Systematic Review and Meta-Analysis

Mass screening *vs* lockdown vs combination of both to control COVID-19: A systematic review

Nadya Johanna,[1] Henrico Citrawijaya,[1] Grace Wangge[2]

[1]Faculty of Medicine, Universitas Indonesia, Jakarta; [2]Southeast Asian Ministers of Education Organization Regional Center for Food and Nutrition (SEAMEO RECFON) / Pusat Kajian Gizi Regional Universitas Indonesia, Central Jakarta, Indonesia

Abstract

Coronavirus disease 2019 (COVID-19) is a global pandemic. Non-pharmacological interventions, such as lockdown and mass testing, remain as the mainstay of control measures for the outbreak. We aim to evaluate the effectiveness of mass testing, lockdown, or a combination of both to control COVID-19 pandemic. A systematic search on 11 major databases was conducted on June 8, 2020. This review is registered in Prospero (CRD420201 90546). We included primary studies written in English which investigate mass screening, lockdown, or a combination of both to control and/or mitigate the COVID-19 pandemic. There are four important outcomes as selected by WHO experts for their decision-making process: incident cases, onward transmission, mortality, and resource use. Among 623 studies, only 14 studies met our criteria. Four observational studies were rated as strong evidence and ten modelling studies were rated as moderate evidence. Based on one modelling study, mass testing reduced the total infected people compared to no mass testing. For lockdown, ten studies consistently showed that it successfully reduced the incidence, onward transmission, and mortality rate of COVID-19. A limited evidence showed that a combination of lockdown and mass screening resulted in a greater reduction of incidence and mortality rate compared to lockdown only. However, there is not enough evidence on the effectiveness of mass testing only.

Introduction

COVID-19 is a highly infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The virus is transmitted from human to human through droplets produced when sick people cough or sneeze.[1] SARS-CoV-2 causes viral pneumonia which may progress to acute respiratory distress syndrome. Severe cases and death are more common in individuals with underlying comorbidities such as hypertension, cardiovascular disease, or diabetes mellitus.[2]

As of the early of June 2020, an effective pharmacological intervention or vaccine for COVID-19 is not yet available. Thus, public health measures including quarantine, isolation, and massive screening become the main measures in containing the outbreak. Quarantine and/or mass screening have been applied in several countries. Two studies conducted in China, reported that utilizing both quarantine and isolation was an effective control measure to decrease the peak number of COVID-19 infections, slow down the time of peak infections, and reduce the reproductive number of the virus.[3,4] Singapore and South Korea used several control measures including early detection by means of surveillance and aggressive contact tracing. For surveillance systems, Singapore has scaled up SARS-CoV-2 RT-PCR laboratory testing capacity with 2,200 tests held in a day within a 5.7 million population. The control measures have been successful in containing the spread of the virus in Singapore since the increase of cases does not exhibit exponential growth.[5] South Korea implemented mass SARS-CoV-2 testing, linked to contact tracing, and self-isolation. These interventions led to a reduction of daily new cases from 284 new cases on February 26, 2020 to 84 new cases on March 17, 2020.[6,7]

The implementation of such public health strategies has sparked some discussion on which strategy is the most effective and cost efficient to prevent infectious diseases. In this systematic review, we aim to analyze the effectiveness of lockdown, mass testing, or a combination of both in reducing the incidence, onward transmission, and mortality due to COVID-19, also the resource use analysis of each strategy.

Methods

Protocol and registration

This systematic review was conducted in accordance with the PRISMA guidelines.[8] We conducted a systematic review on the effectiveness of mass screening and/or lockdown to control the

coronavirus outbreaks. This systematic review is registered in Prospero (CRD42020190546).

Eligibility criteria for inclusion of studies

We included non-randomized studies of interventions as the best available empirical evidence. In addition, we also included modelling studies, as empirical studies were not yet available. Cohort studies, case-control studies, time series, interrupted time series, and case series were also included. We excluded case reports and systematic review. The references of systematic reviews were carefully reviewed.

Population

The target population are the community population of countries which implemented mass screening and lockdown to mitigate and/or control the COVID-19 pandemic. We also included studies on SARS, MERS, and other influenza epidemic or pandemic as indirect evidence. We included all countries regardless of the prevalence rate.

Intervention

Intervention measures included mass screening, lockdown, a combination of both, or in combination with other physical measures, *e.g.* physical distancing, hand hygiene, isolation, school measures/ closures, workplace measures / closures. We decided to only include mass screening with molecular test, such as RT-PCR and other nucleic acid amplification tests, which is the gold standard for the confirmation of COVID-19 diagnosis.[9] Lockdown is a temporary condition imposed by governmental authorities (*e.g.* during emergency) in which people are required to stay in their homes and refrain from or limit activities outside the home involving public contact. Individuals who work in the essential occupational fields (*e.g.* healthcare, public works, law enforcement, and food supply) to public health and safety may continue working during a lockdown. We excluded travel- and border-related screening and measures.

Control

We had two types of controls which were: 1) community population before being involved in any of the physical measures, and 2) community population in which no physical measure was implemented for control and/or mitigation of the epidemic or pandemic and only routine care was provided for the infected people.

