BMJ Open

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040413
Article Type:	Protocol
Date Submitted by the Author:	13-May-2020
Complete List of Authors:	LOPES-JÚNIOR, LUÍS CARLOS; Universidade Federal do Espirito Santo, Nursing Department Bomfim, Emiliana; University of Saskatchewan College of Medicine, Department of Medicine Pessanha, Raphael Manhães ; Universidade Federal do Espirito Santo, Nursing Department Schuab, Sara Isabel Pimentel Carvalho ; Universidade Federal do Espírito Santo, Nursing Department Lima, Regina Aparecida Garcia; Universidade de Sao Paulo Campus de Ribeirao Preto
Keywords:	INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

***Title Page** – BMJ Open*

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Luís Carlos Lopes-Júnior[1*], RN, Ph.D. E-mail: lopesjr.lc@gmail.com
Emiliana Bomfim[2], RN, MSc., Ph.D candidate. E-mail: e.bomfim@usask.ca
Raphael Manhães Pessanha[1], RN student. E-mail: rafa.09pessanha@gmail.com
Sara Isabel Pimentel Carvalho Schuab[1], RN student. E-mail: sarapimentel2009@hotmail.com
Regina Aparecida Garcia de Lima[3], RN, Ph.D. E-mail: limare@eerp.usp.br

Affiliations and addresses: [1]Federal University of Espírito Santo (UFES). Vitoria, ES, Brazil. [2]University of Saskatchewan, College of Medicine. Saskatoon, SK, Canada. [3]University of São Paulo (USP) at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil.

Corresponding author: Luís Carlos Lopes-Júnior. Adjunct Professor of the Nursing Department /Health Sciences Center at the Federal University of Espírito Santo (UFES), Av. Marechal Campos, 1468 – Maruípe, Zip Code: 29.043-900, Vitória, ES, Brazil. E-mail: [lopesjr.lc@gmail.com], Phone: +55(27)99249-7217. ORCID: https://orcid.org/0000-0002-2424-6510

Acknowledgements
None do declare.

Author Contributions: LCLJ conceptualized and designed the protocol, drafted the initial manuscript and reviewed the manuscript. EB, RMP, SISPCS, RAGL and LCLJ defined the concepts and search items, data extraction process as well as methodological appraisal of the studies. EB, RMP, SISPCS, and LCLJ planned the data extraction and statistical analysis. RAGL, EB and LCLJ provided critical insights. All authors have approved and contributed to the final written manuscript.

Funding: No financial support.

Data Statement section: PROSPERO registration number: CRD42020182724. Available in: Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020182724

Word Count: 2868 words.

Disclaimer: The views of the authors do not necessarily reflect those of the NHS, NIHR or the Department of Health.

Competing interests: None.

Sponsorship: None.

Patient consent: Not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

ABSTRACT

Introduction: Since the World Health Organization declared COVID-19 as a pandemic, the exponential spreading of the new coronavirus has been the focus of attention for scientists, governments and populations. One of the great concerns and challenges in several countries, mainly for low and middle-income ones, refers to the notification and monitoring of COVID-19's cases. The wide availability of antibody tests would be an important advance in the control of COVID-19, but there is still no systematic review and meta-analysis to confirm it, and currently, this is the biggest challenge faced by many countries worldwide. We aim to synthesize and critically evaluate the scientific evidence on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19.

Methods and analysis: A systematic review will be held in eight databases: MEDLINE, ISI of Knowledge, CENTRAL, EMBASE, SCOPUS, LILACS, PsycINFO and CNKI, with no restriction regarding the publication date or languages. Primary outcomes will include the better notification, control and timely monitoring of COVID-19 cases. Study selection will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist. Methodological appraisal of the studies will be assessed by the Cochrane Risk-of-Bias Tool for Randomized Controlled Trials, besides MINORS for assessing the risk-of-bias for Non-Randomized Studies. A narrative synthesis of the findings will be structured around the type of intervention, target population characteristics, focused on the primary outcome and intervention/exposure follow-up. Additionally, if sufficient data are available, a meta-analysis will be conducted using Hedges' g score for both fixed and random effect models. I^2 statistics will be used to assess heterogeneity.

Ethics and dissemination: Ethical approval is not required once primary data will not be collected. Findings will be disseminated widely via peer-reviewed publication as well as in different media, such as, symposia, congresses.

PROSPERO registration number: CRD42020182724.

Keywords: COVID-19; Coronavirus; Coronavirus Infections; Testing; Effectiveness; Public Health; Health Surveillance.

Strengths and limitations of this study:

- This systematic review protocol reduces the possibility of duplication, gives transparency to the methods and processes that will be used, reduces possible biases and also will be allows peer review.
- We will offer highest level of evidence for Health Surveillance support for shared decision making from the healthcare providers, stakeholders and governments from this systematic review for control of COVID-19.
- This systematic review will be the first to evaluate critically the scientific evidences on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19. This study will be relevant to address this gap in the literature with regards to achieving better notification, control and timely monitoring of COVID-19 cases as well as guiding strategies and health policies decision-making to the several countries.
- The scarcity of randomized controlled trials as well as observational studies undertaken on this particular topic, the publication bias of the original researches and the methodological quality of the grey literature found may be the main limitations of the study.

INTRODUCTION

Recent cases of pneumonia in Wuhan, China, have led to the discovery of a new type of zoonotic Coronavirus - an enveloped RNA virus, commonly found also in humans capable of causing respiratory, enteric, liver and neurological disorders. [1] Despite COVID-19 has a low lethality of around 3%, transmissibility is high, [1] with respiratory secretions being the main means of spreading SARS-CoV-2. [2] Since the World Health Organization to declared COVID-19 a pandemic on March 11, 2020, [3] the SARS-CoV-2 spreading has been the focus of attention for scientists, government officials, and populations. [4]

A study on observations of SARS-CoV-2 infections in China, using a networked metapopulation dynamics and Bayesian inference models to infer epidemiological characteristics associated with COVID-19, estimated that the rate of transmission of undocumented infections per person was 55% of documented infections. However, due to their greater number, undocumented infections were the source of infection for 79% of documented cases. [5] SARS-CoV2 is already circulating in 212 countries and territories worldwide, with 4,241,956 infected and 286,492 deaths recorded on May 11, 2020, [6] being the Brazil the new epicenter of the pandemic [7] with 165,475 confirmed cases and 11,309 deaths so far. [6]

One of the great concerns and challenges of COVID-19 in several countries, especially for low and middle income, refers to the notification of cases. [8] The definitions of suspected cases, as expected, were changed as the transmission situation changed over time. Notification platforms have also undergone modifications over the months. It is worrying the volume of changes that occurred in such a short time, especially in relation to notification platforms. It is not possible to know whether these changes arrive in a timely manner, especially in populous, middle and low-income countries. [9] The coexistence of several criteria and platforms can generate serious failures in the Health Surveillance system, resulting in underreporting, the magnitude of which is difficult to be estimated. Indeed, the main reason for criticism of the Health Surveillance process in several countries there has been a low capacity for mass testing. [8 10]

One of the crucial issues that the World Health Organization (WHO) has pointed out, is that testing all suspected cases is essential for controlling the pandemic. [11] However, inadequate access to diagnostic tests still exists globally and the confusion among health professionals and the public about prioritizing tests and interpreting results is still a reality. [10 12] The lack of diagnostic tests and laboratory capacity for the detection of COVID-19 in many

countries, for example in Brazil, it had led the Ministry of Health to limit testing only to severe cases, with the justification that testing does not change the treatment to be offered. [13]

It should be noted that the incubation period from infection to the first symptom of COVID-19 is typically 5 to 7 days, with an interval of 4-14 days. The diagnosis of the current infection depends on tests to detect viruses in various body fluids. [10 12] Nasopharyngeal smears (swab) are more sensitive than oropharyngeal smears and are better when the first symptoms appear. [14 15 16 17 18] However, the gold standard for diagnostic testing is the detection of viral RNA by molecular methods, mainly by reverse-transcriptase polymerase chain reaction (RT-PCR).

New systems are being evaluated for faster detection of major viral sequences [16 19 20] and a variety of antigen detection devices have been developed, however, their performance varies widely. In countries such as Korea South, mass testing programs, contact tracking and isolation contributed to early infection control. [21] As the epidemic progresses, the focus is on symptomatic patients and health professionals who are at the forefront of COVID-19 and their families. Testing symptomatic patients for their current infection when they attend health services can inform the tracking and prevention and control of infections, particularly in the screening of patients for COVID-19 referral centers / hospitals. [10 12]

The World Meters Network, based on consolidated official data, raises some questions that are quite relevant in terms of differences in testing. [6] Comparing countries by the capacity of testing per million inhabitants from official data, there are expressive differences. For example, on one hand, the United States has already tested 9,700,658 individuals on May 11, 2020, i.e., 29,307 per 1,000,000,000 inhabitants. Brazil, on the other hand, tested 339,552 individuals to date, representing 1,597 per 1,000,000,000 inhabitants, placing Brazil in a very unfavorable situation in terms of the control of COVID-19 comparing the testing capacity of other countries. [6]

Without symptomatic testing, it will be difficult to isolate patients and quarantine communicants. Thus, the production of diagnostic kits for COVID-19 and the laboratory capacity to perform the testing of symptomatic patients urgently need to be expanded. [10 12] It is hypothesized that the wide availability of antibody tests would be an important advance in the control of COVID-19, but there is still no systematic review and meta-analysis to confirm it, and currently, this is the biggest challenge faced by many countries. Hence, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) checklist as guidance, [22] we propose a systematic and a reproducible strategy to query the literature about the effectiveness of mass testing for control of COVID-19 worldwide.

RESEARCH AIMS

The purpose of this systematic review was to synthesize and critically evaluate the scientific evidence on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19.

