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# Early insights from statistical and mathematical modeling of key epidemiologic parameters of COVID-19

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2	Article Summar	v Line:	The summary	y of current	knowledge on	parameters of d	isease

- 3 transmission will be essential for further planning and response of the COVID -19 epidemic.
- 4 Running Title: Key Epidemiological Parameters of COVID-19
- 5 Keywords: COVID-19; epidemiological parameters; mathematical modelling.
- 6 Title Key Epidemiological Parameters of COVID-19: A Review of Early Insights from
- 7 Statistical and Mathematical Modelling
- 8

9 Authors: The WHO COVID-19 Modelling Parameters Gro
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10 <sup>1</sup> Members of the group are listed at the end of the article.

11 Abstract

We report key epidemiological parameter estimates for COVID-19 identified in peerreviewed publications, pre-print articles, and online reports.

Range estimates for incubation period were 1.8 to 6.9 days, serial interval 4.0 to 7.5 days, and doubling time 2.3 to 7.4 days. The effective reproductive number varied widely, with reductions attributable to interventions. Case burden and infection fatality ratios increased with age. Implementation of combined interventions could significantly reduce cases and delay epidemic peak up to one month.

These parameters for transmission, disease severity and intervention effectiveness are
critical for guiding policy decisions. Estimates will likely change as new information becomes
available.

22 Introduction

On December 31, 2019, Chinese authorities notified the World Health Organization 23 (WHO) of a pneumonia cluster of unknown etiology in Wuhan. (1): A novel coronavirus was 24 subsequently isolated. As of March 7, 2020, the disease and causative agent, officially named 25 COVID-19 and SARS-CoV-2 respectively, had resulted in 101,927 cases and 3,486 deaths in 94 26 countries spanning 6 continents.(2) The spectrum of illness ranged from asymptomatic infection. 27 to mild disease (e.g., fever, dry cough and myalgias), pneumonia and death. Roughly 20% of 28 cases require hospitalization for shortness of breath; death is associated with increasing age and 29 underlying comorbidities (e.g., hypertension, cardiovascular disease and diabetes).(3) 30

Here, we review important parameters of COVID-19 transmission dynamics from 31 statistical and mathematical modeling studies using epidemiologic data reported in the first 60 32 days of the epidemic. We estimate the key components that contribute to future modeling on the 33 effects of non-pharmaceutical interventions (NPIs) and to inform critical resource allocation 34 decisions.(4) Data estimates are current as of March 6, 2020, a few days before WHO 35 characterized COVID-19 as a pandemic on March 11, 2020 (WHO Director General remarks, 36 https://www.youtube.com/watch?v=sbT6AANFOm4&feature=youtu.be), and subject to change 37 as more information becomes available. 38

39 Methods and Results

40	We reviewed the literature on key epidemiological parameters (Table 1) relating to the
41	COVID-19 epidemic. This is not a formal systematic review as the epidemic is rapidly
42	unfolding, and useful data sources exist that have not yet been peer-reviewed. We searched the
43	peer-reviewed and gray literature, including pre-prints, research reports, and forum posts.
44	Searches for individual parameters were conducted from February through March 6, 2020 on
45	PubMed, medRxiv, bioRxiv, arXiv, SSRN, Research Square, Virological, Imperial College
46	COVID reports, and Wellcome Open Research. Search terms centered on the various names of
47	the disease and virus over the course of the epidemic ("nCoV", "COVID", "SARS-CoV-2",
48	"novel coronavirus"), and keywords relating to each of the epidemiologic parameters or
49	characteristics considered (see Supplementary Table 1). Genetic epidemiology estimates, such as
50	evolutionary rate and time from last common ancestor were selected from Virological
51	(http://virological.org/). Articles in English and Chinese were included if they used mathematical
52	or statistical methods for adjustment of different biases and if they were either: i) Peer-reviewed
53	or ii) non-peer reviewed requiring established methods (i.e., clarity about the data used, known
54	statistical methods, and reported uncertainty).(5-8)

55

For each parameter, characteristics such as study population, assumptions, and analytical
methods were summarized when patterns were discernible across estimates. Estimates were
summarized as ranges to reflect remaining uncertainty. No meta-analyses were performed.

59

 $60 R_0 and R$ 

- 61 One of the key early indicators of transmissibility of a novel pathogen is  $R_0$ , the basic
- 62 reproduction number, which represents the average number of people infected by an incident
- 63 individual in a fully susceptible population. Values for  $R_0$  above one are considered a critical
- 64 threshold for epidemic growth. Mean  $R_0$  estimates for Hubei Province, China ranged widely, 2.1-
- 5.1 (peer-reviewed) and 2.0-7.7 (Majumder and Mandl, unpub. data,
- 66 <u>https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3524675;</u> Liu et al., unpub. data,
- 67 <u>https://www.biorxiv.org/content/10.1101/2020.01.25.919787v2</u>; Mizumoto et al., unpub. data,
- 68 <u>https://www.medrxiv.org/content/10.1101/2020.02.12.20022434v2.full.pdf;</u> Zhou, unpub. data,
- 69 <u>https://www.medrxiv.org/content/10.1101/2020.02.15.20023440v2.full.pdf;</u> Sun et al., unpub.
- data, https://www.medrxiv.org/content/10.1101/2020.02.17.20024257v1), reflecting a variety of
- assumptions and methods utilized and data uncertainty (Figure 1).(9–14) A subset of more recent
- restimates accounted for the broad restrictions implemented on January 23 in Hubei explicitly and
- 73 were lower than earlier estimates (1.0-2.9); Sun et al., unpub. data,
- 74 <u>https://www.medrxiv.org/content/10.1101/2020.02.17.20024257v1</u>; Xu et al., unpub. data,
- 75 <u>https://www.medrxiv.org/content/10.1101/2020.02.25.20024398v1</u>; Wan et al., unpub. data,
- 76 <u>https://www.medrxiv.org/content/10.1101/2020.02.16.20023804v1</u>). Mean  $R_0$  estimates for
- provinces outside of Hubei or for all of China were similar to those for Hubei before the
- implementation of travel restrictions (peer-reviewed range: 0.4-3.9; preprint range: 0.6-6.4; Liu
- 79 et al., unpub. data, <u>https://www.biorxiv.org/content/10.1101/2020.01.25.919787v2</u>; Sun et al.,
- 80 unpub. data, <u>https://www.medrxiv.org/content/10.1101/2020.02.17.20024257v1</u>; Xu et al.,
- 81 unpub. data, <u>https://www.medrxiv.org/content/10.1101/2020.02.25.20024398v1</u>; Tindale et al.,
- 82 unpub. data, <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1</u>; Shen et al.,
- 83 unpub. data, <u>https://www.biorxiv.org/content/10.1101/2020.01.23.916726v1</u>; Wang et al., unpub.

- 84 data, <u>https://www.medrxiv.org/content/10.1101/2020.02.29.20029421v1.full.pdf;</u> Ku et al.,
- unpub. data, <u>https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3543589</u>; Song et al., unpub.
- 86 data, <u>http://medrxiv.org/lookup/doi/10.1101/2020.02.29.20029421</u>).(11,14–17)  $R_0$  estimates for China
- and cases outside China attributed to exportation (peer-reviewed range: 2.1-3.2; preprint range:
- 88 2.1–5.7; Read et al., unpub. data,
- 89 <u>https://www.medrxiv.org/content/10.1101/2020.01.23.20018549v2.full.pdf;</u> Zhang and Wang,
- 90 unpub. data, <u>https://www.biorxiv.org/content/10.1101/2020.01.25.919688v3;</u> Zhou et al., unpub.
- 91 data, <u>https://www.medrxiv.org/content/10.1101/2020.02.06.20020941v1.full.pdf;</u> Volz et al.,
- 92 unpub. data, https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-
- 93 <u>fellowships/Imperial-College---COVID-19---genetic-analysis-FINAL.pdf</u>),(14,18,19),estimates
- for the Diamond Princess cruise ship (mean  $R_0$  of approximately 2.2),(20) and estimates for
- 95 Singapore and Republic of Korea (range: 2.6-3.2; Tindale et al., unpub. data,
- 96 <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1</u>) were generally lower. A
- 97 meta-analysis of seven early COVID-19 studies that accounted for uncertainty in assumptions
- 98 estimated an  $R_0$  of 2.9 (95% CI: 2.1-4.5; Park et al., unpub. data,
- 99 <u>https://www.medrxiv.org/content/10.1101/2020.01.30.20019877v4</u>).