Outcomes

There are four important outcomes as selected by WHO experts for their decision-making process: incident cases, onward transmission, mortality, and resource use. Incidence rate is reported separately for suspect, probable, and confirmed case as defined by WHO.[10] Onward transmission could be described by both the basic reproduction number (R_0), which is the expected number of individuals infected by one confirmed individual when he or she enters a fully susceptible population,[11] and the doubling time, which is the number of days for total cases to double at the current growth rate.[12] Resource use included the analysis of direct and indirect costs (*e.g.* test kits, personal protective equipment, pay cut) for the implementation of each strategy.

Information sources and search strategy

Two authors independently conducted a systematic search of the literature published in English up until June 8, 2020 in Cochrane Library, Directory of Open Access Journals, CINAHL, MEDLINE, Proquest, Pubmed, Sage Journals, Science Direct,

Scopus, World Health Organization (WHO) Global Index Mediscus, and Wiley. These following keywords were used in Cochrane Library, Directory of Open Access Journals, EBSCO (CINAHL, MEDLINE), Proquest, Pubmed, Sage, Scopus, WHO Global Index Mediscus, and Wiley: *((screening) OR (mass screening) OR (rapid screening) OR (rapid molecular test) OR (rapid molecular assay) OR (GeneXpert)) AND (quarantine OR lockdown) AND (coronavirus OR (COVID-19) OR (MERS-CoV) OR (MERS) OR (SARS-CoV) OR (SARS) OR influenza) AND infection.* Meanwhile, for ScienceDirect, we used these following keywords: *((screening) OR (rapid molecular test)) AND (quarantine OR lockdown) AND (coronavirus OR (COVID-19) OR (MERS) OR (SARS)) AND infection.* The filter "abstract" was applied to CINAHL, MEDLINE, Sage Journals, and Wiley; the filter "abstract" and "scholarly journals" were applied to Proquest; the filter "title, abstract, or keywords" was applied to ScienceDirect and Scopus; the filter "title, abstract, or subject" was applied to WHO Global Index Mediscus; and the filter "all fields" was applied to Cochrane Library, Directory of Open Access Journals, and Pubmed. No limitation of years used in the searching.

Besides the extensive searching, authors NJ and HC independently screened reference lists of relevant systematic reviews and included relevant studies. Clinical trial registers (clinical trials.gov) and preprint databases (such as medRxiv, bioRxiv, and arvix.org) were also reviewed carefully.

Study selection

The search results were imported to the Mendeley program to manage the studies and remove the duplicates. Two authors independently screened all the titles and abstracts to retrieve eligible studies. The authors then retrieved the full texts of all included abstracts and screened all full-text publications independently. In each stage of screening, any disagreement about eligibility will be discussed with a third author until an agreement was reached. The PRISMA flow diagram was used to report the screening and selection results.

Data extraction

The required information from each full-text were extracted data into a standardized table separately by two authors and cross-checked for completeness and correctness. For cohort studies, the data items were author, publication year, country, study design, objective, characteristics of study participants, description of intervention, description of control, important confounding factors, and results. The data items for modelling studies were author, year, type of model, setting, time, data source and participants, interventions, and results. If there is any unclear or incomplete data in the full-text was found, authors will attempt to contact the author of the original report to provide the details. Any discrepancies will be resolved by discussion, referring to the relevant study paper. If resolution is not possible, however, a third author, who is not involved in the extraction process, will be consulted.

Risk of bias assessment of included studies

Two authors independently appraised the risk of bias for each eligible study using the modified quality assessment tools from Effective Public Health Practice Project (EPHPP).[13] The assessed domains included selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs, and global rating. Raters rated the individual domains as strong, moderate, or weak quality which was translated to low risk, low risk*, or high risk of bias. Disagreements among the raters was solved by discussion with a third author.

Data synthesis

Only studies with moderate and strong global rating (based on the EPHPP bias assessment tools) were included to prevent any bias from poor quality studies. The minimum number of studies for each outcome measure to be deemed eligible for analysis was two.

Descriptive synthesis

The study location, study design, intervention, and control of each included study were arranged in a summary table. The results of each included study were described in another summary table. Frequencies of each outcome measures were reported to find any pattern in relation to the context of the measures.

Quantitative synthesis

Both random effects and fixed effect data pooling will be conducted, if applicable. Subgroup analysis will be conducted for the types of intervention combinations, if the data is available.

Results

Study selection

The searching process done on June 8, 2020 is demonstrated in Figure 1. We excluded a total of 20 papers: 9 papers were not a research study (a review, letter to editor, or narrative text), 2 papers did not have the correct population (the studies were done in high-risk people only), 9 papers had improper intervention/control (such as quarantine, isolation, contact tracing, and many other physical measures without implementing either mass screening or lock-down).