METHODS AND ANALYSIS

Search Strategy

Search strategy will be undertaken using resources for enhance methodological transparency and improve the reproducibility of the findings as well as evidence synthesis, following the PRISMA-P checklist. [22] Additionally, using the PICO (Population/ Intervention/Comparison/Outcomes) acronym [23] we elaborated the research question for this review, for ensuring the systematic search of the literature: *"What is the scientific evidence from studies about the effectiveness of the capacity to testing symptomatic patients for the control of the COVID-19 pandemic?"* Approval of this systematic review protocol was obtained by The PROSPERO – International Prospective Register of Systematic Reviews, under Registration Number CRD42020182724.

Studies will be searched using eight databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, ISI of Knowledge via Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), Excerpta Medica database (EMBASE), SCOPUS, Latin American and Caribbean Health Sciences Literature (LILACS), Psychology Information (PsycINFO) and Chinese National Knowledge Infrastructure (CNKI). There will be no restriction regarding the publication dates or languages for this systematic review. Additionally, secondary searches in other sources, such as, into the registration site of clinical trials (e.g. ClinicalTrials.gov), The British Library and Google Scholar. The reference section of the included studies will be hand searched for additional relevant studies. The search strategy will comprise for only key terms according to a pre-established PICO acronym. It is stand out that two researchers (LCLJ and EB) will carry out the search strategy in all databases independently. Also, the bibliographic software EndNote (https://www.myendnoteweb.com/) as well as Rayyan™ app (*Qatar Computing Research Institute)* [24] will be used to store, organize, and manage all the references and ensure a systematic and comprehensive search.

Firstly, we will identify the existence of specific subject headings index in each database (such as MeSH terms, Emtree terms, PsycINFO Thesaurus and DeCS-Health Science Descriptors) and their synonyms (keywords). The search terms were combined using the Boolean operators "AND" and "OR". [25] Subsequently, the search strategy combining MeSH terms and keywords that will be used in MEDLINE (via PubMed) and adjusted to the other databases will be as depicted in Table 1.

Table 1 Concepts and search items

Databases	Search strategy
MEDLINE ISI of Knowledge CENTRAL EMBASE SCOPUS LILACS PsycINFO CNKI	**#1** (("Infant" [MeSH Terms] OR "Child, Preschool" [MeSH Terms] OR "Adolescent" [MeSH Terms] OR "Young Adult" [MeSH Terms] OR "Adult" [MeSH Terms] OR "Aged" [MeSH Terms] OR "Aged, 80 and over" [MeSH Terms]))
	#2 (("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]) OR ("COVID-19"[All Fields] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields]) OR "Pandemics"[MeSH Terms])
	#3 (("COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 testing" [All Fields] OR "LAMP assay" [Supplementary Concept] OR "LAMP assay COVID-19" [All Fields] OR LAMP assay SARS-CoV-2" [All Fields] OR OR LAMP assay Coronavirus Infections/*diagnosis [All Fields]))
	#4 #1 AND #2 AND #3

Abbreviations: MEDLINE, Medical Literature Analysis and Retrieval System Online; CENTRAL, Cochrane Central Register of Controlled Trials; EMBASE, Excerpta Medica Database; LILACS, Latin American and Caribbean Health Sciences Literature; PsycINFO, Psychology Information; CNKI, Chinese National Knowledge Infrastructure.

Study Selection

The PICO acronym [Population (P), Interventions/Exposure (I), Comparators (C) and Outcomes (O)] are detailed in Table 2.

Table 2 Inclusion and exclusion criteria

PICO Acronym [23]	Inclusion criteria	Exclusion criteria
P – Population	Infant, Child, Adolescents, Young Adult, Adult and Aged (according to MeSH terms)* of both sexes, of any ethnicity, and symptomatic and / or suspect for COVID-19.	–
I – Intervention/Exposure	COVID-19 testing	Testing for other previous pandemics
C – Comparison	Symptomatic individuals for COVID-19 who have not been tested	–
O – Outcome	The primary outcomes includes better notification, control and timely monitoring of COVID-19 cases	–

Abbreviations: MeSH, Medical Subject Headings; COVID-19, Coronavirus Disease 2019.
* In this systematic review we will using as a definition the following terms in accordance with the MeSH terms indexing, such as "Infant" - a child between 1 and 23 months of age; "Child, Preschool"- a child between the ages of 2 and 5; "Child"- a person 6 to 12 years of age; "Adolescent"- a person 13 to 18 years of age; "Young Adult"- a person between 19 and 24 years of age; "Adult"- a person having attained full growth or maturity. Adults are of 19 through 64 years of age; "Aged"- a person 65 through 79 years of age; "Aged, 80 and over"- a person 80 years of age and older.

Regarding the study design, we will include all designs with quantitative approach (descriptive studies, observational studies and experimental studies), as well as the gray literature (editorials, opinion articles, reviews, clinical guidelines, conference proceedings, abstracts, book chapters, etc.) as recommended by the Cochrane Handbook. [26] Thus, studies that have investigated epidemiological and clinical aspects of testing the symptomatic and suspected population for COVID-19 will be included in this systematic review. Nevertheless, studies evaluating the mass testing for other Severe Acute Respiratory Syndromes (SRAG) than COVID-19 will be excluded. The selection of studies will also be carried out by two reviewers independently (LCLJ and EOB) and blindly. After this selection, a third reviewer (RAGL) will be responsible for analyzing and deciding on the inclusion or exclusion of each article, especially in relation to those containing a conflicting decision. In this inclusion stage of articles, we will use the Rayyan™ application, developed by the *Qatar Computing Research Institute*, [24] as an auxiliary tool in the archiving, organization and selection of articles. With regards to the setting of the population to be testing we will include people living in community, nursing homes, also outpatients and hospitalized people.

Screening and Data Extraction

First of all, the screening of studies will be based on the information retrieved in their titles and abstracts and will be carried out by two independent researchers (LCLJ and EB).

When the reviewers disagree, the article will be reevaluated and, if the disagreement persisted, a third reviewer (RAGL) will make a final decision, using Rayyan™ app. Secondly, the full-paper screening will be done by the same independent investigators. In order to measure inter-coder agreement in each screening phase, Cohen's kappa will be performed. Once consensus is reached on the selected studies, a standardized form based on previous studies [27] [28] [29] [30] will be used for data extraction. Information to be extracted including four domains: I) identification of the study (article title; journal title; impact factor; authors; country of the study; idiom; publication year; host institution of the study [hospital; university; research center; single institution; multicenter study]; conflict of interest and study sponsorship); ii) methodological characteristics (study design; study objective or research question or hypothesis; sample characteristics, e.g. sample size, age, race, baseline characteristics; groups and controls; recruitment methods and study completion rates; stated length of follow-up; validated measures; statistical analyses, adjustments; iii) main findings and implications for clinical practice; and iv) conclusions. The same two reviewers will be carried out the data extraction independently. Discrepancies between the reviewers will be resolved either by discussion or, in the lack of agreement, by a third reviewer (RAGL).

Methodological appraisal

The internal validity and risk of bias for RCTs will be assessed with the appraisal tool from the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0, [26] which assesses which assesses the seven domains: I) Randomization Sequence Allocation; II) Allocation concealment; III) Blinding of participants and team involved; IV) Blindness of outcome evaluators; V) Incomplete outcomes; VI) Report of selective outcome and VII) Other sources of bias. Based on these domains evaluated, studies are classified as at risk of low, high or uncertain bias. For assessing Non-Randomized Controlled Trials, the Methodological Index for Non-Randomized Studies (MINORS), [31] will be used. This instrument MINORS contains eight items for non-comparative studies: 1) A clearly stated aim; 2) Inclusion of consecutive patients; 3) Prospective collection of data; 4) Endpoints appropriate to the aim of the study; 5) Unbiased assessment of the study endpoint; 6) Follow-up period appropriate to the aim of the study; 7) Loss to follow-up less than 5%; and 8) Prospective calculation of the study size. [31] Again, the same two reviewers (LCLJ and EB) will held the critical appraisal independently. Disagreements will be resolved by a third reviewer (RAGL). The risk of bias for each outcome across individual studies will be

summarized as a narrative statement and supported by a risk of bias table. A review-level narrative summary of the risk of bias will also be depicted.

Data synthesis

Narrative syntheses about the risk of bias of RCT will be made for the included and analyzed studies. The studies will be classified according to the risk of bias as follows: "low" if all the main domains were classified as "low risk"; "Uncertain" if one or two main domains were classified as "uncertain risk"; and "high" if more than two main domains have been classified as "uncertain" or "high risk". When no information was available, we assigned "uncertain risk". [32] For assessing the Non-Randomized Studies, each item from MINORS will be rated from 0 to 2, which means: the score 0 indicates that the information was not reported, 1 indicated that the information was inadequately reported, and 2 that the information was adequately reported. [31] We will provide a qualitative synthesis of the findings from the included studies, structured around the type of intervention, target population characteristics, focused on the primary outcome and intervention follow-up. In order to select particular studies for data synthesis, we will consider the subgroups based on study design (RCT, non-randomized studies), risk of bias assessments (for example, low, uncertain and high risk of bias), sample size, the relevance of the evidence (outcome, population/context, or intervention) comprising to the research question, or the certainty of the evidence, directness in relation to the research question).

Informal methods will involve ordering tables or structuring figures such as methodological characteristics (for example, study design), subpopulations (for example, sex, age), intervention components, and/or contextual/setting factors. The assessment of the certainty of the evidence will search to take into consideration the precision of the synthesis finding (confidence interval if available), the number of studies and participants, the consistency of effects across studies, the risk of bias of the studies, how directly the included studies address the planned question (directness), and the risk of publication bias. [33]

Study findings will be presented in tables or graphs in the same way as the syntheses are reported in the narrative text to facilitate the comparison of findings from each included study. Key characteristics, such as study design, sample size, and risk of bias, which may affect interpretation of the data, will be also presented. Outcomes will be analyzed according to sex and population subgroups (children, adolescents, young adults, adults and the elderly), and also according to classification of country (low, middle or high-income country).