100

High variability in  $R_0$  estimates can result from a mix of data (e.gs., time period of cases analyzed; data available by onset date), methods (e.gs.,  $R_0$  as a component of early exponential growth; fitting case data to compartmental models), and assumptions (e.gs., serial intervals; case ascertainment). In particular, serial interval estimates directly affect  $R_0$ : shorter serial intervals suggest that fewer transmission events are required for rapid growth. However, most  $R_0$ 

106 estimates reviewed here employed serial intervals values between 7.5 (COVID-19) and 8.4

107 (SARS); these differences likely had limited effects.(7,9)

109	Importantly, $R_0$ reflects average transmission, not individual-level transmission.
110	Variability (dispersion) among individual-level contacts and transmission potential can lead to
111	many individuals infecting no additional people, while others infect many as previously observed
112	for the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome
113	(MERS).(21,22) This pattern has also been observed for COVID-19 with estimates of the
114	dispersion parameter below one (e.g., 0.5 in Singapore (Tariq et al. unpub. data,
115	https://www.medrxiv.org/content/10.1101/2020.02.21.20026435v4.full.pdf), 0.54 in China (14),
116	0.58 in Shenzhen (16). This implies that a minority of cases may cause the majority of infections,
117	e.g., in Shenzhen, 8.9% of cases were found to cause 80% of infections. (16) Rigorous contact
118	tracing data are needed to improve these estimates and identify opportunities to tailor
119	interventions accordingly. (23)
120	Explicit estimates of the time-varying or effective reproduction number, $R$ (often referred
121	to as $R_t$ or $R_E$ ), can identify changes in transmission over time as a result of interventions and
122	acquired immunity. Mean estimates of $R$ before January 23 generally fall within the 2.3 to 2.6
123	range (peer-reviewed) and 3.9 to 6.2 range (preprints; Liu et al., unpub, data,
124	https://www.biorxiv.org/content/10.1101/2020.01.25.919787v2; Wang et al., unpub. data,
125	https://www.medrxiv.org/content/10.1101/2020.03.03.20030593v1).(24,25) Shortly after the
126	travel restrictions, <i>R</i> estimates ranging from 0.4-1.0 (peer-reviewed) to 0.2-3.4 (preprints)
127	indicated a decrease in transmission in Wuhan and other parts of China (Liu et al., unpub data,

- 128 <u>https://www.biorxiv.org/content/10.1101/2020.01.25.919787v2</u>; Mizumoto et al., unpub. data,
- 129 <u>https://www.medrxiv.org/content/10.1101/2020.02.12.20022434v1.full.pdf;</u> You et al., unpub.
- 130 data, <u>https://www.medrxiv.org/content/10.1101/2020.02.08.20021253v2.full.pdf;</u> Wan et al.,
- 131 unpub. data, https://www.medrxiv.org/content/10.1101/2020.02.16.20023804v1; Ku et al.,
- unpub. data, <u>https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3543589</u>; Wang et al., unpub.
- 133 data, <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20030593v1.full.pdf;</u> Chong et al.,
- unpub. data, https://www.medrxiv.org/content/10.1101/2020.03.02.20028704v1.full.pdf; Chen et
- al.,unpub data, <u>https://arxiv.org/pdf/2003.00305v1.pdf</u>).(16,24) In Singapore and the Republic of
- 136 Korea, declines in *R* estimates also suggest decreases in transmission; 1.1 to 0.7 as of February
- 137 14 in Singapore, and 1.5 (95% CI: 1.4, 1.6) in Republic of Korea up to February 27 (Tariq et al.,
- 138 unpub. data, https://www.medrxiv.org/content/10.1101/2020.02.21.20026435v6.full.pdf).(26)
- 139 The *R* estimate for the Diamond Princess cruise ship suggests high transmission before and
- immediately after movement restrictions on the ship (median *R* of 12.1 [95% CrI: 8.2, 17.2] on
- 141 February 7, two days post-quarantine), with rapid decrease thereafter (median *R* of 0.35 [95%
- 142 CrI: 0.02, 2.19] as of February 18).(27) Together, these estimates suggest  $R_0$  is high, yet

143 intensive interventions can reduce transmissibility (*R*) substantially.

144

#### 145 Incubation period

The incubation period is the time between infection and symptom onset. Seven studies
(10 estimates) were included in this review; range 1.8 to 9.0 days (Figure 2, Supplemental Tables
2 & 3; Tindale et al., unpub. data,

149 <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1</u>; Lu et al., unpub. data,

150 <u>https://www.medrxiv.org/content/10.1101/2020.02.19.20025031v1</u> ).(9,28–31) Amon
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- articles in peer-reviewed literature, the mean incubation period was 1.8 to 6.9 days.(9,28–31)
- 152

153 Serial interval

- 154 The serial interval is the average time between symptom onset of a primary and
- transmission associated secondary case. Seven studies (10 estimates) estimated the mean serial
- interval between 4.0 and 7.5 days (Figure 3, Supplemental Tables 2 & 3; Tindale et al., unpub.
- 157 data, <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1;</u> Zhao et al., unpub.
- 158 data, <u>https://www.medrxiv.org/content/10.1101/2020.02.21.20026559v1</u>).(9,31–34) Ganyni et al.
- estimated the mean generation interval of 5.21 in Singapore and 3.95 in Tianjin China.(34)
- 160

### 161 Doubling time

- 162 The doubling time is the average time period it takes for the daily case count to double.
- 163 Utilizing both genetic and case data over several locations and time periods, 11 studies estimated
- a mean doubling time of 2.3 to 7.4 days (Figure 4, Supplemental Tables 2 & 3; Rambaut, unpub.
- data, <u>http://virological.org/t/phylodynamic-analysis-176-genomes-6-mar-2020/356;</u> Bedford,
- 166 unpub. data, <u>http://virological.org/t/phylodynamic-estimation-of-incidence-and-prevalence-of-</u>
- 167 <u>novel-coronavirus-ncov-infections-through-time/391</u>; Pinotti et al., unpub. data,
- 168 <u>https://www.medrxiv.org/content/10.1101/2020.02.24.20027326v1</u>; Zhao et al., unpub. data,
- 169 <u>https://www.medrxiv.org/content/10.1101/2020.02.06.20020941v1;</u> Volz et al., unpub. data,

- 170 <u>https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-</u>
- 171 <u>College---COVID-19---genetic-analysis-FINAL.pdf</u>).(9,11,15,18,19,35)
- 172
- 173 Infectious period
- 174 The infectious period is the period of time in which an infected host, with or without
- symptoms, can transmit to susceptible individuals. One estimate (You et al., unpub. data,
- 176 <u>https://www.medrxiv.org/content/10.1101/2020.02.08.20021253v2</u>). Based on data from 67
- 177 cases, estimated a mean infectious period of 10.91 days (standard deviation, 3.95 days). Little is
- 178 known about how characteristics of an infected person, such as age, severity and clinical
- 179 progression, affect overall infectious period estimates.
- 180
- 181 Severity
- 182 Clinical progression
- We did not identify mathematical or statistical models that examine clinical disease
  progression. We include empiric findings detailed in the WHO China mission report, which has
  been used to inform other models.(36)
- 186
- 187 Within China

The majority of >75,000 cases of COVID-19 reported through March 6 have been from
Hubei province. Among 55,924 confirmed cases in China as of February 20, the median age was

51 years (range 2 days-100 years) with most between 30–69 years (77.8%). The clinical
distribution was: 80.4% mild/moderate, 13.8% severe and 6.1% critically ill (Supplemental
Table 4). Only 2.4% of reported cases were among persons < 19 years old.(36) Severe disease</li>
was reported among those with increased age (over 60) and comorbidities such as hypertension,
diabetes, cardiovascular disease, chronic respiratory disease, and cancer.(37) Fatality estimates
have come primarily from elderly Wuhan residents,(38) suggesting substantially higher lethality
compared with outside Hubei (Figure 5).