Study characteristics

Our searches identified 14 relevant studies,[3,4,12,14-24] all of these focused on COVID-19. There were 10 modelling studies,[3,4,14-16,19-22,24] 3 retrospective cohort studies,[12,17,18] and 1 time series analysis,[23] covering 8 countries (China, France, Italy, Spain,
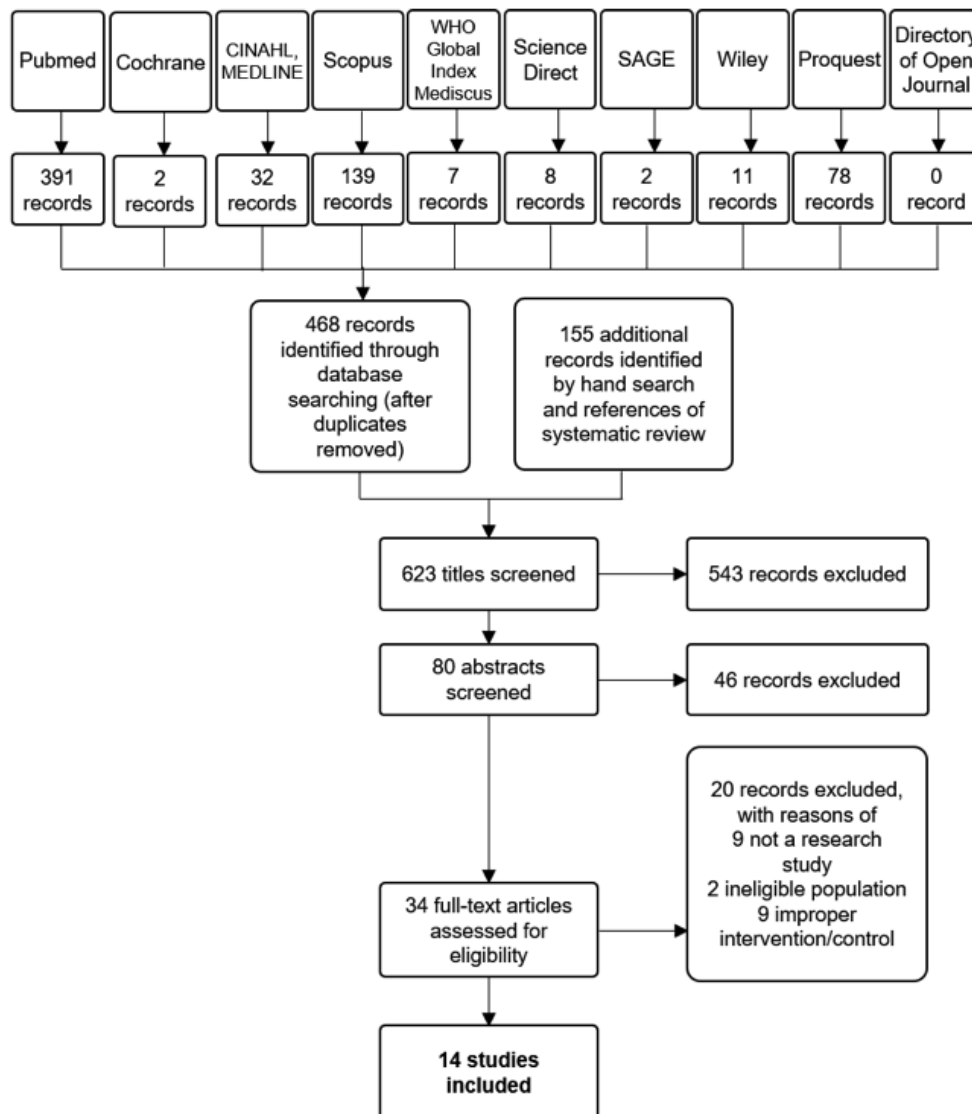

Figure 1. Searching diagram.

United Kingdom, United States, Russia, and Indonesia) from 3 continents. We could not identify any similar studies on SARS, MERS, or other influenza virus infection as indirect evidence. We also could not identify any study on the cost effectiveness of mass screening, lockdown, and a combination of both. Due to the heterogeneity of the study designs and effect measures, we could not continue with data pooling and only conducted systematic qualitative review. The characteristics of included studies are described in Table 1.

Risk of bias of included studies

Based on the EPHPP bias assessment tool, we rated all 4 observational studies[12,17,18,23] as strong evidence. Of the modelling studies, we rated all 10 modelling studies[3,4,14-16,19-22,24] as moderate evidence, the detailed assessment is illustrated in Table 2.

Results of individual studies

The summary of results of each study is presented in Table 3. The detailed characteristics of included studies is presented in Appendix 1.

Synthesis of results

Mass testing

We could identify one modelling study[22] on mass screening effectiveness compared to no mass testing. The mass testing method modeled by Taipale et al.[22] was weekly mass testing on day 20-100 after the first 100 cases were identified in a population of 10000 people. Taipale et al.[22] projected that mass testing would reduce the total infected people from 80% (with no mass testing) to 20% of the total population. Moreover, the mortality rate also reduced significantly from 0.66% (no mass testing) to 0.19% with mass testing.[22]

Lockdown

There was a total of 10 studies reporting the effectiveness of lockdown. There is a consistent evidence[3,12,14,16,17,20,21,23,24] that lockdown was effective in reducing the number of new infected cases, except for one modelling study by Taipale et al.[22] which predicted that 80% of the total population would be infected either

Table 1. Characteristics of included studies.