Furthermore, whenever possible, continuous and dichotomous outcomes will be pooled together for meta-analysis purposes. All effect sizes will be transformed into a

common metric, in order to make them comparable across studies – the bias-corrected standardized difference in means by Hedges' g score, for both fixed and random effect models. Heterogeneity will be assessed using I^2. [34]

Patient and public involvement, ethics and dissemination

Since this is a systematic review protocol the participant recruitment as well as their involvement was not applicable. Moreover, any amendments to this protocol will be documented with reference to saved searches and analysis methods, which will be recorded in bibliographic databases for data collection and synthesis. In addition, our findings will be disseminated via peer-reviewed publication as well as in different media, such as, symposia, and congresses.

DISCUSSION

One of the strengths of the proposed systematic review is to apply a reproducible and transparent procedure for systematic review of the literature. In this protocol, we clearly describe the types of studies, participants, intervention and outcomes that will be considered according to the research question, as well as the data sources, search strategy, data extraction methods (including critical appraisal of the studies included) and data synthesis. [35] By publishing the research protocol, we reinforce the clarity of the strategy and minimize the risk of bias, i.e., selective outcome reporting. [35] These results shall provide high-level evidence to inform, support and customize shared decision making from the healthcare providers, stakeholders and governments.

Potential limitations of this systematic review might include the heterogeneity of measures and outcomes evaluated and the potentially reduced number of studies in subgroup analyses (give the recent COVID-19 outbreak), which may influence the external validity.

Antibody tests are used primarily to determine whether a person has ever had COVID-19. Specific IgM and IgG antibodies should begin to be detectable after 4-5 days, with positive IgM antibodies in 70% of symptomatic patients on days 8 to 14 and 90% of the total positive antibody tests on days 11 to 24. [36] [37] The testing of all symptomatic patients, according to the Imperial College study and the Chinese experience, [38] is essential for the strategy of combining recommended measures to contain the epidemic to be successful. [38]

While the virus spreads worldwide, the scientific community are doing many efforts to generate and spread knowledge about COVID-19. On February 13, 2020, the COVID-19

vocabulary had already been added to the MeSH terms as a subject descriptor indexed in the Medical Literature Analysis and Retrieval System Online - MEDLINE database. On May 11, the new coronavirus had already been cited in 10,750 publications indexed in PubMed, including descriptive analyzes of the first cases, analysis of genomic sequences, epidemiological analyzes, mathematical and statistical models to monitor the new virus and define action strategies, in addition to clinical outcomes, and the unbridled search for the treatment of the new coronavirus. However, there is still no systematic review on the actual effectiveness of testing COVID-19 symptomatic patients for the control and monitoring of cases.

In this sense, the present systematic review will delivery relevant evidence on the on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19 in order to address this gap in the literature with regards to achieving better notification, control and timely monitoring of COVID-19 cases as well as guiding important strategies and health policies decision-making to the several countries.

REFERENCES

1 Zhu N, Zhang D, Wang W, *et al*. A novel Coronavirus from patients with pneumonia in China, 2019. *N Eng J Med* 2020;**382**:727-733. doi: 10.1056/NEJMoa2001017 pmid: https://pubmed.ncbi.nlm.nih.gov/31978945/

2 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol* 2019;**17**:181-92. doi: 10.1038/s41579-018-0118-9 pmid: https://pubmed.ncbi.nlm.nih.gov/30531947/

3 Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. *BMJ* 2020;**368**:m1036. doi: 10.1136/bmj.m1036 pmid: https://pubmed.ncbi.nlm.nih.gov/32165426/

4 Wang C, Horby, PW, Hayden FG, *et al*. A novel coronavirus outbreak of global health concern. *Lancet* 2020;**395**:470–473. doi: 10.1016/S0140-6736(20)30185-9 pmid: https://pubmed.ncbi.nlm.nih.gov/31986257/

5 Li R, Pei S, Chen B, *et al*. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science* 2020;**16**:eabb3221. doi: 10.1126/science.abb3221 pmid: https://pubmed.ncbi.nlm.nih.gov/32179701/

6 Roser M, Ritchie H, Ortiz-Ospina E. Coronavirus Disease (COVID-19) – Statistics and Research. Our World in Data. Available from: https://ourworldindata.org/coronavirus. Accessed: Apr 2020.

7 The Lancet. COVID-19 in Brazil: "So what?". *Lancet.* 2020;**395**:1461. doi: S0140-6736(20)31095-3

8 Turci MA, Holliday JB, de Oliveira NCVC. A Vigilância Epidemiológica diante do Sars-Cov-2: desafios para o SUS e a Atenção Primária à Saúde. *APS em Revista* 2020;**2**:44-55. doi:10.14295/aps.v2i1.70

9 De Oliveira WK, *et al.* Guia de Vigilância Epidemiológica: Emergência de Saúde Pública de Importância Nacional pela Doença pelo Coronavírus 2019. 3 ed. Brasília: Ministério da Saúde; 2020.

10 Beeching NJ, Fletcher TE, Beadsworth MBJ. Covid-19: testing times. *BMJ* 2020;**369**:1403. doi: 10.1136/bmj.m1433

11 World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. WHO: 2020.

12 Peto J. Covid-19 mass testing facilities could end the epidemic rapidly. *BMJ* 2020;**368**:1163. doi: 10.1136/bmj.m1163

13 Rocha, C. A dificuldade do Brasil de aplicar testes em massa na pandemia. [atualizado em 10 de abril de 2020; acesso em 11 de abril de 2020]. Disponível em: https://www.nexojornal.com.br/expresso/2020/04/10/A-dificuldade-do-Brasil-de aplicar-testes-em-massa-na-pandemia

14 Zhang W, Du RH, Li B, *et al.* Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 2020;**9**:386-389. doi: 10.1080/22221751.2020.1729071

15 Wang W, Xu Y, Gao R, *et al.* Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA,* 2020. doi:10.1001/jama.2020.3786

16 Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections—the state of the art. *Emerg Microbes Infect* 2020;**9**:747-56. doi: 10.1080/22221751.2020.1745095

17 Carver C, Nick J. Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. *Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford* (2020).

18 Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, *et al.* SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med 2020;***382**:1177-9. doi: 10.1056/NEJMc2001737

19 Sheridan C. Fast, portable tests come online to curb coronavirus pandemic. *Nat Biotechnol* 2020;**38**:515-518. doi:10.1038/d41587-020-00010-2.

20 Moore SC, Penrice-Randal R, Alruwaili M, Dong X, Pullan ST, Carter D, *et al.* Amplicon based MinION sequencing of SARS-CoV-2 and metagenomic characterisation of nasopharyngeal swabs from patients with COVID-19. *MedRxiv* 2020. doi: 0.1101/2020.03.05.20032011.

21 Kim YJ, Sung, Heungsup S, Chang-Seok, Hur M. COVID-19 Testing in South Korea: Current Status and the Need for Faster Diagnostics. *Ann Lab Med* 2020;**40**:349-350.

22 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;**4**:1. doi: 10.1186/2046-4053-4-1

23 Methley AM, Campbell S, Chew-Graham C, *et al*. PICO, PICOS and SPIDER. A comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC Health Serv Res* 2014;**14**:579. doi: 10.1186/s12913-014-0579-0

24 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*2016;**5**(1):210.

25 Lopes-Júnior LC, Rosa MADRP, Lima RAG. Psychological and Psychiatric Outcomes Following PICU Admission: A Systematic Review of Cohort Studies. *Pediatr Crit Care Med* 2018;**19**:e58–e67.

26 Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. *The Cochrane Collaboration.* Chichester, UK: John Wiley & Sons 2011.

27 Lopes-Júnior LC, Bomfim EO, Nascimento LC, *et al.* Non-pharmacological interventions to manage fatigue and psychological stress in children and adolescents with cancer: an integrative review. *Eur J Cancer Care* 2016;**25**:921–935. doi: 10.1111/ecc.12381

28 Lopes-Júnior, Cruz LAP, Leopoldo VC, *et al*. Effectiveness of Traditional Chinese Acupuncture versus Sham Acupuncture: a Systematic Review. *Rev Lat Am Enferm* 2016;**24**:e2762. doi: 10.1590/1518-8345.0647.2762

29 Gonçalves CA, Lopes-Júnior LC, Nampo FK, *et al*. Safety, efficacy and immunogenicity of therapeutic vaccines in the treatment of patients with high-grade cervical intraepithelial neoplasia associated with human papillomavirus: a systematic review protocol. *BMJ Open* 2019;**9**:e026975. doi: 10.1136/bmjopen-2018-026975

30 Lopes-Júnior LC, Lima RAG, Olson K, *et al*. Systematic review protocol examining the effectiveness of hospital clowns for symptom cluster management in pediatrics. *BMJ Open* 2019;**9**:e026524. doi: 10.1136/bmjopen-2018-026524

31 Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003; **73**(9):712-6.

32 Laurant M, Biezen MVD, Wijers N, *et al*. Nurses as substitutes for doctors in primary care. *Cochrane Database Syst Rev* 2018;**7**:CD001271. doi: 10.1002/14651858.CD001271.pub3

33 Campbell M, McKenzie JE, Sowden A, *et al*. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ* 2020;**368**:l6890. doi: 10.1136/bmj.l6890

34 Egger M, Smith GD, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34. doi: 10.1136/bmj.315.7109.629

35 Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. *JAMA* 2002;**287**:2831–4. doi: 10.1001/jama.287.21.2831

36 Zhao J, Yuan Q, Wang H, *et al.* Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis* 2020:ciaa344. doi: 10.1093/cid/ciaa344 32221519

37 Li Z, Yi Y, Luo X, *et al.* Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol* 2020. doi: 10.1002/jmv.25727 32104917

38 World Health Organization. *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19).* Geneva: World Health Organization; 2020. (WHO technical report).