197 *Outside China* 

The age-distribution of cases and deaths detected outside China has been wider than that within China.(38) This difference may result from higher sensitivity surveillance for travelers compared to cases within China, particularly in countries on high alert, such as Thailand and Japan, which implemented temperature screening at airports. In general, early severe cases are more likely to be detected than mild cases resulting in higher severity estimates early on. Cases among travelers might also generally be younger due to age-specific differences in travel.

A broader spectrum of clinical severity has been observed in travel-associated and locally acquired cases reported outside of China, likely reflecting more robust surveillance for SARS-CoV-2. Severity ranges from asymptomatic infection, to symptoms such as fever and fatigue, as well as mild to severe respiratory symptoms including cough and pneumonia. Cases have been reported in persons with previously good health and no known comorbidities.(39) Differences in severity have also been observed within transmission chains.(40–43)

211 Case and Infection Fatality Ratio

212	The case fatality ratio (CFR) is the proportion of cases which result in death. There are
213	several variations of CFR, including symptomatic (sCFR), laboratory-confirmed (cCFR),
214	hospitalization (HFR), and infection (IFR). Eleven studies, estimating either CFR or a variation
215	of CFR, were included in this review (Figure 5). Most estimates were based on data from China.
216	However, a few are from outside China or from the Diamond Princess cruise ship (38,44)
217	Estimates of CFR generally did not include specific case definitions, and ranged from 0.9% to
218	18.9%. Moreover, CFR is highly variable across situations (i.e., general population, hospitalized
219	or critically ill). Critically ill patients' central estimates range between 8.0% and 28.7% (Deng et
220	al., unpub. data, https://www.medrxiv.org/content/10.1101/2020.03.04.20031005v1). Notably,
221	IFR seems to be more consistent across studies, with central estimates around 0.6% in two peer-
222	reviewed studies from mainland China (38,44), yet higher at 3.3% in Hubei, China, 3% in
223	Northern Italy (Hauser et al., unpub. data,
224	https://www.medrxiv.org/content/medrxiv/early/2020/03/30/2020.03.04.20031104.full.pdf), and
225	and lower at 0.2% to 1.6% in Asia and Europe (Figure 5 and Supplementary Table 5).
226	
227	There was evidence of a strong age-gradient in both CFR and IFR, with the elderly being
228	at a higher risk.(42) IFR presents a strong age gradient, with an IFR of 0.007% in children,
229	between 1.9% and 4.6% in those aged 60-69, and between 7.8% and 18% in those aged >80 (38).
230	Hospitalization rates were also age dependent:<0.04% in children, 11.8% in those aged 60-69
231	and 18.4% among those aged 80 or more (38).

- 233 Viral Evolution and Genomic Epidemiology
- Virus genome sequences from a representative sample of cases can be used for
- calculating the evolutionary rate, date of introduction to the human population, size of outbreak,
- and estimating the reproduction number.(45–48) The evolutionary rate is the rate at which
- mutations accumulate per base pair in the genome over the course of a year. Estimates have
- ranged from  $0.8 \times 10^{-3}$  to  $1.2 \times 10^{-3}$  (Table 2; Sciré et al., unpub. data,
- 239 <u>http://virological.org/t/update-2-evolutionary-epidemiological-analysis-of-128-genomes/423;</u>
- 240 Duchene et al., unpub. data, <u>http://virological.org/t/temporal-signal-and-the-evolutionary-rate-of-</u>
- 241 <u>2019-n-cov-using-47-genomes-collected-by-feb-01-2020/379</u>; Hill and Rambaut, unpub. data,
- 242 <u>http://virological.org/t/phylodynamic-analysis-of-sars-cov-2-update-2020-03-06/420;</u> Rambaut,
- 243 unpub. data, <u>http://virological.org/t/phylodynamic-analysis-176-genomes-6-mar-2020/356;</u>
- 244 Bedford, unpub. data, <u>http://virological.org/t/phylodynamic-estimation-of-incidence-and-</u>
- 245 prevalence-of-novel-coronavirus-ncov-infections-through-time/391). These evolutionary rates
- are similar to that of MERS-CoV and SARS-CoV-1. The data suggests that the COVID-19
- outbreak was started by a single spillover event occurring in late 2019 (Table 2), and supported
- by first case reported data in December 2019 (Sciré et al., unpub. data,
- 249 <u>http://virological.org/t/update-2-evolutionary-epidemiological-analysis-of-128-genomes/423;</u>
- 250 Duchene et al., unpub. data, <u>http://virological.org/t/temporal-signal-and-the-evolutionary-rate-of-</u>
- 251 <u>2019-n-cov-using-47-genomes-collected-by-feb-01-2020/379</u>; Hill and Rambaut, unpub. data,
- 252 http://virological.org/t/phylodynamic-analysis-of-sars-cov-2-update-2020-03-06/420; Rambaut,
- unpub. data, <u>http://virological.org/t/phylodynamic-analysis-176-genomes-6-mar-2020/356;</u>
- 254 Bedford, unpub. data, <u>http://virological.org/t/phylodynamic-estimation-of-incidence-and-</u>
- 255 prevalence-of-novel-coronavirus-ncov-infections-through-time/391; Volz et al., unpub. data,

- 256 https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-
- 257 <u>College---COVID-19---genetic-analysis-FINAL.pdf</u>).(49) Analysis of viral genomes can also be
- used to estimate doubling time and reproduction number.
- 259
- 260 Effectiveness of Non-Pharmaceutical Interventions (NPIs)
- 261 NPIs include interventions at individual and community levels. At the individual level, NPIs
- examined in modeling studies included voluntary home isolation or quarantine (Supplementary
- Table 6). At the community level, NPIs included school and workplace closures and canceling or
- 264 postponing large public gatherings (see Supplementary Table 7 for definitions). Modeling can be
- used to estimate the effectiveness of components of these interventions (e.g. case detection), the
- interventions themselves (e.g. case isolation) or combinations of interventions (e.g. case and
- contact isolation). In total, 29 articles were identified; of these, 17 met the inclusion criteria for
- this review (Table 3; Pinotti et al., unpub. data,
- 269 <u>https://www.medrxiv.org/content/10.1101/2020.02.24.20027326v1</u>; Niehus et al., unpub. data,
- 270 <u>https://www.medrxiv.org/content/10.1101/2020.02.13.20022707v2</u>; Gostic et al., unpub. data,
- 271 <u>https://www.medrxiv.org/content/10.1101/2020.01.28.20019224v2</u>; Adiga et al., unpub. data,
- 272 <u>https://www.medrxiv.org/content/10.1101/2020.02.20.20025882v2</u>; Lai et al., upub. data,
- 273 <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029843v3.full.pdf;</u> Zhang et al., unpub.
- data, <u>https://www.medrxiv.org/content/10.1101/2020.03.04.20031187v1</u>; Clifford et al., unpub.
- data, <u>https://cmmid.github.io/topics/covid19/screening-outbreak-delay.html;</u> Bhatia et al., unpub.
- 276 data https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-

- 277 <u>fellowships/Imperial-College-COVID19-international-surveillance-21-02-</u>
- 278 <u>2020.pdf</u>).(11,15,18,50–55)
- 279
- 280 Case screening and detection
- 281 Recent articles have addressed the efficacy of screening and detection by surveillance
- systems in different countries (Pinotti et al., unpub. data,
- 283 <u>https://www.medrxiv.org/content/10.1101/2020.02.24.20027326v1</u>; Niehus et al., unpub. data,
- 284 <u>https://www.medrxiv.org/content/10.1101/2020.02.13.20022707v2;</u> Bhatia et al., unpub. data
- 285 https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-
- 286 <u>College-COVID19-international-surveillance-21-02-2020.pdf</u>).(50) Two studies used data from
- 287 Singapore (known for having a reliable health reporting system) as benchmarks to estimate the
- sensitivity of surveillance systems in other countries (Niehus et al., unpub. data,
- 289 <u>https://www.medrxiv.org/content/10.1101/2020.02.13.20022707v2;</u> Bhatia et al., unpub. data
- 290 https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-
- 291 <u>College-COVID19-international-surveillance-21-02-2020.pdf</u>). Both articles agreed that only a
- fraction of cases (22%-64%) are captured by surveillance systems, varying by country. A more
- recent study found similar results (36% detected cases), and lower ascertainment when
- 294 repatriations were considered (Pinotti et al., unpub. data,
- 295 <u>https://www.medrxiv.org/content/10.1101/2020.02.24.20027326v1</u>).
- 296
- 297 Case isolation and quarantine of contacts