Article reference (First author, year)	Study location	Study design	Intervention	Control
Dolbeault et al.[14], 2020	France	SEIR modelling study	Lockdown A: a big single group Lockdown B: a majority of population under lockdown + a minority (2% of the population) with higher social interaction than before lockdown, i.e. health workers	Before lockdown
Gongalsky et al.[15], 2020	Moscow, London, New York	SEIAR modelling study	Mass group RT-PCR testing (5000 tests/ big city) Rapid isolation of superspreaders Quarantine Schools and universities are closed Offices, trains, and groceries are partially quarantined Non-essential workers work remotely	No mass testing
Hoertel et al.[16], 2020	France	Stochastic agent-based micro-simulation modelling study	Lockdown: 8 weeks and 16 weeks Post-lockdown social distancing, mask usage, extra protection for vulnerable population, quarantine, contact tracing, molecular tests for all contacts	No lockdown
Hou et al.[3], 2020	Wuhan	SEIR modelling study	Lockdown	No lockdown
Ji et al.[17], 2020	Hubei	Retrospective cohort study	Lockdown Real-time syndromic surveillance, health screening, quarantine, social isolation, compulsory outdoor mask usage, monitoring, reporting	Before lockdown
Lau et al.[18], 2020	China	Retrospective cohort study	Lockdown Change in diagnostic criteria	Before lockdown
Putra et al.[19], 2020	Indonesia	SEIR modelling study	Lockdown (implemented on the last week of March 2020)	Before lockdown
Rao et al.[20], 2020	U.S.	Model based predictions	Lockdown in several states (implemented by the end of March 2020)	Before lockdown
Signorelli et al.[21], 2020	Italy	Modelling study	Lockdown (started on March 9, 2020)	Mass testing only
Taipale et al.[22], 2020	-	Standard SEIR modelling study	Scenario A1: mass testing on day 20-100 and self-quarantine of infected individuals Scenario A2: no lockdown, no mass testing Scenario B1: lockdown on day 20-100, mass testing after day 100 Scenario B2: lockdown on day 20-100, no mass testing	Lockdown only
Tang et al.[4], 2020	Hubei	SEIR modelling study	Lockdown	Before lockdown
Tellis et al.[12], 2020	U.S.	Retrospective cohort study	Lockdown	No lockdown
Tobias[23], 2020	Italy and Spain	Interrupted time-series analysis	Lockdown	Before lockdown
Zhao et al.[24], 2020	Wuhan, Hubei, and China	SUQC modelling study	Lockdown and other preventive measures	Before lockdown

SEIR, suspected, exposed, infected, recovered; SEIAR, suspected, exposed, infected, admitted, recovered; RT-PCR, reverse transcription polymerase chain reaction; SUQC, susceptible, un-quarantine infected, quarantine infected, confirmed infected.

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with or without lockdown. Relaxing lockdown will result in a higher suspected, quarantined, and confirmed cases.[4] Other than that, delaying lockdown also resulted in a higher total of cases.[12]

Five studies[4,14,18,19,24] were consistent in reporting that lockdown was an effective strategy for reducing onward transmission of COVID-19. Dolbeault et al.[14], Zhao et al.[24], Tang et al.[4], Putra et al.[19] all reported that lockdown resulted in a reduction of reproduction number of SARS-CoV-2, ranging from 1.5-10 before lockdown to 0.0792-3 after lockdown.

Lockdown could also lower the mortality due to COVID-19.[16,22,23] Tobias[23] presented that 2 weeks of lockdown lowered the daily mortality rate by 41.7 to 9.1%. According to Hoertel et al.[16], the cumulative mortality was 30% lower with lockdown compared to no lockdown. However, Taipale et al.[22] predicted that there would only be a slight difference of the number of deaths between lockdown and no lockdown, 0.57% and 0.66% respectively. The reduction of daily mortality rate can be enhanced by tightening lockdown.[23]

Combination of mass testing and lockdown

Compared to only lockdown, the addition of mass testing to lockdown has shown some promising results. A modeling study by Taipale et al.[22] showed that the addition of mas testing to lockdown successfully reduced the number of infected people from 80% to 20% and the mortality rate from 0.57% to 0.16% compared to only lockdown. Taipale and colleagues used a lockdown scheme for day 20-100 after the first case was discovered, followed by a weekly mass testing of a random part of the population after day 100. However, there is no significant different in terms of the total infected people (2,000 people vs 2,000 people) and mortality rate (0.19% and 0.16%) between mass testing and the combination of mass testing and lockdown. The incidence in mass testing only is 200 new cases/ day until around day 80, while the combination of lockdown and mass testing resulted in around 125 new cases/ day from day 100-150 (or after the mass testing began) and significantly reduced thereafter.[22]

Discussion

Control measures including lockdown and massive testing strategy are conducted in many countries around the world as a response to COVID-19 outbreak. To our best knowledge, this is the first systematic review comparing the mass screening and lockdown effectiveness in controlling COVID-19 pandemic. The evidence is still very limited as 6 out of the 14 included studies are preprint and 10 out of the 14 included studies are modelling studies, made based on limited data sets and predicted assumptions. Most of the studies did not take into account the heterogeneity of infectiousness, incubation period, and recovery time, immunity of recovered patients, deceased patients, various social interactions, age structure, and many other contributing factors.