Reporting checklist for protocol of a systematic review.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	1 and 2
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	1
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Sources	#5a	Indicate sources of financial or other support for the review	1

Sponsor	#5b	Provide name for the review funder and / or sponsor	1
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	1
Rationale	#6	Describe the rationale for the review in the context of what is already known	3 and 4
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5 and 6
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5 and 6
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5 and 7
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7 and 8
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study	8

		level, or both; state how this information will be used in data synthesis	
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	9
	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	9
	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9 and 10
	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	9 and 10
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

BMJ Open

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040413.R1
Article Type:	Protocol
Date Submitted by the Author:	25-Jun-2020
Complete List of Authors:	LOPES-JÚNIOR, LUÍS CARLOS; Universidade Federal do Espirito Santo, Nursing Department Bomfim, Emiliana; University of Saskatchewan College of Medicine, Department of Medicine Silveira, Denise Sayuri Calheiros da; Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto, Department of Biochemistry and Immunology Pessanha, Raphael Manhães ; Universidade Federal do Espirito Santo, Nursing Department Schuab, Sara Isabel Pimentel Carvalho ; Universidade Federal do Espírito Santo, Nursing Department Lima, Regina Aparecida Garcia; Universidade de Sao Paulo Campus de Ribeirao Preto
Primary Subject Heading:	Public health
Secondary Subject Heading:	Health policy, Public health
Keywords:	INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

***Title Page** – BMJ Open*

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Luís Carlos Lopes-Júnior[1*], RN, Ph.D. E-mail: luisgen@usp.br
Emiliana Bomfim[2], RN, MSc., Ph.D candidate. E-mail: e.bomfim@usask.ca
Denise Sayuri Calheiros da Silveira[3], BS, Ph.D., in Immunology. E-mail: sayuri_denise@yahoo.com.br
Raphael Manhães Pessanha[1], Nursing student. E-mail: rafa.09pessanha@gmail.com
Sara Isabel Pimentel Carvalho Schuab[1], Nursing student. E-mail: sarapimentel2009@hotmail.com
Regina Aparecida Garcia de Lima[4], RN, Ph.D. E-mail: limare@eerp.usp.br

Affiliations and addresses: [1]Federal University of Espírito Santo (UFES). Vitoria, ES, Brazil. [2]University of Saskatchewan, College of Medicine. Saskatoon, SK, Canada. [3]University of São Paulo (USP) at Ribeirão Preto Medical School. Ribeirão Preto, SP, Brazil. [4]University of São Paulo (USP) at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil.

Corresponding author: Luís Carlos Lopes-Júnior. Adjunct Professor of the Nursing Department /Health Sciences Center at the Federal University of Espírito Santo (UFES), Av. Marechal Campos, 1468 – Maruípe, Zip Code: 29.043-900, Vitória, ES, Brazil. E-mail: [luisgen@usp.br], Phone: +55(27)99249-7217. ORCID: https://orcid.org/0000-0002-2424-6510

Acknowledgements
None do declare.

Author Contributions: LCLJ conceptualized and designed the protocol, drafted the initial manuscript and reviewed the manuscript. EB, DSCS, RMP, SIPCS, RAGL and LCLJ defined the concepts and search items, data extraction process as well as methodological appraisal of the studies. EB, DSCS, RMP, SIPCS, and LCLJ planned the data extraction and statistical analysis. RAGL, EB, DSCS, LCLJ provided critical insights. All authors have approved and contributed to the final written manuscript.

Funding: No financial support.

Data Statement section: PROSPERO registration number: CRD42020182724. Available in: Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020182724

Word Count: 3515 words.

Disclaimer: The views of the authors do not necessarily reflect those of the NHS, NIHR or the Department of Health.
Competing interests: None.
Sponsorship: None.
Patient consent: Not required.
Provenance and peer review: Not commissioned; externally peer reviewed.

ABSTRACT

Introduction: Since the COVID-19 outbreak has been declared a pandemic by the WHO, the new coronavirus spreading has been the focus of attention of scientists, governments and communities around the world. One of the great concerns and challenges, mainly in low and middle-income countries, is the notification and monitoring of COVID-19's cases. The large-scale availability of the test is a fundamental aspect in the control of COVID-19, but this is currently the biggest challenge faced by many countries in the world. We aim to synthesize and critically evaluate the scientific evidence on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19.

Methods and analysis: A systematic review will be conducted through eight databases: MEDLINE, ISI-of-Knowledge, CENTRAL, EMBASE, SCOPUS, LILACS, PsycINFO and CNKI, from inception until June 30, 2020. No restriction regarding the publication date, settings or languages will be employed. Primary outcomes will include sensitivity as well as the specificity of the tests for COVID-19. Study selection will follow the PRISMA checklist. Methodological appraisal of the studies will be assessed by the Cochrane Risk-of-Bias tool for Randomized Controlled Trials, besides MINORS for Non-Randomized Studies and Newcastle-Ottawa Scale for case-control or cohort studies. Findings will be structured according to the test type, target population characteristics, focused on the primary outcomes (sensitivity and specificity). Additionally, if sufficient data are available, a meta-analysis will be conducted. Pooled standardized mean differences and 95% CIs will be calculated. Heterogeneity between the studies will be determined by the I^2 statistics. Subgroup analyzes will be also performed. Publication bias will be assessed with funnel plots and Egger's test. Heterogeneity will be explored by random-effects analysis.

Ethics and dissemination: Ethical approval was not required. Findings will be disseminated widely via peer-reviewed publication and presented at conferences related to this field.

PROSPERO registration number: CRD42020182724.

Keywords: COVID-19; Coronavirus; Coronavirus Infections; Testing; Effectiveness; Public Health Nursing; Health Surveillance.

Strengths and limitations of this study:

- We will offer evidence for health surveillance support in order to help decision makers (i.e. healthcare providers, stakeholders and governments) regarding COVID-19 control.
- This systematic review will be the first to critically evaluate the scientific evidence about the effectiveness of testing capacity for symptomatic individuals of COVID-19.
- This study will be relevant to address the gap in the literature with regards to achieving better notification, control and timely monitoring of COVID-19 cases as well as guiding strategies and health policies in several countries.
- This systematic review protocol reduces the possibility of duplication, due to the transparency of the methods and processes that will be used, in addition, it reduces possible biases and also allows peer review.
- The sensitivity and specificity of the tests varies widely by test and may be the main limitation of this systematic review, in addition to the publication bias of the original researches and the methodological appraisal of the studies.

INTRODUCTION

In December 2019, an increased number of pneumonia-like cases in Wuhan, China, have led to the discovery of a new type of zoonotic Coronavirus - an enveloped RNA virus, commonly found also in humans capable of causing respiratory, enteric, liver and neurological disorders. [1] Despite the low lethality of COVID-19, around 3%, its transmissibility is high, [1] with respiratory secretions being the main means of spreading SARS-CoV-2. [2] Since the World Health Organization declared COVID-19 outbreak a pandemic on March 11, 2020, [3] the new coronavirus spreading has been the focus of attention for scientists, government officials, and communities around the world. [4]

A study on observations of SARS-CoV-2 infections in China, using a networked metapopulation dynamics and Bayesian inference models to infer epidemiological characteristics associated with COVID-19, estimated that the rate of transmission of undocumented infections per person was 55% of documented infections. However, due to their greater number, undocumented infections were the source of infection for 79% of documented cases. [5] SARS-CoV2 is already circulating in 213 countries and territories worldwide, with 8,914,787 infected and 466,718 deaths recorded on June 20, 2020, [6] making Brazil the new epicenter of the pandemic [7] with 1,070,139 confirmed cases and 50,058 deaths so far. [6]

One of the greatest concerns and challenges in several countries, especially for low and middle-income countries, refers to the notification of cases. [8] Notification platforms have undergone modifications over the months. [9] In addition, the coexistence of several criteria and platforms can generate serious failures in the health surveillance system, resulting in underreporting. Indeed, the main reason for criticism of how health surveillance in being employed in several countries is the low capacity for mass testing. [8 10]

Another crucial issue that the World Health Organization (WHO) has pointed out, is that testing all suspected cases is essential for pandemic control. [11] However, the access to diagnostic tests remains a challenge globally, besides the confusion among health professionals and the population about prioritizing tests and interpreting results.[10 12] The limited availability of diagnostic tests and laboratory capacity for the detection of COVID-19 in many countries, for example in Brazil, had led the Minister of Health to limit testing only for severe cases. The Minister of Health justified its decision by stating that, in mild cases, it

does not matter if the person tests negative or positive, the treatment to be delivered is the same if it is a suspected mild case. [13]

It should be noted that the incubation period from the infection to the appearance of the first symptoms is typically 5 to 7 days, but up to14 days. The final diagnosis depends on tests to detect viruses in various body fluids. [10 12] Nasopharyngeal smears are more sensitive than oropharyngeal smears and are more effective at early stages of symptom development. [14 15 16 17 18] However, the gold standard test is the detection of viral RNA by molecular methods, mainly by reverse-transcriptase polymerase chain reaction (RT-PCR).

New methods are being evaluated for faster detection of major viral sequences [16 19 20] and a variety of antigen detection devices have been developed, however, their performance varies widely. In countries such as Korea South, mass testing programs, contact tracking and isolation, contributed to early infection control. [21] As the epidemic progresses, the focus is on symptomatic patients and health professionals who are on the frontline of COVID-19 response. Testing symptomatic patients can inform about contact tracing, prevention and control of potential new infections. [10 12]

Based on consolidated official data, the Our World in Data raises some questions that are quite relevant in terms of differences in testing capacity. [6] Comparing countries by the testing capacity per one thousand inhabitants from official data, there are expressive differences between countries. The United States has already tested 27,784,614 individuals on June 20, 2020, i.e., 83,9 per 1,000 inhabitants. On the other hand, Brazil has tested 2,409,830 individuals to date, representing 11,3 per 1,000 inhabitants. In order words, currently, the United States has a testing capacity of the 7.4 times greater than that of Brazil. [6]

Without symptomatic testing only, it will be difficult to isolate patients and quarantine communicants. Thus, increasing the production of diagnostic kits and increasing the laboratory capacity is an urgent issue in Brazil as well as in low and middle-income countries . [10 12] It is hypothesized that a significant increase in the large-scale testing capability would be an important advance in the control of COVID-19 in Brazil and other countries, as this is currently the biggest challenge faced by many countries in the world. Hence, this systematic review protocol, adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) reporting standards[22] proposes a systematic and a reproducible strategy to query the literature about the effectiveness of mass testing for control of COVID-19.