298	One study considered different scenarios in which the reproduction number and
299	transmission before symptom onset were varied to study the controllability of the outbreak.(50)
300	The authors found that as R <sub>0</sub> increased, the percentage of contacts to be traced increased. The
301	delay between symptom onset and isolation also affected the controllability of the outbreak. For
302	values of $R_0 > 2.5$ , contact tracing and isolation were successful at stopping transmission when <
303	1% of transmission occurred before symptom onset. For these two parameters, case isolation
304	alone would be unlikely to control transmission within 3 months.
305	
206	Traveler screening
306	Traveler screening
307	Two studies considered models in which passengers are screened before departing an
308	area with local transmission and upon arrival to destination (Gostic et al., unpub. data,
309	https://www.medrxiv.org/content/10.1101/2020.01.28.20019224v2).(51), demonstrating that a
310	relatively low number of cases would likely be detected (34%-54%). Different factors affect the
311	under-detection of cases, including country ability to detect them. Some of those factors include
312	asymptomatic infections, infections with mild clinical symptoms, limited care-seeking behavior,
313	case definition, and under-recognition of cases by clinicians. A third study suggests that exit and
314	entry screening combined with traveler sensitization can delay a local outbreak by $\geq 83$ days,
315	with no > 1 infected traveler per week (Clifford et al., unpub. data,
316	https://cmmid.github.io/topics/covid19/screening-outbreak-delay.html).
317	

318 Travel restrictions

On January 23, 2020, travel bans were implemented from Wuhan city. Within China, this 319 resulted in a delay of three days, on average, of disease arrival.(52) Cities, implementing the ban 320 before their first case was detected observed fewer cases than cities implementing the ban after 321 their first case.(52) Another study found that 130 cities in China had >50% chance of having a 322 COVID-19 case imported from Wuhan in the three weeks preceding the implementation of travel 323 restrictions, suggesting that there were cases outside of Wuhan before the travel ban.(15) 324 Analysis of the effect of the Wuhan travel ban, including the implementation of long-range travel 325 restrictions on January 23, showed no noticeable difference for the epidemic trajectory of 326 Wuhan, while delaying the occurrence of cases for other locations in China by three days.(18) 327 Another study found that travel restrictions would delay the epidemic spread throughout China 328 by two days.(53) 329

330

Internationally, several countries implemented travel bans. One modeling study estimated how travel restrictions from China impacted time of arrival of the infected individuals (Adiga et al., unpub. data, <u>https://www.medrxiv.org/content/10.1101/2020.02.20.20025882v2</u>). It found that countries in Africa and South America would likely observe the biggest delay, 11 and 9 day, respectively. Another study found that travel reductions of up to 90% of had only a modest effect unless paired with public health interventions and behavioral changes to achieve a considerable reduction in disease transmission.(18)

338

339

Cancellation of events and public gatherings

One study analyzed a range of interventions such as suspending public transport, closing entertainment venues, and banning public gatherings.(52) Varying by city and number of control measures adopted, the study found that cities that implemented a Level 1 response (at least two control measures) before the first case was confirmed had 37% fewer cases in the week after the first case identified compared with cities that started control thereafter. Locations that closed entertainment venues and banned public gatherings early in the outbreak reported fewer cases during the first week.

347

Finally, four studies estimated the effects of transmission reduction in China when NPImitigation strategies were combined (Lai et al., upub. data,

350 <u>https://www.medrxiv.org/content/10.1101/2020.03.03.20029843v3.full.pdf</u>).(11) The combined

interventions significantly reduced the number of cases observed and delayed epidemic peak by

 $\frac{>1}{>1}$  month. It was found that earlier intervention of social distancing could significantly limit the

epidemic in mainland China. The number of infections could have been reduced up to 98.9%,

and the number of deaths reduced by 99.3% as of Feb 23, 2020 (Zhang et al., unpub. data,

355 <u>https://www.medrxiv.org/content/10.1101/2020.03.04.20031187v1</u>). A different group found

that following the implementation of control measures, growth rates became negative in most

357 locations, and that drastic control measures implemented in China substantially mitigated

358 COVID-19 spread.(55)

359

361 Community behavior modification

362 One research group performed an online survey after the first case of COVID-19 was 363 reported in Hong Kong. Their results showed that 39%-88% of the people surveyed had adopted 364 social distancing measures.(54)

#### 365 **Discussion**

Modeling can provide estimates of disease transmission parameters for planning and 366 response during epidemics. Investigators around the world have been trying to understand the 367 368 transmission dynamics and severity of disease, as well as the effects that different interventions have had on the course of the epidemic through advanced analytics and modeling. However, 369 transmission parameter estimates are limited by the availability and comprehensiveness of data 370 early in the epidemic. Some parameters can be estimated from genetic sequencing data, but these 371 estimates are heavily influenced by biases in sampling and inaccuracies in sequencing. Although 372 efforts to collect and share clinical, epidemiological, and sequence data have been remarkably 373 timely, there remain outstanding gaps in knowledge. 374

375

Several parameters presented in this review are context specific, such as  $R_0$  values or CFR measurements. Although the characteristics of SAR-CoV-2 are unlikely to change, responses to transmission will vary. Several factors affect the trajectory of an epidemic in different locations, such as population density, health system infrastructure, transportation robustness, cultural practices, and poverty levels.(56) Available data from China may not be

reflective of secular trends elsewhere. As other countries develop more cases, more robust datawill be available for modeling and extrapolation for countries not yet affected.

383

Challenges in assessing severity of clinical outcomes during an new emerging epidemic 384 have been discussed in-depth elsewhere and are not covered here. (7,8) However, there remain 385 four challenges. First, early in an outbreak, data are heavily biased towards severe cases. 386 Estimates of the CFR in those patients with known outcomes may be biased upwards until the 387 extent of clinically milder disease is determined. Second, there is a period between onset of 388 symptoms and final clinical outcome (death vs survival).(57.58) During a growing epidemic, the 389 final clinical outcome of most reported cases is typically unknown. This is particularly true with 390 COVID-19 where severely ill patients may be hospitalized for many days. The crude CFR will 391 underestimate the fatality risk among early epidemic cases. (7,8,58) Third, while the epidemic is 392 growing there will be a bias towards having observed cases with recent symptom onset and 393 outcomes. Therefore, estimates should be adjusted for the growth rate of the epidemic.(8) Fourth, 394 over-representation of men, elderly people with co-morbidities and people with respiratory risk 395 factors (smoking, etc.) may result from observation bias or exposure differences and affect CFR 396 estimates. 397

398

Country preparedness and clinical care capacity will affect patient outcomes. Delayed
diagnosis and treatment, limited knowledge of the natural history of infection, and rapid
escalation of cases can affect clinical outcomes Thus, fatality in patients cared for very early in a
country's epidemic may be greater than for later patients.(7) More information on the proportion

of individuals requiring healthcare, level (outpatient, inpatient and intensive care) and duration
of care required are essential for predicting healthcare needs as the epidemic progresses.

405

406	Pre-symptomatic or asymptomatic transmission, if substantial, might have critical
407	implications for control efforts. Empiric evidence of such potential transmission includes: i) a
408	serial interval and generation time that were estimated shorter than the incubation period,
409	(Tindael et al., unpub.data, https://www.medrxiv.org/content/10.1101/2020.03.03.20029983v1;
410	Lu et al., unpub. data, <u>https://www.medrxiv.org/content/10.1101/2020.02.19.20025031v1</u> ); ii)
411	similarly high viral load in asymptomatic and symptomatic cases;(34,59) and iii) documentation
412	of cases infected by pre-symptomatic or asymptomatic carriers in cluster investigations.(60-63)
413	If asymptomatic infectious carriers are not characterized appropriately in models, epidemic
414	infection rates would be underestimated, while the severity and the effectiveness of interventions
415	would be overestimated, potentially leading to implementation of ineffective interventions.
416	Serological studies will be critical for understanding the role of asymptomatic transmission.
417	
418	Early evidence suggests that travel restrictions result in only modest decreases in the
419	importation of cases. However, combined with other social distancing measures and behavior
420	changes, travel restrictions may be a useful addition. Modeling can be extremely valuable in
421	providing counterfactuals aimed at disentangling the effects of different NPIs. Documentation of
422	timing, type of NPI, and compliance rate will be needed to estimate the effectiveness of the
423	different interventions.