Mass testing

We could only identify a modeling study[22] on the clinical effectiveness of solely weekly mass testing to mitigate COVID-19. Taipale et al.[22] projected that mass testing would drastically reduce the total infected people from 80% to 20% of the total population. Moreover, the mortality rate also reduced significantly from 0.66% to 0.19% with mass testing. The mass testing method used was the weekly mass testing on day 20-100 after the first 100 cases were identified in a population of 10,000 people.[22]

Taipale et al.[22] also compared the effectiveness of several mass testing techniques. Testing everyone at the same time is the best strategy to control an outbreak, followed by testing everyone in a certain period and last by a random sampling.[22] In reality, due to limited tests and manpower, the preferable option could be testing everyone in a certain period, e.g. geographical sweep where infected individuals are prevented from crossing to other areas. In low-resource settings, random sampling might be the only possible way. This method is less efficient than testing part of the population in a certain period because some individuals are tested twice, while some not at all. This method will miss some infected individuals. However, in order to put an outbreak under control, the most important thing is to make sure that the generation of new cases per current case is less than one or the reproductive number remains less than one.

Table 2. Risk of bias assessment using EPHPP (Effective Public Healthcare Panacea Project) tools.

First author, year	Selection bias	Study design	Confounders	Blinding	Data collection method	Withdrawals and dropouts	Global rating
Dolbeault et al.,[14] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Gongalsky et al.,[15] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Hoertel et al.,[16] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Hou et al.,[3] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Ji et al.,[17] 2020	+++	++	+++	++	+++	+++	+++
Lau et al.,[18] 2020	+++	++	+++	++	+++	+++	+++
Putra et al.,[19] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Rao et al.[20] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Signorelli et al.[21] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Taipale et al.,[22] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Tang et al.,[4] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Tellis et al.,[12] 2020	+++	+	+++	Can't tell	Can't tell	++	++
Tobias[23], 2020	+++	++	+++	++	+++	+++	+++
Zhao et al.,[24] 2020	+++	++	+++	++	+++	+++	+++

+++, strong; ++, moderate; +, weak.

Table 3. Results summary of included studies.

