjar F. Measurement Method for Evaluating the Lockdown Policies during the COVID-19 Pandemic. International journal of environmental research and public health. 2020;17(15).