This paper is subject to additional limitations. To utilize the latest information, we included a number of pre-print reports that have not been formally peer-reviewed. Additionally, there is a heavy reliance on data from China, due to the period considered. Given the recent geographic spread of COVID-19, there may be a range of future estimates that will differ from those reported here. Finally, we have not performed a formal assessment of possible biases of the estimates examined in this paper, and therefore cannot exclude that some estimates reported are affected by unmeasured sources of biases.

432

As the COVID-19 epidemic progresses, ongoing refinement and validation of key 433 434 epidemiological parameters will help inform the global public health response. Defining optimal surveillance methods, laboratory testing, contact tracing parameters, quarantine measures, 435 hospital acute care capacities, and many other operational factors, depends on estimates of the 436 epidemiological parameters summarized in this paper. One of the largest knowledge gaps are 437 those of asymptomatic or pre-symptomatic infectious potential and the occurrence of subclinical 438 infections. In the absence of efficacious vaccines and therapeutics, developing an evidence-base 439 for NPIs will remain a critical tool for effective local, national, and global outbreak control. 440 Better data will enable mathematical and statistical modeling to more precisely predict how 441 different NPIs can be combined to produce efficient epidemic control. 442

443

Our summary provides estimates through the first 10 weeks of the COVID-19 epidemic
that are needed for operational planning, scenario-building for contingency planning and
forecasting to inform today's preparedness and response efforts. Data from outbreaks in newly

- 447 affected countries and new data stemming from sero-prevalence and transmission studies will
- 448 provide insights currently unavailable. Documenting and evaluating NPIs will help public health
- and government decision makers to implement the most effective epidemic control measures.

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670

## 671 Tables

#### Table 1. Key parameters and definitions

Parameter	Definition
Basic Reproduction Number (R₀)	The average number of people infected by a single infected individual in a fully susceptible population
Time-varying or effective reproduction number (R, R <sub>t</sub> , R <sub>E</sub> )	The average number of people infected by an infected individual in a population in the context of changing transmission patterns such as those resulting from interventions and acquired immunity
Incubation Period	The time between infection and symptom onset
Serial Interval	The average time between symptom onset of a primary case and symptom onset of linked secondary cases
Generation Interval	The average time between infection of a primary case and infection of linked secondary cases
Doubling Time	The average time period it takes for the daily case count to double
Infectious Period	The period of time in which an infected host, with or without symptoms, can transmit an infectious agent to susceptible individuals, directly or indirectly
Case Fatality Ratio (CFR)	The proportion of cases which result in death (with case defined in numerous ways)
Infection Fatality Ratio (IFR)	The proportion of all infections (including confirmed, symptomatic, asymptomatic, etc.) which result in death
Mean Evolutionary rate	The average rate at which mutations accumulate per base pair in the genome over the course of a year

Table 2. Summary of Estimates of Mean Evolutionary Rate and Most Recent Common Ancestor(MRCA)

Mean Evolutionary Rate (95% CI)*	MRCA (95% CI)	Number of Genomes in Analysis	Clock Model**	Growth Model	Source
-	29 Nov 2019 (8 Nov 2019 – 16 Dec 2019)	23	Strict	Constant	Rambaut, unpub. data, http://virologic al.org/t/phylog enetic- analysis-of-23- ncov-2019- genomes- 2020-01- 23/335
1.23x10 <sup>-3</sup> (0.56x10 <sup>-</sup> <sup>3</sup> - 1.98x10 <sup>-3</sup> )	21 Nov 2019 (23 Oct 2019 - 13 Dec 2019)	51	Strict	Exponential	Duchene et al., unpub. data, http://virologic al.org/t/tempor al-signal-and- the- evolutionary- rate-of-2019- n-cov-using- 47-genomes- collected-by- feb-01- 2020/379.
1.29x10 <sup>-3</sup> (0.535x10 <sup>-4</sup> - 2.15x10 <sup>-3</sup> )	14 Nov 2019 (28 Sept 2019- 13 Dec 2019)	51	UNCL***	Exponential	Duchene et al., unpub. data, http://virologic al.org/t/tempor al-signal-and- the- evolutionary- rate-of-2019- n-cov-using- 47-genomes- collected-by- feb-01- 2020/379.
0.9x10 <sup>-3</sup> (0.5x10 <sup>-3</sup> - 1.4x10 <sup>-3</sup> )	3 Dec 2019 (30 Oct 2019- 17 Dec 2019)	51	Strict	Exponential	Bedford, unpub. data, http://virologic al.org/t/phylod ynamic- estimation-of- incidence-and- prevalence-of- novel- coronavirus- ncov- infections- through-

					time/391.
0.92x10 <sup>-3</sup> (0.33x10 <sup>-</sup> <sup>3</sup> - 1.46x10 <sup>-3</sup> )	29 Nov 2019 (28 Oct 2019 - 20 Dec 2019)	75	Strict	Exponential	Rambaut, unpub. data, http://virologic al.org/t/phylod ynamic- analysis-176- genomes-6- mar-2020/356. Accessed March 4, 2020
1.04x10 <sup>-3</sup> (0.71x10 <sup>-</sup> <sup>3</sup> - 1.4x10 <sup>-3</sup> )	3 Dec 2019 (16 Nov 2019 - 17 Dec 2019)	116	Strict	Exponential	Hill and Rambaut, unpub. data, http://virologic al.org/t/phylod ynamic- analysis-of- sars-cov-2- update-2020- 03-06/420
7.41x10 <sup>-4</sup> (4.91x10 <sup>-</sup> <sup>4</sup> - 1.02x10 <sup>-3</sup> )	27 Nov 2019 (7 Nov 2019- 11 Dec 2019)	128	Strict	Birth Death Model	Sciré et al., unpub. data, http://virologic al.org/t/update -2- evolutionary- epidemiologic al-analysis-of- 128- genomes/423

# 676 \* confidence interval

<sup>677</sup> \*\*The Clock Model is a technique that uses the mutation rate to estimate the time of emergence.

678 (47)

679 \*\*\*Uncorrelated

# Table 3. Summary of the studies of non-pharmaceutical interventions (NPI)

Non-pharmaceutical intervention	Summary/Results	Source
Case detection	(27% - 37%) cases detected*	Bhatia et al., unpub. data, https://www.impe rial.ac.uk/media/ii mperial- college/medicine/ sph/ide/gida- fellowships/Imper ial-College- COVID19- international- surveillance-21- 02-2020.pdf
Case detection	38% (22%-64%) cases detected	Niehus et al., unpub. data, https://www.medr xiv.org/content/1 0.1101/2020.02. 13.20022707v2
Case screening and detection	(36%-65%) cases detected*	Pinotti et al., unpub. data, https://www.medr xiv.org/content/1 0.1101/2020.02. 24.20027326v1
Case isolation and contact tracing	Delay of onset symptoms to isolation has a high impact on the results, affecting the controllability of the outbreak. Results vary by scenario.	50
Travel screening	34% (20%-50%) travelers identified through both departure and arrival screening using symptoms or risk screening	Gostic et al., unpub. data, https://www.medr xiv.org/content/1 0.1101/2020.01. 28.20019224v2
Travel screening	46.5% (35.9% - 57.7%) travelers not detected through thermal screening	51

Travel screening	Syndromic screening and traveler sensitization in combination could delay outbreaks in yet unaffected countries up to 83 days (75% 36 days, 97.5% 8 days)	Clifford et al., unpub. data, https://cmmid.git hub.io/topics/covi d19/screening- outbreak- delay.html
Travel reduction (transport suspension)	Delay of 2.91 days (95% CI: 2.54-3.29) for the arrival of the disease to other cities in China.	52
Travel reduction (travel quarantine)	130 cities in China had ≥ 50% chance of having a COVID-19 case imported from Wuhan in the 3 weeks preceding the quarantine	15
Travel restrictions	Travel restriction imposed on Wuhan delay the epidemic for 3 days	18
Travel reduction (airline suspensions)	Travel restriction imposed on China will delay the disease in other countries, the biggest delay being in Africa (11 days) and South America (9 days)	Adiga et al., unpub. data, https://www.medr xiv.org/content/1 0.1101/2020.02. 20.20025882v2;
Travel reduction	Travel restriction will delay the epidemic for 2 days.	53
Cancellation of mass gathering	37% fewer cases when the interventions started before the first case.	52
Combination of NPI	66%, 86%, and 95% fewer cases depending on the timing of the interventions	Lai et al., upub. data, https://www.medr xiv.org/content/1 0.1101/2020.03. 03.20029843v3.f ull.pdf
Combination of NPI	50% fewer cases if transmissibility reduced by 25% in all cities in China. Delay of epidemic peak for one month.	11