Outcome	Number of studies	Outcome summary
Incidence	**Mass testing** 1 modeling study (Taipale *et al.*[22])	**Mass testing** Taipale *et al.*[22] Taipale modeled a weekly mass testing of a random part of the population (10,000 people) on day 20-100 after the first case was found. This type of mass testing would effectively reduce the number of infected people compared to no mass testing, 2,000 infected people vs 8,000 infected people respectively.
	Lockdown 9 modelling studies (Dolbeault *et al.*[14]; Hoertel *et al.*[16]; Hou *et al.*[3]; Rao *et al.*[20]; Signorelli *et al.*[21]; Taipale *et al.*[22]; Tang *et al.*[4]; Tellis *et al.*[12]; Zhao *et al.*[24]), 1 retrospective cohort study (Ji *et al.*[17]), and 1 time series analysis (Tobias[23])	**Lockdown** Dolbeault *et al.*[14] A total lockdown resulted in a reduction of the number of infected people (4% to 1%) compared to before lockdown. Lockdown with a minority (2%) of the population having an increased social interaction (i.e. health workers, supermarket cashiers) resulted in a decrease of infected people (4% to 2%) compared to before lockdown. However, almost all individuals (81%) of the minority group got infected.
	Lockdown and mass testing 2 modelling studies (Gongalsky *et al.*[15]; Taipale *et al.*[22])	Hoertel *et al.*[16] Both 8- and 16-week lockdowns resulted in a reduction of cumulative incidence (∞10%). An 8-week lockdown followed by mandatory post quarantine social distancing and mask usage reduced the cumulative incidence by ∞35%, adding extra protection for the most vulnerable population (aged ≥65 or having at least one comorbidity) until the pandemic ends (calculated to be on week 38th) to these resulted in a ∞60% reduction compared to no lockdown and adequate in preventing a second epidemic wave. Hou *et al.*[3] Reduction of contact rate by strict isolation and quarantine can effectively decrease the peak number of COVID-19 infections, but may postpone the peak time of infections. Ji *et al.*[17] In Huangshi, right after Jan 24, 2020 (day 1 of lockdown), the epidemic curve flattened. Feb 1, 2020 (day 9 of lockdown) was the peak of total COVID-19 cases. No new cases were detected after Feb 26, 2020 (day 34 of lockdown). After 48 days of lockdown, the lockdown was lifted and normal life can continue. Rao *et al.*[20] Adherence rate of lockdown and other preventive measures was important in determining the effectiveness of lockdown. A complete lockdown in the U.S. or 2 months could lower the daily new cases of COVID-19 by 72-85% compared to prior to lockdown. If 10% of the unidentified susceptible and 20% of the unidentified infected do not adhere to lockdown, the daily new cases would rise to 172-190% of the daily new cases before lockdown. Moreover, an adherence rate of only 50% would result in over 500,000 cases by the end of June. Signorelli *et al.*[21] The timing of lockdown appeared to be a crucial factor in determining its effectiveness on mitigating new cases. The lockdown in Italy was more effective in the Central-Southern region than in the Northern regions because they implemented the lockdown early when there were only a few cases. The highest new notified cases were estimated to be 6,500 cases on day 13 of lockdown, followed by a decrease. Taipale *et al.*[22] Taipale predicted that the number of infected people would not differ between lockdown and no lockdown as 80% of the population would be infected at the end. Tang *et al.*[4] Relaxing the lockdown and other intervention measures will result in a higher suspected, quarantined, and confirmed cases, thus postpone the epidemic peak. Tellis *et al.*[12] As of May 1, 2020, delaying lockdown for a week increased the total cases by 8-32%. Without lockdown, the total case increased by 45-128%. Tobias[23] After around 2 weeks of lockdown, the daily confirmed cases in Italy reduced from 21.6% to 12.5%. In Spain, it dropped from 38.5% to 11.9% in 2 weeks. After that, Italy and Spain tightened their lockdowns. After 2 weeks of stricter lockdown, the daily confirmed cases in Italy went down to -2.0%. After a week of stricter lockdown in Spain, it went down to -2.7%. Both countries succeeded in putting the COVID-19 pandemic under control. Zhao *et al*[24] Strengthening lockdown would reduce the total number of infected people. Increasing the quarantine rate from 0.4 to 0.6 reduced the number of infected people from 63,000 to 50,000 cases in Wuhan. **Lockdown and mass testing** Gongalsky *et al.*[15] Identifying and isolating superspreaders in cities conducting strong quarantine (London and New York City) led to a 4.5-to-4.8-fold decrease in the number of infected populations. In cities with weak quarantine (Moscow) an 8-fold decrease in the number of infected populations was found. Taipale *et al.*[22] Taipale compared lockdown and mass testing to lockdown only. The addition of mass testing to lockdown successfully reduced the number of infected people from 80% to 20%.
Onward transmission	**Lockdown** 4 modelling studies (Dolbeault *et al.*[14]; Putra *et al.*[19]; Tang *et al.*[4]; Zhao *et al*[24]) and 1 retrospective cohort (Lau *et al.*[18])	**Lockdown** Dolbeault *et al.*[14] The basic reproduction rate was reduced from 2.33 before lockdown to 1.37 during lockdown. However, the outbreak peak was delayed from day 40 to day 105 with lockdown The end of the outbreak was also delayed from day 90 to day 200 with lockdown. Lau *et al.*[18] Lockdown was associated with a decrease in the COVID-19 growth rate, shown by an increase of doubling time of total COVID-19 cases from 2 days before lockdown to 4 days during the lockdown in China. Putra *et al.*[19] Lockdown reduced the basic reproduction number from 10 to around 3 in 3 weeks in Indonesia. Tang *et al.*[4] Lockdown on January 23, 2020 resulted in reduction of reproductive number of COVID-19 in Hubei from 6.39 to 0.28 and China from 6.00 to 0.08 on February 9, 2020 (day 18 of lockdown). Zhao *et al.*[24] The reduction of the reproductive number of COVID-19 is proportionally related to the strictness level of quarantine. This is illustrated by a reduction of reproductive number of COVID-19 in Wuhan from 4.71 to 0.75, Hubei (excluding Wuhan) from 5.93 to 0.61, and China (excluding Hubei) from 1.53 to 0.58 with moderately strict quarantine. By implementing a stricter lockdown, Wuhan could further decrease the basic reproduction number to 0.48.
Mortality	**Mass testing** 1 modeling study (Taipale *et al.*[22])	**Mass testing** Taipale *et al.*[22] Taipale predicted that weekly mass testing on day 20-100 after the first 100 cases were identified would result in a lower mortality rate compared to no mass testing, 0.19% and 0.66%, respectively.
	Lockdown 2 modelling studies (Hoertel *et al.*[16]; Taipale *et al.*[22]) and 1 time series analysis (Tobias[23])	**Lockdown** Hoertel *et al.*[16] The cumulative mortality was 30% lower with either 8- or 16 week-lockdown compared to no lockdown. In addition to the lockdown, when a post-quarantine social distancing was applied, the reduction would be 46%. Furthermore, if it was combined with mandatory mask usage, there would be 73% reduction compared to no lockdown. Giving extra protection for the most vulnerable population (aged ≥65 or having at least one comorbidity) until the end of pandemic (week 38th) resulted in a 90% reduction compared to no lockdown. Taipale *et al.*[22] Taipale predicted that lockdown on day 20-100 after the first 100 cases were found resulted in a lower number of death cases compared to no lockdown, 0.57% and 0.66%, respectively. Tobias[23] After around 2 weeks of lockdown, the daily mortality cases of COVID-19 in Italy reduced from 21.6% to 12.5%. In Spain, it went down from 59.3% to 17.6% in 2 weeks. Thereafter, Italy and Spain tightened their lockdowns. After around 2 weeks of stricter loc down in Italy, the daily mortality cases went further down to -2.0%. Meanwhile, in Spain, after a week of stricter lockdown, it went further down from 17.6% to -1.8%, putting the COVID-19 pandemic under control in both countries.
	Lockdown and mass testing 1 modeling studies (Taipale *et al.*[22])	**Lockdown and mass testing** Taipale *et al.*[22] Taipale compared lockdown on day 20-100 after the first 100 cases were found and lockdown with weekly mass testing of a random part of the population. Lockdown fo lowed by mass testing resulted in a lower mortality rate compared to only mass testing and only lockdown, 0.16%, 0.19%, 0.57% respectively.