RESEARCH AIMS

The purpose of this systematic review is to synthesize and critically evaluate the scientific evidence on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19.

METHODS AND ANALYSIS

Search Strategy

Search strategy will be performed using resources to enhance methodological transparency and improve the reproducibility of the findings, following the PRISMA-P guidelines. [22] In addition, using the PICO (Population/ Intervention/Comparison/Outcomes) acronym[23] we elaborated the research question of this review, for ensuring the systematic search of the literature: *"What are the scientific evidence from studies about the effectiveness of the testing capacity for symptomatic patients for COVID-19 pandemic control?"*. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on April 2020 (registration number CRD42020182724).

Article searches will be conducted in the following specialized and general databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, ISI of Knowledge via Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), Excerpta Medica database (EMBASE), SCOPUS, Latin American and Caribbean Health Sciences Literature (LILACS), Psychology Information (PsycINFO) and Chinese National Knowledge Infrastructure (CNKI), from inception until June 30, 2020. The grey literature will be searched in five additional sources: ProQuest Dissertations and Theses Global, Mascot/Wotro, Effective Public health Practice Projects, Public Health Grey Literature Sources, Health Evidence. No restriction regarding the publication date, the setting or languages will be considered in this systematic review. Additionally, secondary searches in other sources, such as the website of clinical trials (e.g. ClinicalTrials.gov), The British Library and Google Scholar will be also performed. The reference section of the included studies and citing studies will be hand searched for additional relevant studies. The search strategy will comprise for only key terms according to a pre-established PICO acronym. It is stand out that two researchers (LCLJ and EB) will carry out the search strategy in all databases independently. Also, the bibliographic software EndNote (https://www.myendnoteweb.com/) as well as Rayyan™ app (*Qatar Computing Research*

Institute) [24] will be used to store, organize, and manage all the references and ensure a systematic and comprehensive search.

Firstly, we will identify the existence of specific subject headings index in each database (such as MeSH terms, Emtree terms, PsycINFO Thesaurus and DeCS-Health Science Descriptors) and their synonyms (keywords). The search terms will be combined using the Boolean operators "AND" and "OR". [25] The search strategy combining MeSH terms and keywords which will be used in MEDLINE is depicted in the Table 1 and will be adapted to meet each databases' specific syntax requirements.

Table 1 Concepts and search items

Databases	Search strategy
MEDLINE ISI of Knowledge CENTRAL EMBASE SCOPUS LILACS PsycINFO CNKI	**#1** (("Infant" [MeSH Terms] OR "Child, Preschool" [MeSH Terms] OR "Adolescent" [MeSH Terms] OR "Young Adult" [MeSH Terms] OR "Adult" [MeSH Terms] OR "Aged" [MeSH Terms] OR "Aged, 80 and over" [MeSH Terms])) **#2** (("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields]) OR ("COVID-19"[All Fields] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields]) OR "Pandemics"[MeSH Terms]) **#3** (("COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 testing" [All Fields] OR "2019 novel coronavirus disease testing" [All Fields] OR "COVID19 antibody testing" [All Fields] OR "SARS2 testing" [All Fields] OR "2019-nCoV testing" [All Fields] OR "COVID-19 antibody testing" [All Fields] OR "COVID-19 blood antibody testing" OR "SARS-CoV-2 infection antibody testing" [All Fields] OR "COVID-19 serological testing" [All Fields] OR "COVID19 serological testing" [All Fields] OR "Serology Testing for COVID-19" [All Fields] OR "COVID-19 serological testing" [All Fields] OR "Serology Testing for COVID-19" [All Fields] OR "SARS-CoV-2 infection serological testing" [All Fields] OR"LAMP assay" [Supplementary Concept] OR "LAMP assay COVID-19" [All Fields] OR LAMP assay SARS-CoV-2" [All Fields] OR LAMP assay Coronavirus Infections/*diagnosis [All Fields] OR "2019-novel coronavirus real-time reverse transcriptase diagnostic panel" [All Fields] OR "2019-nCoV RT-PCR diagnostic panel" [All Fields] OR "COVID-19 nucleic acid testing" [All Fields] OR "SARS-CoV-2 infection nucleic acid testing" [All Fields] OR "COVID19 nucleic acid testing"

[All Fields] OR))

#4 #1 AND #2 AND #3

Abbreviations: MEDLINE, Medical Literature Analysis and Retrieval System Online; CENTRAL, Cochrane Central Register of Controlled Trials; EMBASE, Excerpta Medica Database; LILACS, Latin American and Caribbean Health Sciences Literature; PsycINFO, Psychology Information; CNKI, Chinese National Knowledge Infrastructure.

Study Selection

The PICO acronym [Population (P), Interventions/Exposure (I), Comparators (C) and Outcomes (O)] is detailed in the Table 2.

Table 2 Inclusion and exclusion criteria

PICO Acronym [23]	Inclusion criteria	Exclusion criteria
P – Population	Infant, Child, Adolescents, Young Adult, Adult and Aged (according to MeSH terms)* of all genders, of any ethnicity, and symptomatic and / or suspect for COVID-19.	–
I – Intervention/Exposure	Testing for COVID-19	Testing for other previous pandemics
C – Comparison	Symptomatic individuals for COVID-19 who have not been tested	–
O – Outcome	The primary outcomes includes sensitivity as well as the specificity of the tests.	–

Abbreviations: MeSH, Medical Subject Headings; COVID-19, Coronavirus Disease 2019.
* In this systematic review we will use the definitions in accordance with the MeSH terms indexing, such as "Infant" - a child between 1 and 23 months of age; "Child, Preschool"- a child between the ages of 2 and 5; "Child"- a person 6 to 12 years of age; "Adolescent"- a person 13 to 18 years of age; "Young Adult"- a person between 19 and 24 years of age; "Adult"- a person having attained full growth or maturity. Adults are of 19 through 64 years of age; "Aged"- a person 65 through 79 years of age; "Aged, 80 and over"- a person 80 years of age and older.

Regarding the study design, we will include all designs with quantitative approach (descriptive, observational and experimental studies), as well as the gray literature (editorials, opinion articles, reviews, clinical guidelines, conference proceedings, abstracts, book chapters, etc.) as recommended by the Cochrane Handbook.[26] Thus, studies that have investigated epidemiological and clinical aspects of testing capacity for symptomatic and suspected patients for COVID-19 will be included in this systematic review. Nevertheless, studies evaluating mass testing for other Severe Acute Respiratory Syndromes (SARS) than COVID-19, will be excluded. With regards to population characteristics, will be included people living in the communities, nursing homes, outpatients and hospitalized people.

The primary outcomes of this systematic review include sensitivity as well as the specificity of the tests for COVID-19. Sensitivity measures how often a test correctly

generates a positive result for people who have the condition that is being tested for (also known as the "true positive" rate). A test that's highly sensitive will flag almost everyone who has the disease and not generate many false-negative results. For instance, a test with 90% sensitivity will correctly return a positive result for 90% of people who have the disease but, will return a negative result - a false-negative - for 10% of the people who have the disease and should have tested positive. [27] Specificity measures a test's ability to correctly generate a negative result for people who don't have the condition that's being tested for (also known as the "true negative" rate). A high-specificity test will correctly rule out almost everyone who does not have the disease and will not generate many false-positive results. For example, a test with 90% specificity will correctly return a negative result for 90% of people who don't have the disease but, will return a positive result - a false-positive - for 10% of the people who don't have the disease and should have tested negative). [27] In other words, sensitivity is the proportion of patients with disease who have a positive test, or the true positive rate and the specificity is the proportion of patients without disease who have a negative test, or true negative rate. These terms describe the operating characteristics of a test and can be used to gauge the effectiveness of a test result. [28]

The screening and selection of studies will also be carried out by two reviewers (LCLJ and EB) independently and blindly. After this selection, a third reviewer (RAGL) will be responsible for analyzing and deciding on the inclusion or exclusion of each article, especially in relation to those containing a conflicting decision. The Rayyan™ application, developed by the *Qatar Computing Research Institute*, [24] will be used as an auxiliary tool for data management.

Screening

After importing documents retrieved from the initial searches, duplicates will be removed, and two reviewers (LCLJ and EB) will independently screen the studies for based on their titles and abstracts. If good agreement is achieved between reviewers (at least 80 percent) then each will proceed to full article screening. If there is less than 80 percent agreement, the articles will be reevaluated, and the disagreements discussed and resolved by consensus, but if the disagreement persist, a third reviewer (RAGL) will make a final decision, using Rayyan™ app.

Data Extraction

Full text screening will be done by the same independent investigators. In order to measure inter-coder agreement in each screening phase, Cohen's kappa will be performed. Once consensus is reached on the selected studies, a standardized form based on previous

studies [29 30 31 32 33 34] will be used for data extraction. Information to be extracted including four domains: I) identification of the study (article title; journal title; impact factor; authors; country of the study; language; sources of funding; publication year; host institution of the study [hospital; university; research center; single institution; multicenter study]; conflict of interest and study sponsorship); ii) methodological characteristics (study design; study objective or research question or hypothesis; sample characteristics, e.g. sample size, age, eligibility criteria, ethnicity, baseline characteristics; groups and controls; recruitment methods and study completion rates; comparator group; timeframe for follow-up; co-interventions; validated measures; costs and/or remuneration related to participation; statistical analyses, adjustments; iii) main findings and implications for clinical practice; and iv) conclusions. The same two reviewers will be carried out the data extraction independently. Discrepancies between the reviewers will be resolved either by discussion or, in the lack of agreement, by a third reviewer (RAGL).