Combination of NPI	Drastic control measures implemented in China have substantially mitigated the spread of COVID-19	34
Combination of NPI	Earlier intervention of social distancing could significantly limit the epidemic in mainland China. The number of infections could be reduced up to 98.9%, and the number of deaths could be reduced by up to 99.3% as of Feb 23, 2020	Zhang et al., unpub. data, <u>https://www.medr</u> <u>xiv.org/content/1</u> <u>0.1101/2020.03.</u> 04.20031187v1
Community behavior modification	At least 42% of the people interviewed have modified daily behavior.	54

## 682 \*point estimates

# 684 Legends for Figures

685	Figure 1. Basic reproduction number ( $R_0$ ) estimates by date of last reported cases
686	analyzed and location. Points are mean or median estimates and error bars indicate 90% (12, 13,
687	18) or 95% bounds (i.e. confidence or credible intervals). International-China estimates are those
688	using international cases or exported cases from China to infer $R_0$ in China or Hubei. Estimates
689	for China refer to R <sub>0</sub> estimates at the national or province level, except for those exclusive
690	estimating $R_0$ for Hubei (China-Hubei).
691	Figure 2. Estimated incubation period based on search in peer-reviewed (top) and gray
692	literature (bottom). Point are mean, triangles are median estimates (if applicable) and error bars
693	indicate confidence (blue) or credible intervals (red).
694	Figure 3. Estimated serial interval based on search in peer-reviewed literature (top) and
695	gray literature (bottom). Point are mean estimates, triangles are median estimates (if applicable)
696	and error bars indicate confidence (blue) or credible intervals (red).
697	
698	Figure 4. Estimated doubling time based on search in peer-reviewed literature (top) and
699	gray literature (bottom). Point are mean estimates and error bars indicate confidence (blue) or
700	credible intervals (red).
701	
702	Figure 5. Summary of CFR and IFR estimates. Point are mean or median estimates and

error bars indicate confidence (dotted line) or credible intervals (full line). Red color refers to

704 Peer-reviewed and blue to non-Peer-reviewed papers.

# 705 Supplementary Figures and Tables

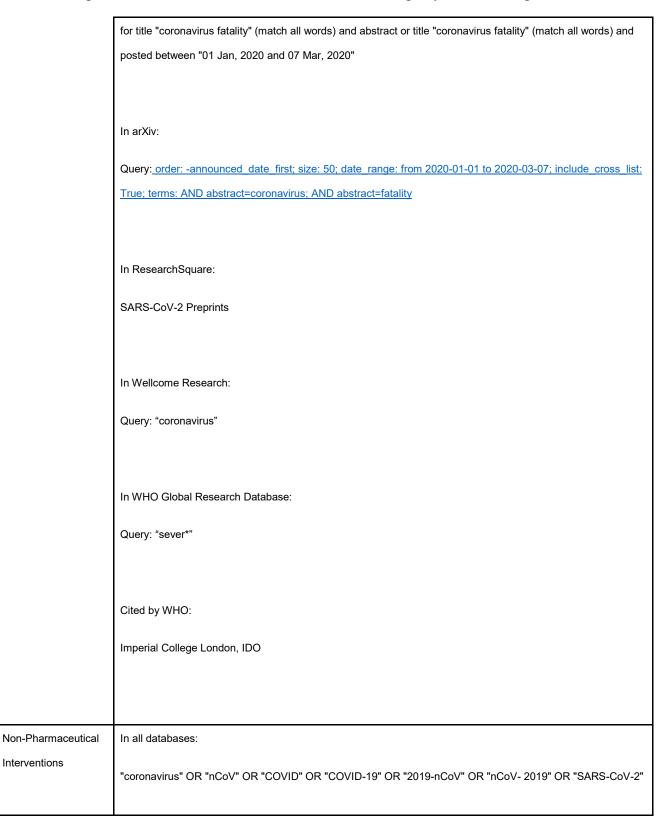
### 706 Supplementary Table 1- Search Terms

Торіс	Search Terms
Virus Evolution	"nCoV", "2019-nCoV", "nCoV-2019", "COVID", "COVID-19", "novel coronavirus", "SARS-CoV-2"
	AND
	"evolution*" or "phylogenetics"
Incubation period	In PubMed, medRxiv, bioRxiv and arXiv:
	#1: "incubation period"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	#3: #1 AND #2
	In SSRN:
	#1: "incubation period"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	#3: #1 AND search within each of the term in #2
	In research square, Virological, and Wellcome Open Research:

	#1: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
	CoV-2"
	Then read through all the papers
Serial interval	In PubMed:
	#1: "serial interval" OR "generation interval" OR "generation time" OR "serial distribution" OR "secondary infections" OR "secondary cases"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	#3: #1 AND #2
	In medRxiv, bioRxiv, and arXiv:
	#1: "serial interval"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
	CoV-2"
	#3: #1 AND #2
	In SSRN:
	#1: "serial interval"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
	CoV-2"
	#3: #1 AND search within each of the term in #2
	In research square, Virological, and Wellcome Open Research:

	#1: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	Then read through all the papers
Generation interval	In PubMed and arXiv:
	#1: "generation interval"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	#3: #1 AND #2
	In medRxiv and bioRxiv:
	"generation interval" for full text or abstract or title (match whole all)
	In SSRN:
	#1: "generation interval"
	#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	#3: #1 AND search within each of the term in #2
	In research square, Virological, and Wellcome Open Research:
	#1: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS- CoV-2"
	Then read through all the papers

In PubMed, medRxiv, bioRxiv and arXiv:
#1: "doubling time" OR "growth rate"
#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
CoV-2"
#3: #1 AND #2
In SSRN:
#1: "doubling time" OR "growth rate"
#2: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
CoV-2"
#3: #1 AND search within each of the term in #2
In research square, Virological, and Wellcome Open Research:
#1: "coronavirus" OR "nCoV" OR "COVID" OR "COVID-19" OR "2019-nCoV" OR "nCoV-2019" OR "SARS-
CoV-2"
Then read through all the papers
In PubMed:
("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "2019-ncov"[All Fields] OR "COVID-19"[All Fields]
OR "COVID"[All Fields] OR "SARS-COV-2"[All Fields] OR "ncov"[All Fields] OR "ncov-2019"[All Fields]) AND
"2019/12/31 00.00"[MHDA] : "2020/03/06 23.59"[MHDA] AND ("fatality"[All Fields] OR "Case Fatality"[All Fields]
OR "Infection Fatality"[All Fields])
In biorXiv & medrXiv:



- Supplementary Table 2. Summary of the published study included in the review of incubation
- 710 period, serial interval, doubling time and generation interval.