On the cost effectiveness of mass testing, we could not find any relevant study comparing no mass testing with mass testing. However, we found two modelling studies comparing the cost effectiveness of mass group testing and mass individual testing.[25,26] These modelling studies consistently showed that mass group testing for COVID-19 using RT-PCR could be a much cheaper alternative to mass individual testing with the same or even higher level of sensitivity, especially in low prevalence (≤1%) areas. The group size is inversely related to the prevalence ratio, as it allows a bigger group size. This could be the solution for the extensive strain on global supply chains for molecular test reagents.[27]

Lockdown

Given that COVID-19 is known to spread mostly by direct or close contact between humans, there is a clear rationale for preventing contact between infectious and susceptible people. With a long incubation period (up to 14 days), there would be a lot of asymptomatic people and thus it is hard to isolate asymptomatic people from susceptible populations. Even though transmission by asymptomatic individuals is much less likely than those who develop symptoms,[28] lockdown puts everyone in quarantine and leaves no or minimum risk of community transmission.

We found consistent but low-quality evidence related to lockdown effectiveness in reducing the onward transmission of SARS-CoV2.[4,14,18,19,24] A SEIR modelling study by Tang et al.[4], showed that lockdown drastically decreased the effective reproductive number from >6 to <1 only in 8 days in China and 10 days in Hubei, putting the outbreak under control. Similar result was shown by another modeling study in Wuhan, Hubei, and China. Zhao et al.[24] stated that a stricter lockdown resulted in a greater reduction of reproductive number. However, other SEIR modelling studies in France and Indonesia showed that lockdown alone was unable to lower the reproductive number to below 1.[14,19] The reduced effectiveness of lockdown in the modelling study by Dolbeault et al.[14] might be caused by the loose lockdown implemented. Meanwhile, in a modelling study by Putra et al.[19], the reproductive number was significantly reduced from 10 to 3 in 3 weeks and stayed the same for the next 3 weeks, but the lockdown method was not clearly described.

All relevant studies[3,12,14,16,17,20,21,23,24] predicted that lockdown would decrease the daily new and total confirmed cases compared to before or no lockdown, except for one modelling study by Taipale et al.[22] which predicted that 80% of the total population would be infected either with or without lockdown. The lockdown illustrated by Taipale et al.[22] was lockdown from day 20-100 after the first 100 cases were detected without any preventive measures after day 100. Most studies predicted that the peak time of infection would occur earlier, except for Dolbeault et al.[14] and Hou et al.[3] who predicted that it would be delayed.

For the duration of lockdown, the included studies studied a wide variety of lockdown duration (14 days to 200 days). Some studies also did not mention the lockdown duration,[3,12,18,21,24] some of it might be due to the persistent lockdown that was still taking place at the time of the study. A 2-week lockdown successfully reduced the daily confirmed and mortality cases in Italy and Spain by 42-69% and 58-70%, respectively.[23] However, this study described that an addition of 1-2 weeks of stricter quarantine is needed to halt the increase of daily confirmed cases or to eliminate the COVID-19 pandemic. Ji et al.[17] reported another successful COVID-19 lockdown in controlling the pandemic. After 34 days of complete lockdown in Huangshi, Hubei, there was no new COVID-19 case. The lockdown was lifted on day 48 and the normal life has been continued. Hoertel et al.[16] showed that a minimum of an 8 week of lockdown should be commenced, followed by post quarantine social distancing, mask usage, and extra protection for vulnerable populations until the end of the pandemic was enough to prevent a second pandemic wave. The duration of lockdown should be determined by considering the effective reproduction number, daily new confirmed cases, daily death cases, and the public adherence of other preventive measures. Relaxing or lifting lockdown too early would lead to a second pandemic wave and delay the epidemic peak.[4]

The timing of lockdown also plays an important role in determining the lockdown effectiveness. Tellis et al.[12] showed that delaying a lockdown for a week resulted in an 8-32% increase of total COVID-19 cases in the United States. Executing lockdown as early as possible is essential to contain the transmission and avoid nationwide outbreaks.