Methodological appraisal

The internal validity and risk of bias for RCTs will be assessed with the appraisal tool from the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0, [26] which assesses the following seven domains: I) Randomization Sequence Allocation; II) Allocation concealment; III) Blinding of participants and team involved; IV) Blindness of outcome evaluators; V) Incomplete outcomes; VI) Report of selective outcome and VII) Other sources of bias. Based on these domains evaluated, studies are classified as at risk of low, high or uncertain bias. For assessing Non-Randomized Controlled Trials, the Methodological Index for Non-Randomized Studies (MINORS), [35] will be used. This instrument MINORS contains eight items for non-comparative studies: 1) A clearly stated aim; 2) Inclusion of consecutive patients; 3) Prospective collection of data; 4) Endpoints appropriate to the aim of the study; 5) Unbiased assessment of the study endpoint; 6) Follow-up period appropriate to the aim of the study; 7) Loss to follow-up less than 5%; and 8) Prospective calculation of the study size. [35] With regards to the case-control or cohort studies, we will use the Newcastle-Ottawa Scale to evaluate its methodological quality. [36] Using the Newcastle-Ottawa Scale, the case–control and cohort studies will be given star ratings in 3 categories —Selection (maximum 4 stars), Comparability (maximum 2 stars), and Outcome (maximum 3 stars)—with a maximum score of 9 stars. [36] The same two reviewers (LCLJ and EB) will hold the quality assessment independently. Disagreements will be resolved by a third reviewer (RAGL).

Data synthesis

A qualitative synthesis on the risk of bias of RCT will be made for the included and analyzed studies. The studies will be classified according to the risk of bias as follows: "low" if all the main domains were classified as "low risk"; "Uncertain" if one or two main domains were classified as "uncertain risk"; and "high" if more than two main domains have been classified as "uncertain" or "high risk". When no information is available, we will assign "uncertain risk". [37] For assessing the Non-Randomized Studies, each item from MINORS will be rated from 0 to 2, which means: the score 0 indicates that the information was not reported, 1 indicated that the information was inadequately reported, and 2 that the information was adequately reported. [35] Regarding the case–control and cohort studies assessing by the Newcastle-Ottawa Scale the quality of these studies will be adjudicated based on previous study [38]: good quality: Selection ≥3 stars AND Comparability ≥1 stars AND Outcome ≥2 stars; fair quality: Selection 2 stars AND Comparability ≥1 stars AND Outcome ≥2 stars; poor quality: Selection ≤1 Star OR Comparability 0 stars OR ≤1 stars. [38]

In addition, we will complete a narrative synthesis, providing a comprehensive descriptive summary around the type of test for COVID-19, study design, target population characteristics, focused on the primary outcome (sensitivity as well as the specificity of the tests for COVID-19). It will be also presented in the text and table format the methodological characteristics of the studies, subpopulations characteristics, test characteristics, as well as sensitivity and specificity of them. The assessment of the certainty of the evidence will take into consideration the precision of the synthesis finding (i.e. confidence interval if available), the number of studies and participants, the consistency of effects across studies, the risk of bias of the studies, how directly the included studies address the planned question (directness), and the risk of publication bias. [39]

Study findings will be presented in tables or graphs in the same way as the syntheses are reported in order to facilitate the comparison of similarities and differences in design and outcomes between studies. Key characteristics, such as study design, sample size, and risk of bias, sensitivity as well as the specificity, which may affect interpretation of the data, will be also presented. Outcomes will be analyzed according to sex and population subgroups (children, adolescents, young adults, adults and the elderly), test for COVID-19 type, and also according to the classifying countries by income (high, upper-middle, lower-middle, and low), based on The World Bank Classification using the Gross National Income (GNI) per capita. [40]

Meta-analyses will be conducted if there is sufficient homogeneity in study design and study subjects among selected articles. Therefore, continuous and dichotomous outcomes will

be pooled together for meta-analysis purposes. Quantitative data from each study will be extracted and inserted into an Excel sheet by two independent reviewers. Statistical analyses will be carried out using the Statistical Package for the Social Sciences - SPSS, version 18.0 (SPSS, Inc., Chicago, IL, USA).

Standardized mean differences (SMD) and 95% CI will be used to calculate the effect sizes, [41] [42] included in our meta-analysis will have reported the differences in testing for COVID-19. All effect sizes will be transformed into a common metric, in order to make them comparable across studies—the bias-corrected standardized difference in means (Hedges' g). For continuous outcome measures, standardized mean differences (SMDs) and risk ratio (RR) for categorical outcomes will be considered for the final assessment from individual studies. SMD was chosen as a measure of pooled results considering the likely variability in the measuring scales for continuous outcomes. [42] The effect size will be interpreted by Cohen's proposal: 0.20 corresponds to a small effect size, 0.50 corresponds to a medium effect size and 0.80 corresponds to a large effect size. [43]

A random effects model will be selected under the assumption that studies included in the meta-analysis have been carried out with heterogeneous populations. Heterogeneity will also be tested by the I^2 statistic, which can quantify the heterogeneity ranging from 0% (no heterogeneity) to 100% (the differences between the effect sizes can completely be explained by chance alone), and the interpretations of the percentages are as follows: 0%–40% indicates potentially unimportant heterogeneity, 30%–60% indicates moderate heterogeneity, 50%–90% indicates substantial heterogeneity and 75%–100% indicates considerable heterogeneity. [42] To explore the heterogeneity across studies, subgroup analysis will be performed using a mixed effects model according to the following variables: according to sex and population subgroups (children, adolescents, young adults, adults and the elderly), test for COVID-19 type, and also according to the classifying countries by income (high, upper-middle, lower-middle, and low).

Patient and public involvement

Since this is a systematic review protocol no patients and public will be involved.

Ethics and dissemination

Due to the characteristics of this study design, the ethical evaluation was not required. The findings of this systematic review will be disseminated through peer-reviewed publication as well as in different media, such as, symposia, and congresses related to this field. Moreover, any amendments to this protocol will be documented with reference to the

saved searches and analysis methods, which will be recorded in bibliographic databases, for data collection and synthesis.

DISCUSSION

One of the strengths of the proposed systematic review is to apply a reproducible and transparent procedure for systematic review of the literature. In this protocol, we clearly describe the types of studies, participants, intervention and outcomes that will be considered according to the research question, as well as the data sources, search strategy, data extraction methods (including critical appraisal of the studies included) and data synthesis. [35] By publishing the research protocol, we reinforce the clarity of the strategy and minimize the risk of bias, i.e., selective outcome reporting. [44] These results shall provide evidences in order to inform, support and customize shared decision making from healthcare providers, stakeholders and government personnel.

Since the sensitivity and specificity of the tests for COVID-19 varies widely by test, this might be the main limitation of this systematic review, in addition to the publication bias of the original studies and the methodological appraisal of the studies, which may influence the external validity.

The testing of all symptomatic patients, according to the Imperial College study and the Chinese experience, [45] is essential to contain the epidemic. Although positive tests for COVID-19 are clinically useful, negative tests need to be interpreted with caution, taking into account the pre-test probability of disease. This has important implications for physicians to interpret tests and policymakers who design diagnostic algorithms for COVID-19. The Chinese handbook of COVID-19 prevention and treatment states "*if the nucleic acid test is negative at the beginning, samples should continue to be collected and tested in the following days*". [46] False negatives carry substantial risks; for instance, patients can be transferred to wards not covered by COVID-19, leading to the spread of hospital-acquired COVID-19 infection; caregivers can also spread the infection to vulnerable dependents. [28 47] Hence, clear evidence-based guidelines on repeated testing are needed to reduce the risk of false negatives. Finally, physicians must ensure that patients are informed about the limitations of the tests. Patients with a single negative test, but with symptoms that are suggestive of COVID-19, should be advised to isolate themselves according to the guidelines for suspected COVID-19, once no test is 100% accurate. [28 47]

In this sense, the present systematic review will delivery relevant evidence on the effectiveness of testing capacity for symptomatic individuals for the control of COVID-19.

Ultimately, we will provide evidence to help the health sector achieving better notification, control and timely monitoring of COVID-19 cases, as well as guiding important strategies and health policy decision makers of several countries.

REFERENCES

1 Zhu N, Zhang D, Wang W, *et al*. A novel Coronavirus from patients with pneumonia in China, 2019. *N Eng J Med* 2020;**382**:727-733. doi: 10.1056/NEJMoa2001017 pmid: https://pubmed.ncbi.nlm.nih.gov/31978945/

2 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol* 2019;**17**:181-92. doi: 10.1038/s41579-018-0118-9 pmid: https://pubmed.ncbi.nlm.nih.gov/30531947/

3 Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. *BMJ* 2020;**368**:m1036. doi: 10.1136/bmj.m1036 pmid: https://pubmed.ncbi.nlm.nih.gov/32165426/

4 Wang C, Horby, PW, Hayden FG, *et al*. A novel coronavirus outbreak of global health concern. *Lancet* 2020;**395**:470–473. doi: 10.1016/S0140-6736(20)30185-9 pmid: https://pubmed.ncbi.nlm.nih.gov/31986257/

5 Li R, Pei S, Chen B, *et al*. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science* 2020;**16**:eabb3221. doi: 10.1126/science.abb3221 pmid: https://pubmed.ncbi.nlm.nih.gov/32179701/

6 Roser M, Ritchie H, Ortiz-Ospina E & Hasell J. Coronavirus Pandemic (COVID-19) Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource]

7 The Lancet. COVID-19 in Brazil: “So what?”. *Lancet.* 2020;**395**:1461. doi: S0140-6736(20)31095-3

8 Turci MA, Holliday JB, de Oliveira NCVC. A Vigilância Epidemiológica diante do Sars-Cov-2: desafios para o SUS e a Atenção Primária à Saúde. *APS em Revista* 2020;**2**:44-55. doi:10.14295/aps.v2i1.70

9 De Oliveira WK, *et al.* Guia de Vigilância Epidemiológica: Emergência de Saúde Pública de Importância Nacional pela Doença pelo Coronavírus 2019. 3 ed. Brasília: Ministério da Saúde; 2020.