Study	Study setting	Incubation period	Serial interval	Doubling time	Generation interval
		(days)	(days)	(days)	(days)
Backer 2020	88 confirmed	Mean: 6.4,	NA	NA	NA
(28)	cases detected	Median: NA,			
	outside of	SD: 2.3,			
	Wuhan from 20	95% Crl: 5.6 to 7.7 based			
	Jan 2020 to 28	on Weibull distribution			
	Jan 2020				
Chinazzi 2020	Modeling study	NA	NA	4.2 (90% CI: 3.8 to 4.7)	NA
[18]				based on reporting	
				dates	
Du 2020a [15]	Modeling study	NA	NA	7.31 (95% Crl: 6.26 to	NA
				9.66) based on onset	
				dates	
Ganyani 2020	Modeling study	NA	Mean: 5.21,	NA	Mean: 5.20,
(34)			Median: NA,		Median: NA,
			SD: 4.32,		SD: 1.72,
			95% Crl: -3.35 to		95% Crl: 3.78 to 6.78
			13.94 in Singapore		in Singapore

Ganyani 2020	Modeling study	NA	Mean: 3.95,	NA	Mean: 3.95,
(34)			Median: NA,		Median: NA,
			SD: 4.24,		SD: 1.51,
			95% Crl: -4.47 to		95% Crl: 3.01 to 4.91
			12.51 in Tianjin, China		in Tianjin, China
Jung 2020	Modeling study	NA	NA	2.39 (95% CI: 1.93 to	
(19)				3.15) from 20 exported	
				cases reported by 24	
				Jan 2020, calculated by	
				growth rate of 0.29	
				(95% CI: 0.22 to 0.36)	
				based on reporting	
				dates	
Leung 2020	175 confirmed	Mean: 1.8,	NA	NA	
(30)	patients in China	Median: NA,			
	from 20 Jan	SD: NA,			
	2020 to 12 Feb	95% CI: 1.0 to 2.7			
	2020	based on travelers to			
		Hubei fitting to Weibull			
		distribution;			
Leung 2020	175 confirmed	Mean: 7.2,	NA	NA	
(30)	patients in China	Median: NA,			
	from 20 Jan	SD: NA,			
	2020 to 12 Feb	95% CI: 6.1 to 8.4			
	2020	based on non-travelers			
		fitting to Weibull			
		distribution			

Li 2020 (9)	425 confirmed	Mean: 5.2,	Mean: 7.5,	7.4 (95% CI: 4.2 to
	cases in Wuhan	Median: NA,	Median: NA,	14.0) based on onset
	as of 22 Jan	SD: NA,	SD: 3.4,	dates
	2020	95% CI: 4.1 to 7.0	95% CI: 5.3 to 19.0	
		based on log-normal	based on gamma	
		distribution	distribution	
Linton 2020	158 confirmed	Mean: 5.6,	NA	NA
(29)	cases in and	Median: NA,		
	outside of	SD: NA,		
	Wuhan as of 31	95% Crl: 5.0 to 6.3		
	Jan 2020 (52	based on 158 cases;		
	cases when			
	excluding			
	Wuhan			
	residents)			
Linton 2020	158 confirmed	Mean: 5.0,	NA	NA
Linton 2020 (29)	158 confirmed cases in and	Mean: 5.0, Median: NA,	NA	NA
			NA	NA
	cases in and	Median: NA,	NA	NA
	cases in and outside of	Median: NA, SD: NA,	NA	ΝΑ
	cases in and outside of Wuhan as of 31	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0	NA	ΝΑ
	cases in and outside of Wuhan as of 31 Jan 2020 (52	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0	NA	ΝΑ
	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0	NA	ΝΑ
	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0	NA	ΝΑ
	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0	NA Mean: 4.7,	NA
(29)	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents)	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases		
(29) Nishiura 2020	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents) 28 infector-	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases	Mean: 4.7,	
(29) Nishiura 2020	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents) 28 infector- infectee pairs	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases	Mean: 4.7, Median: 4.0,	
(29) Nishiura 2020	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents) 28 infector- infectee pairs from published	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases	Mean: 4.7, Median: 4.0, SD: 2.9,	
(29) Nishiura 2020	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents) 28 infector- infectee pairs from published research articles	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases	Mean: 4.7, Median: 4.0, SD: 2.9, 95% Crl: 3.7 to 6.0	
(29) Nishiura 2020	cases in and outside of Wuhan as of 31 Jan 2020 (52 cases when excluding Wuhan residents) 28 infector- infectee pairs from published research articles as of 12 Feb	Median: NA, SD: NA, 95% Crl: 4.2 to 6.0 based on 52 cases	Mean: 4.7, Median: 4.0, SD: 2.9, 95% Crl: 3.7 to 6.0 based all 28 pairs	

Nishiura 2020	18 pairs with	NA	Mean: 4.8,	NA
(33)	highest certainty		Median: 4.6,	
	from published		SD: 2.3,	
	research articles		95% Crl: 3.8 to 6.1	
	as of 12 Feb		based on 18 certain	
	2020		pairs fitting to Weibull	
			distribution	
Sanche 2020	Modeling study	NA	NA	2.4 (95% CI: 1.9, 3.3)
(35)				based on onset dates
Wu 2020 (11)	Modeling study	NA	NA	6.4 (95% Crl: 5.8 to
				7.1) based on onset
				dates
Zhang 2020	8579 confirmed	Mean: 5.2,	Mean: 5.1,	NA
(31)	cases reported	Median: NA,	Median: NA,	
	outside Hubei in	SD: NA,	SD: NA,	
	China as of 17	95% CI: 1.8 to 12.4	95% CI: 1.3 to 11.6	
	Feb 2020 (only	based on log-normal	based on gamma	
	49 cases with no	distribution	distribution	
	travel history			
	to/from			
	Wuhan/Hubei)			

- 713 Supplementary Table 3. Summary of the study included in the review of incubation period, serial
- interval, doubling time based on search in gray literature

Study	Study setting	Incubation period	Serial interval (days)	Doubling time (days)
		(days)		
Bedford,	53 publicly available nCoV	NA	NA	7.2 (95% CI: 5.0 to 12.9)
unpub. data, http://virologic	genomes collected			based on sample
al.org/t/phylod ynamic-	between 24 Dec, 2019			collection dates
estimation-of- incidence-and- prevalence-of- novel-	and 4 Feb, 2020			
<u>coronavirus-</u> <u>ncov-</u> infections- through-				
<u>time/39</u> Lu et al.,	265 confirmed cases in	Mean: 6.4,	NA	NA
unpub. data, https://www.m	Shanghai before 7 Feb	Median: NA,		
edrxiv.org/cont ent/10.1101/2	2020 (only 27 had credible	SD: NA,		
<u>020.02.19.200</u> 25031v1	contact information)	95% CI: 5.3 to 7.6		
		based on Weibull		
		distribution		
Pinotti et al.,	Modeling study	NA	NA	2.67 (95% CI: 2.24 to
unpub. data, <u>https://www.m</u>				3.30) importations from
edrxiv.org/cont ent/10.1101/2				Hubei, calculated by
<u>020.02.24.200</u> 27326v1				growth rate of 0.26 (95%
				CI: 0.21 to 0.31) based
				on reporting dates

Rambaut, unpub. data, http://virologic al.org/t/phylod ynamic- analysis-176- genomes-6- mar-2020/356	75 genomes in 12 Feb 2020, 86 genomes in 24 Feb 2020	NA	NA	6.2 (95% CI: 4.1 to 12.3) 75 genomes based on sample collection dates
Rambaut, unpub. data, <u>http://virologic</u> al.org/t/phylod <u>ynamic-</u> analysis-176- <u>genomes-6-</u> mar-2020/356	75 genomes in 12 Feb 2020, 86 genomes in 24 Feb 2020	NA	NA	7.2 (95% CI: 4.7 to 16.3) 86 genomes based on sample collection dates
Tindale et al., unpub. data, https://www.m edrxiv.org/cont ent/10.1101/2 020.03.03.200 29983v1	93 confirmed cases in Singapore from 19 Jan 2020 to 26 Feb 2020	Mean: 7.11, Median: 6.55, SD: NA, 95% CI: 6.13 to 8.25 based on Weibull distribution	Mean: 4.56, Median: NA, SD: 0.95, 95% Cl: 2.69 to 6.42 based on expectation- maximization approach	NA
Tindale et al., unpub. data, https://www.m edrxiv.org/cont ent/10.1101/2 020.03.03.200 29983v1	125 confirmed cases in Tianjin from 21 Jan 2020 to 22 Feb 2020	Mean: 9.02, Median: 8.62, SD: NA, 95% CI: 7.92 to 10.2 based on Weibull distribution	Mean: 4.22, Median: NA, SD: 0.4, 95% Cl: 3.43 to 5.01 based on expectation- maximization approach	NA