Other than timing, the strictness of quarantine was also an important factor. Dolbeault et al.[14], Rao et al.[20], Tang et al.[4], Tobias[23], and Zhao et al.[24] demonstrated that the stricter the quarantine, the lower the reproduction number and the total number of infected people would be. Dolbeault et al.[14] demonstrated that even by allowing a minority (2%) of the population having a higher social interaction level than before lockdown (e.g. health care workers, supermarket cashiers), the total infected population would be higher than in a complete lockdown situation, 2% and 1% respectively. Furthermore, 81% of the minority group would be infected. This highlights the importance of adequate prevention measures on individuals with a high level of social interactions. Rao et al.[20] also illustrated that if only 50% of the public adhere to lockdown and other preventive measures implemented by the end of March, the daily new cases in June would be over 500,000 cases or 17 times the average new COVID-19 cases in April (29,000 cases/ day). This would quickly lead to a disastrous overcapacity of the national or even international health system. On the other hand, if a complete lockdown was taken place, it could lower the daily new cases to 4,300-8,000 cases in May, slowly eliminating the pandemic.[20]

Combination of lockdown and mass screening

Compared to only lockdown, the addition of mass testing to lockdown has shown some promising results. A modeling study by Taipale et al.[22] showed that the addition of mas testing to lockdown successfully reduced the number of infected people from 80% to 20% and the mortality rate from 0.57% to 0.16% compared to only lockdown. Taipale et al.[22] used a lockdown scheme for day 20-100 after the first case was discovered, followed by a weekly mass testing of a random part of the population after day 100. However, there is no significant different in terms of the total infected people (2,000 people vs 2,000 people) and mortality rate (0.19% and 0.16%) between mass testing and the combination of mass testing and lockdown. The incidence in mass testing only is 200 new cases/ day until around day 80, while the combination of lockdown and mass testing resulted in a 125 new cases/ day from day 100-150 and significantly reduced after that.[22]

As we can see from the modeling study by Taipale et al.[22], lockdown alone is not adequate in controlling the pandemic as it resulted in a high number of infected people and mortality rate. Without an extensive public screening, pre-symptomatic and asymptomatic transmission cannot be prevented, especially among the essential workers (e.g. health care workers, supermarket cashiers). In a large UK teaching hospital, around 3% of health care workers who did not have any symptom at the time of the sampling was tested positive for SARS-CoV-2 RT-PCR and the viral genome sequencing showed that the majority of HCWs had the same dominant linage, showing that pre-symptomatic and

asymptomatic transmission as a possible way of transmission.[29] These essential workers might further spread the infection to their families.

The extent of lockdown and capacity of mass testing also influenced the effectiveness of these interventions on flattening the incidence and mortality curve, as illustrated by Mahajan *et al.*[30] This study showed that with the same number of tests per day, the stricter the lockdown is, the greater the reduction of confirmed, active, and total death cases. This study also illustrated that with the same level of lockdown, the higher the daily number of tests done per day (8,000 *vs* 4,000 increase of tests per day, saturated at 300,000 and 200,000 tests/ day respectively) would result in lower number of confirmed, active, and total death cases. The relaxation of lockdown increases the transmission rate by 20% and thus leads to around a 50,000 increase of total cases and 3,000 increase in total deaths.[31]

Furthermore, a similar result was presented in a cross-sectional study. Meneghesso *et al.*[31] mentioned that a strict lockdown with a widespread molecular COVID-19 test (40-50 test/million) in Veneto, Italy was effective in accelerating the pandemic peak and preventing the collapse of the healthcare system.[31]

Limitations of study

There are six preprint studies[4,12,15,16,20,22] included in this review, rated as moderate evidence. Therefore, there might still be some future changes which could affect the results of this review. However, these evidences are the best ones to date. Given the urgent need of guidance, we only include papers written in English to eliminate the time needed for formal translation.

The outcomes of this study focused on incidence, transmission, mortality, and resource use of mass testing, lockdown, and a combination of both, as selected by WHO expert panel for the decision making. Psychological impact, economic disruption, and other health adverse effects are several important factors that need to be considered in the decision making of public health intervention policy but was not addressed in this article.

Conclusions

Implications for practice

Lockdown was pretty consistently proven to be effective in mitigating the COVID-19 pandemic by substantially reducing the incidence, onward transmission, and mortality. Despite the limited evidence on mass testing to control COVID-19, random weekly mass testing was effective in reducing the total infected people compared to no mass testing. Based on limited evidence, a combination of both lockdown and mass screening resulted in a greater reduction of incidence and mortality rate compared to lockdown only, but resulted in a similar mortality rate compared to mass testing only.

Implications for research

Studies on the clinical effectiveness of mass testing are still urgently needed. There should also be more studies on the clinical and cost effectiveness of different mass testing and lockdown methods. Moreover, modelling studies on lockdown and mass testing should incorporate more factors (*e.g.* the heterogeneity of infectiousness, incubation period, and recovery time, immunity of recovered patients, deceased patients, various social interactions, age structure) to give a better understanding of the actual implementation.

Correspondence: Nadya Johanna, Faculty of Medicine, Universitas Indonesia, Salemba Raya 6, 10430, Central Jakarta, Jakarta, Indonesia. Tel. +62.85920776688 - Fax: +6.2213912477.
E-mail: nadya.johanna@gmail.com

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