10 Beeching NJ, Fletcher TE, Beadsworth MBJ. Covid-19: testing times. *BMJ* 2020;**369**:1403. doi: 10.1136/bmj.m1433

11 World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. WHO: 2020.

12 Peto J. Covid-19 mass testing facilities could end the epidemic rapidly. *BMJ* 2020;**368**:1163. doi: 10.1136/bmj.m1163

13 Rocha, C. A dificuldade do Brasil de aplicar testes em massa na pandemia. [atualizado em 10 de abril de 2020; acesso em 11 de abril de 2020]. Disponível em: https://www.nexojornal.com.br/expresso/2020/04/10/A-dificuldade-do-Brasil-de aplicar-testes-em-massa-na-pandemia

14 Zhang W, Du RH, Li B, *et al.* Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 2020;**9**:386-389. doi: 10.1080/22221751.2020.1729071

15 Wang W, Xu Y, Gao R, *et al.* Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA,* 2020. doi:10.1001/jama.2020.3786

16 Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections—the state of the art. *Emerg Microbes Infect* 2020;**9**:747-56. doi: 10.1080/22221751.2020.1745095

17 Carver C, Nick J. Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. *Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford* (2020).

18 Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, *et al.* SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med 2020;***382**:1177-9. doi: 10.1056/NEJMc2001737

19 Sheridan C. Fast, portable tests come online to curb coronavirus pandemic. *Nat Biotechnol* 2020;**38**:515-518. doi:10.1038/d41587-020-00010-2.

20 Moore SC, Penrice-Randal R, Alruwaili M, Dong X, Pullan ST, Carter D, *et al.* Amplicon based MinION sequencing of SARS-CoV-2 and metagenomic characterisation of nasopharyngeal swabs from patients with COVID-19. *MedRxiv* 2020. doi: 0.1101/2020.03.05.20032011.

21 Kim YJ, Sung, Heungsup S, Chang-Seok, Hur M. COVID-19 Testing in South Korea: Current Status and the Need for Faster Diagnostics. *Ann Lab Med* 2020;**40**:349-350.

22 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;**4**:1. doi: 10.1186/2046-4053-4-1

23 Methley AM, Campbell S, Chew-Graham C, *et al*. PICO, PICOS and SPIDER. A comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC Health Serv Res* 2014;**14**:579. doi: 10.1186/s12913-014-0579-0

24 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*2016;**5**(1):210.

25 Lopes-Júnior LC, Rosa MADRP, Lima RAG. Psychological and Psychiatric Outcomes Following PICU Admission: A Systematic Review of Cohort Studies. *Pediatr Crit Care Med* 2018;**19**:e58–e67.

26 Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. *The Cochrane Collaboration.* Chichester, UK: John Wiley & Sons 2011.

27 Trevethan R. Sensitivity, specificity, and predictive values: foundations, pliabilities, and pitfalls in research and practice. *Front Public Health.* 2017;**5**:307. doi: 10.3389/fpubh.2017.00307.

28 Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. *BMJ.* 2020;**369**:m1808. doi:10.1136/bmj.m1808

29 Lopes-Júnior LC, Bomfim EO, Nascimento LC, *et al.* Non-pharmacological interventions to manage fatigue and psychological stress in children and adolescents with cancer: an integrative review. *Eur J Cancer Care* 2016;**25**:921–935. doi: 10.1111/ecc.12381

30 Carlos L Lopes-Júnior, Cruz LAP, Leopoldo VC, *et al*. Effectiveness of Traditional Chinese Acupuncture versus Sham Acupuncture: a Systematic Review. *Rev Lat Am Enferm* 2016;**24**:e2762. doi: 10.1590/1518-8345.0647.2762

31 Gonçalves CA, Lopes-Júnior LC, Nampo FK, *et al*. Safety, efficacy and immunogenicity of therapeutic vaccines in the treatment of patients with high-grade cervical intraepithelial neoplasia associated with human papillomavirus: a systematic review protocol. *BMJ Open* 2019;**9**:e026975. doi: 10.1136/bmjopen-2018-026975

32 Lopes-Júnior LC, Lima RAG, Olson K, *et al*. Systematic review protocol examining the effectiveness of hospital clowns for symptom cluster management in pediatrics. *BMJ Open* 2019;**9**:e026524. doi: 10.1136/bmjopen-2018-026524

33 Souza AR, Lima RA, Lopes-Júnior LC. Biomarkers associated with postoperative cardiac surgery clinical outcomes in pediatric intensive care. *Acta Paul Enferm*. 2020;34(1). *Ahead of print.*

34 Rosa GS, Pessanha RM, Schuab SIPC, Nunes KZ, Amorim MHC, Lopes-Júnior-LC. Eficácia das terapias complementares no manejo da dor oncológica em cuidados paliativos: revisão sistemática. *Rev Lat Am Enferm* 2020;**28**. *Ahead of print.*

35 Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003;**73**(9):712-6.

36 Wells GA, Shea B, O'Connell D, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 3 January 2019.

37 Laurant M, Biezen MVD, Wijers N, *et al*. Nurses as substitutes for doctors in primary care. *Cochrane Database Syst Rev* 2018;**7**:CD001271. doi: 10.1002/14651858.CD001271.pub3

38 Burnham JP, Fritz SA, Yaeger LH, Colditz GA. Telemedicine infectious diseases consultations and clinical outcomes: a systematic review. *Open Forum Infect Dis.* 2019;**6**. doi: 10.1093/ofid/ofz517.

39 Campbell M, McKenzie JE, Sowden A, *et al*. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ* 2020;**368**:l6890. doi: 10.1136/bmj.l6890

40 The World Bank. Classifying countries by income. IBRD.IDA. Available from: https://datatopics.worldbank.org/world-development-indicators/stories/the-classification-of-countries-by-income.html

41 Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, *et al.* Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;**34**:101623. doi:10.1016/j.tmaid.2020.101623

42 Silva-Junior FJG, Sales JCS, Monteiro CFS *et al*. The impact of covid-19 pandemic on mental health of young people and adults: a systematic review protocol of observational studies. *BMJ Open*, 2020. doi: 10.1136/bmjopen-2020-039426. *Ahead of print.*

43 Cohen J. *Statistical power analysis for the behavioral sciences*, 2nd. Lawrence Erlbaum Associates 1988.

44 Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. *JAMA* 2002;**287**:2831–4. doi: 10.1001/jama.287.21.2831

45 World Health Organization. *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)*. Geneva: World Health Organization; 2020. (WHO technical report).

46 First Affiliated Hospital of Zhejiang University School of Medicine. Handbook of COVID-19 Prevention and Treatment. 2020. https://gmcc.alibabadoctor.com/prevention-manual 21

47 Burki TK. Testing for COVID-19. *Lancet Respir Med*. 2020;**20**:30247-2. doi:10.1016/S2213-2600(20)30247-2

Reporting checklist for protocol of a systematic review.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	1 and 2
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	1
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Sources	#5a	Indicate sources of financial or other support for the review	1

Sponsor	#5b	Provide name for the review funder and / or sponsor	1
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	1
Rationale	#6	Describe the rationale for the review in the context of what is already known	3 and 4
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5 and 6
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5 and 6
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5 and 7
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7 and 8
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study	8

		level, or both; state how this information will be used in data synthesis	
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	9
	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	9
	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9 and 10
	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	9 and 10
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

BMJ Open

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040413.R2
Article Type:	Protocol
Date Submitted by the Author:	17-Jul-2020
Complete List of Authors:	LOPES-JÚNIOR, LUÍS CARLOS; Universidade Federal do Espirito Santo, Nursing Department Bomfim, Emiliana; University of Saskatchewan College of Medicine, Department of Medicine Silveira, Denise Sayuri Calheiros da; Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto, Department of Biochemistry and Immunology Pessanha, Raphael Manhães ; Universidade Federal do Espirito Santo, Nursing Department Schuab, Sara Isabel Pimentel Carvalho ; Universidade Federal do Espírito Santo, Nursing Department Lima, Regina Aparecida Garcia; Universidade de Sao Paulo Campus de Ribeirao Preto
Primary Subject Heading:	Public health
Secondary Subject Heading:	Health policy, Public health
Keywords:	INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

***Title Page** – BMJ Open*

EFFECTIVENESS OF MASS TESTING FOR CONTROL OF COVID-19: A SYSTEMATIC REVIEW PROTOCOL

Luís Carlos Lopes-Júnior[1*], RN, Ph.D. E-mail: luisgen@usp.br
Emiliana Bomfim[2], RN, MSc., Ph.D candidate. E-mail: e.bomfim@usask.ca
Denise Sayuri Calheiros da Silveira[3], BS, Ph.D., in Immunology. E-mail: sayuri_denise@yahoo.com.br
Raphael Manhães Pessanha[1], Nursing student. E-mail: rafa.09pessanha@gmail.com
Sara Isabel Pimentel Carvalho Schuab[1], Nursing student. E-mail: sarapimentel2009@hotmail.com
Regina Aparecida Garcia de Lima[4], RN, Ph.D. E-mail: limare@eerp.usp.br

Affiliations and addresses: [1]Federal University of Espírito Santo (UFES). Vitoria, ES, Brazil. [2]University of Saskatchewan, College of Medicine. Saskatoon, SK, Canada. [3]University of São Paulo (USP) at Ribeirão Preto Medical School. Ribeirão Preto, SP, Brazil. [4]University of São Paulo (USP) at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil.

Corresponding author: Luís Carlos Lopes-Júnior. Adjunct Professor of the Nursing Department /Health Sciences Center at the Federal University of Espírito Santo (UFES), Av. Marechal Campos, 1468 – Maruípe, Zip Code: 29.043-900, Vitória, ES, Brazil. E-mail: [luisgen@usp.br], Phone: +55(27)99249-7217. ORCID: https://orcid.org/0000-0002-2424-6510

Acknowledgements
None do declare.

Author Contributions: LCLJ conceptualized and designed the protocol, drafted the initial manuscript and reviewed the manuscript. EB, DSCS, RMP, SIPCS, RAGL, and LCLJ defined the concepts and search items, data extraction process as well as methodological appraisal of the studies. EB, DSCS, RMP, SIPCS, and LCLJ planned the data extraction and statistical analysis. RAGL, EB, DSCS, LCLJ provided critical insights. All authors have approved and contributed to the final written manuscript.

Funding: No financial support.

Data Statement section: PROSPERO registration number: CRD42020182724. Available in: Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020182724

Word Count: 3995 words.