8579 confirmed cases	Mean: 5.2,	Mean: 5.1,	NA
reported outside Hubei in	Median: NA.	Median: NA.	
China as of 17 Feb 2020			
(only 49 cases with no	SD: NA,	SD: NA,	
travel history to/from	05% Cl. 1.9 to 12.4	05% Ch 1.2 to 11.6	
Wuhan/Hubei)	95% CI. 1.8 10 12.4	95% CI. 1.3 to 11.6	
	based on log-normal	based on gamma	
	distribution	distribution	
Phylogenetic analysis of	NA	NA	7.1 (95% CI: 3.0 to 20.5)
53 SARS-CoV-2 whole			based on sample
genome sequences			collection dates
01 infactor infactor pairs		Maan: 4.4	NA
	NA		NA
2020 to 15 Feb 2020			
		-	
		distribution	
Modeling Study	NA	NA	2.9 (95% Crl: 2 to 4.1) based on onset dates
	reported outside Hubei in China as of 17 Feb 2020 (only 49 cases with no travel history to/from Wuhan/Hubei) Phylogenetic analysis of 53 SARS-CoV-2 whole genome sequences 21 infector-infectee pairs in Hong Kong from 16 Jan 2020 to 15 Feb 2020	reported outside Hubei in China as of 17 Feb 2020 (only 49 cases with no travel history to/from Wuhan/Hubei) 95% CI: 1.8 to 12.4 based on log-normal distribution Phylogenetic analysis of 53 SARS-CoV-2 whole genome sequences NA 21 infector-infectee pairs in Hong Kong from 16 Jan 2020 to 15 Feb 2020	reported outside Hubei in China as of 17 Feb 2020 (only 49 cases with no travel history to/from Wuhan/Hubei) 55% CI: 1.8 to 12.4 95% CI: 1.3 to 11.6 based on log-normal distribution based on gamma distribution 038 Phylogenetic analysis of S3 SARS-CoV-2 whole genome sequences NA NA 21 infector-infectee pairs in Hong Kong from 16 Jan 2020 to 15 Feb 2020 NA Mean: 4.4, Median: NA, 2020 to 15 Feb 2020 SG CI: 2.9 to 6.7, based on gamma distribution

718 Supplementary Table 4. Frequency of different case severities

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Classification	Definition	Proportion *
Mild/Moderate	non-pneumonia and pneumonia cases	80.9%
Severe	dyspnea, respiratory frequency ≥ 30/minute, blood oxygen saturation ≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% within 24–48 hours	13.8%
Critical	respiratory failure, septic shock, and/or multiple organ dysfunction/failure	6.1%

\* Proportion out of 55,924 cases until Feb 20th

# 725 Supplementary Table 5- Summary of CFR and IFR Estimate Sources

Author	Place	Metr ic	Estimate	Uncertai nty type	Peer- revie wed	Source
Russell et al	China	IFR	0.6 (0.2- 1.3)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32234121
Hauser et al	China Hubei	IFR	3.3 (2-4.7)	95% Crl	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031104v2.full.pdf
Famulare	China Wuhan	IFR	0.9 (0.4- 2.9)	95% CI	No	https://institutefordiseasemodeling.github.io/nCoV- public/analyses/first adjusted mortality estimates and risk assessment/2019-nCoV- preliminary age and time adjusted mortality rate s and pandemic risk assessment.html
Mizumoto et al	China Wuhan	IFR	0.2 (0.2- 0.3)	95% Crl	No	https://www.medrxiv.org/content/10.1101/2020.02.1 2.20022434v1
Russell et al	Diamond Princess	IFR	1.3 (0.4- 3.6)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32234121
Hauser et al	Italy Northern	IFR	3 (2.6-3.4)	95% Crl	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031104v1.full.pdf
Nishiura et al +	mainland China	IFR	NA (0.3- 0.6)	95% CI	Yes	https://www.mdpi.com/2077-0383/9/2/419
Verity et al	mainland China	IFR	0.7 (0.4- 1.3)	95% Crl	Yes	https://www.thelancet.com/journals/laninf/article/PII S1473-3099(20)30243-7/fulltext
Russell et al	China	CFR	1.2 (0.3- 2.7)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32234121
Deng et al	China Hubei	CFR	5.4 (5.3- 5.6)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Mizumoto et al	China Hubei not Wuhan	CFR	0.9 (0.6- 1.3)	95% Crl	No	https://www.medrxiv.org/content/10.1101/2020.02.1 9.20025163v1
Deng et al	China not Hubei	CFR	0.9 (0.8- 1.1)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	China not Wuhan	CFR	3.5 (3.4- 3.8)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	China Wuhan	CFR	6.2 (6.1- 6.4)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Mizumoto et al	China Wuhan	CFR	18.9 (17.1- 20.8)	95% Crl	No	https://www.medrxiv.org/content/10.1101/2020.02.1 9.20025163v1
Russell et al	Diamond Princess	CFR	2.6 (0.9- 6.7)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32234121
Deng et al	mainland China	CFR	4.5 (4.5- 4.7)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Wang et al	China Hubei	sCF R	7.2 (6.6-8)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.02.1 7.20023630v4
Wang et al	China not Hubei	sCF R	1 (0.9-1.2)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.02.1 7.20023630v4
Verity et al	mainland China	sCF R	1.4 (1.2- 1.5)	95% Crl	Yes	https://www.thelancet.com/journals/laninf/article/PII S1473-3099(20)30243-7/fulltext
Famulare	China Wuhan	cCF R	33 (29-37)	95% CI	No	https://institutefordiseasemodeling.github.io/nCoV- public/analyses/first adjusted mortality estimates and risk assessment/2019-nCoV- preliminary age and time adjusted mortality rate s and pandemic risk assessment.html
Jung et al *	mainland China	cCF R	5.3 (3.5- 7.5)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32075152
Jung et al **	mainland China	cCF R	8.4 (5.3- 12.3)	95% CI	Yes	https://www.ncbi.nlm.nih.gov/pubmed/32075152
Verity et al	outside mainland China (non- parametric)	cCF R	4.1 (2.1- 7.8)	95% Crl	Yes	https://www.thelancet.com/journals/laninf/article/PII S1473-3099(20)30243-7/fulltext
Verity et al	outside mainland China (parametric)	cCF R	2.7 (1.4- 4.7)	95% Crl	Yes	https://www.thelancet.com/journals/laninf/article/PII S1473-3099(20)30243-7/fulltext

Wu et al	China Wuhan	HFR	14 (3.9-32)	95% CI	Yes	https://www.eurosurveillance.org/content/10.2807/1 560-7917.ES.2020.25.3.2000044
Deng et al	China Hubei	ciCF R	25.7 (25.4- 26.5)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	China not Hubei	ciCF R	8 (7.5-9.6)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	China not Wuhan	ciCF R	28.8 (28- 31)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	China Wuhan	ciCF R	26.9 (26.6- 27.9)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1
Deng et al	mainland China	ciCF R	24.2 (23.9- 25)	95% CI	No	https://www.medrxiv.org/content/10.1101/2020.03.0 4.20031005v1

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- 727 +. Range based on  $\sim 10\%$  ascertainment
- \*. Fitted to epidemic growth alone
- \*\*. Fitted to epidemic growth along with other parameters

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- 732 Supplementary Table 6- Types of NPIs that could be implemented at the individual and
- 733 community level

	Non-pharmaceutical intervention				
Interventions for individuals	Voluntary home isolation. Separation of ill people with contagious diseases from non- infected persons				
	Voluntary home quarantine. Restriction of people who are presumed to have been exposed to a contagious disease but are not ill, either because they did not become infected or because they are still in the incubation period.				
Community level	School closure (closure of day care facilities, schools and higher education)				
	Workplace closure (closure of non-essential services)				
	Cancel or postpone large public gatherings				

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737 Supplementary Table 7- Definition of NPIs search key words

Торіс	Definition
'case detection', 'case detected'	Detection of cases imported from an affected area
'case isolation and contact tracing'	Isolation of an identified positive case.
'travel screening'	Screening of passengers at port of exit/entry
'travel reduction', 'reduced travel', 'airline suspension'	Mobility reduction of individuals, intra- or inter- city/country.
'school closure'	Closing schools to prevent further transmission
'Cancellation of events and mass gatherings', 'Lockdown'	Cancellation of events and mass gatherings in order to prevent further transmission.
'Community response'	People's psychological and behavioral responses during an outbreak

738 In Table 7 we present a short definition of the search keywords related to the non-pharmaceutical

intervention we are interested in. As there are not specific terms to describe these interventions,

or there are different terms to describe the same kind of intervention, we considered them to be

741 equivalent.