Disclaimer: The views of the authors do not necessarily reflect those of the NHS, NIHR or the Department of Health.
Competing interests: None.
Sponsorship: None.
Patient consent: Not required.
Provenance and peer review: Not commissioned; externally peer-reviewed.

ABSTRACT

Introduction: Since March 2020, when the Corona Virus Disease 2019 (COVID-19) outbreak has been deemed a pandemic by the World Health Organization (WHO), the SARS-CoV-2 spreading has been the focus of attention of scientists, authorities, public health agencies, and communities around the world. One of the great concerns and challenges, mainly in low- and middle-income countries, is the identification and monitoring of COVID-19 cases. The large-scale availability of testing is a fundamental aspect of COVID-19 control, but it is currently the biggest challenge faced by many countries around the world. We aimed to synthesize and critically evaluate the scientific evidence on the influence of the testing capacity for symptomatic individuals in the control of COVID-19.

Methods and analysis: A systematic review will be conducted in eight databases, such as MEDLINE, ISI-of-Knowledge, CENTRAL, EMBASE, SCOPUS, LILACS, PsycINFO, and CNKI, from inception until July 30, 2020. No restriction regarding the language, publication date, or setting will be employed. Primary outcomes will include the sensitivity as well as the specificity of the tests for COVID-19. Study selection will follow the PRISMA checklist. Methodological assessment of the studies will be evaluated by the Cochrane Risk-of-Bias tool for randomized controlled trials, the MINORS for non-randomized studies, and the Newcastle-Ottawa Scale for cohort or case-control studies. Findings will be structured according to the test type and target population characteristics and focused on the primary outcomes (sensitivity and specificity). Moreover, if sufficient data are available, a meta-analysis will be performed. Pooled standardized mean differences and 95% CIs will be calculated. Heterogeneity between the studies will be determined by I^2 statistics. Subgroup analyses will also be conducted. Publication bias will be assessed with funnel plots and Egger's test. Heterogeneity will be explored by random-effects analysis.

Ethics and dissemination: Ethical approval is not required. The results will be disseminated widely via peer-reviewed publication and presentations at conferences related to this field.

PROSPERO registration ID: CRD42020182724.

Keywords: COVID-19; Coronavirus; Coronavirus Infections; Testing; Effectiveness; Public Health Nursing; Health Surveillance.

Strengths and limitations of this study:

- We will offer evidence for health surveillance support in order to help decision makers (i.e., healthcare providers, stakeholders and governments) regarding COVID-19 control.
- This systematic review will be the first to critically evaluate the scientific evidence about the influence of the testing capacity for symptomatic individuals in COVID-19.
- This study will be relevant to address the gap in the literature with regard to achieving better identification, control and timely monitoring of COVID-19 cases and guiding strategies and health policies in several countries.
- This systematic review protocol reduces the possibility of duplication due to the transparency of the methods and processes that will be used; in addition, it reduces possible biases and allows for peer review.
- The sensitivity and specificity of the tests varies widely by test and may be the main limitation of this systematic review, in addition to the publication bias of the original studies and the methodological appraisal of the studies.

INTRODUCTION

In December 2019, an increased number of pneumonia-like cases in Wuhan, China, led to the discovery of a new type of coronavirus—an enveloped RNA virus commonly found in humans and capable of causing respiratory, enteric, liver as well as neurological illness. [1] Despite the low lethality of COVID-19, approximately 3%, its transmissibility is high, [1] with respiratory contact droplet being the main means of spreading the new coronavirus. [2] Since the WHO declared the COVID-19 outbreak a pandemic on March 11, 2020, [3] the spread of the new coronavirus has been the focus of attention of scientists, authorities, public health agencies, government officials, and communities around the world. [4]

Using a networked metapopulation dynamics and Bayesian inference models to gather epidemiological factors associated with COVID-19, a recent study on SARS-CoV-2 infections in China, showed that unreported infections were projected to be 55% as contagious as documented infections, per person. Besides, unreported cases were the source of infection for 79% of reported cases. [5] A total of 213 countries, territories or areas have reported confirmed cases of SARS-CoV-2, with 8.914.787 infected and 466.718 deaths recorded as of June 20, 2020, [6] with Brazil being the new epicenter of the pandemic [7] with 1.070.139 confirmed cases and 50.058 deaths so far. [6]

One of the greatest concerns and challenges in several countries, especially low- and middle-income countries, refers to the identification of cases. [8] Identification platforms have undergone modifications in recent months. [9] In addition, the coexistence of several criteria and platforms can generate serious failures in the health surveillance system, resulting in underreporting. Indeed, the main reason for the problem with how health surveillance is being performed in several countries is the low capacity for mass testing. [8 10]

Another crucial issue that the WHO has pointed out is that testing all suspected cases is essential for pandemic control. [11] However, access to diagnostic tests remains a challenge globally, in addition to the confusion among health professionals and the population about prioritizing tests and interpreting results.[10 12] The limited availability of diagnostic tests and laboratory capacity for the detection of COVID-19 in many countries, for example, in Brazil, has led the Ministry of Health to limit testing only for severe cases. The Ministry of Health justified its decision by stating that, in mild cases, it does not matter if the person tests negative or positive, the treatment to be delivered is the same as if it was a suspected mild case. [13]

It should be noted that the incubation period from infection to the appearance of the first symptoms is typically 5 to 7 days but up to 14 days. The final diagnosis depends on tests to detect viruses in several body fluids. [10 12] Nasopharyngeal smears are more sensitive than oropharyngeal smears and are more effective at early stages of symptom development. [14 15 16 17 18] However, the gold standard test is the detection of viral RNA by reverse-transcriptase polymerase chain reaction (RT-PCR). [10]

New methods are being evaluated for faster detection of major viral sequences, [10 16 19 20] and a variety of antigen detection devices have been developed; however, their performance varies widely. In South Korea, for instance, mass testing programs, contact tracking and isolation contributed to early infection control. [21] As the pandemic progresses, the attention is on symptomatic patients and health professionals who are on the frontline of the COVID-19 response. Testing symptomatic patients can provide information about contact tracing, besides control and prevention of potential new infections. [10 12]

Based on consolidated official data, Our World in Data raises some questions that are quite relevant in terms of differences in testing capacity. [6] Comparing countries by their testing capacity per thousand inhabitants, there are notable differences between countries. The United States has already tested 27.784.614 individuals as of June 20, 2020, i.e., 83.9 per 1.000 inhabitants. On the other hand, Brazil has tested 2.409.830 individuals to date, 11.3 per 1.000 inhabitants. In other words, currently, the United States has a testing capacity 7.4 times greater than that of Brazil. [6]

With only symptomatic testing, it will be difficult to isolate patients and quarantine communicants. Thus, increasing the production of diagnostic kits and laboratory capacity are urgent issues in Brazil as well as in low- and middle-income countries. [10 12] It is hypothesized that a significant increase in large-scale testing capability would be an important advance in the control of COVID-19 in Brazil and other countries, as this is currently the biggest challenge faced by many countries around the world. Hence, this systematic review protocol, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) reporting standards,[22] proposes a reproducible strategy to query the scientific literature on the effectiveness of mass testing for the control of COVID-19.

RESEARCH AIMS

The purpose of this systematic review is to synthesize and critically evaluate the scientific evidence on the influence of the testing capacity for symptomatic individuals in the control of COVID-19.

METHODS AND ANALYSIS

Search Strategy

The search strategy will be performed using resources to enhance methodological transparency and improve the reproducibility of the findings, following the PRISMA-P guidelines. [22] In addition, using the PICO (Population/ Intervention/Comparison/Outcomes) approach,[23] we elaborated the research question of this review to ensure a systematic search of the literature: *"What is the scientific evidence from studies about the influence of the testing capacity for symptomatic patients in COVID-19 pandemic control?"*. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in April 2020 (registration ID: CRD42020182724).

Article searches will be conducted in the following specialized and general databases from inception until July 30, 2020: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, the ISI of Knowledge via Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL), Excerpta Medica dataBASE (EMBASE), SCOPUS, Latin American and Caribbean Health Sciences Literature (LILACS), Psychology Information (PsycINFO) and Chinese National Knowledge Infrastructure (CNKI). The gray literature will be searched in five additional sources: ProQuest Dissertations and Theses Global, Mascot/Wotro, Effective Public Health Practice Projects, Public Health Gray Literature Sources, and Health Evidence. No restriction regarding the publication date, setting or language will be considering in this systematic review. Additionally, secondary searches in other sources, such as the clinical trials website (e.g., ClinicalTrials.gov), The British Library and Google Scholar, will also be performed. The reference sections of the included studies and cited studies will be manually searched for additional relevant studies. The search strategy will comprise only key terms according to a pre-established PICO strategy. Two researchers (LCLJ and EB) will independently carry out the search in all databases. Additionally, the bibliographic software EndNote (https://www.myendnoteweb.com/) as well as the Rayyan™ app (*Qatar Computing Research Institute)* [24] will be used to store, organize, and manage all the references and ensure a systematic and comprehensive search.

First, we will identify the existence of a specific subject heading index in each database (including MeSH terms, Emtree terms, PsycINFO Thesaurus and DeCS-Health Science Descriptors) and their synonyms (keywords). The search terms will be combined using the Boolean operators "AND" and "OR". [25] The search strategy combining MeSH terms

and keywords that will be used in MEDLINE is depicted in Table 1; it will be adapted to meet each database's specific syntax requirements.

Table 1 Concepts and search items

Databases	Search strategy
MEDLINE ISI of Knowledge CENTRAL EMBASE SCOPUS LILACS PsycINFO CNKI	**#1** (("Infant" [MeSH Terms] OR "Child, Preschool" [MeSH Terms] OR "Adolescent" [MeSH Terms] OR "Young Adult" [MeSH Terms] OR "Adult" [MeSH Terms] OR "Aged" [MeSH Terms] OR "Aged, 80 and over" [MeSH Terms])). **#2** (("Coronavirus" [MeSH Terms] OR "Coronavirus"[All Fields]) OR ("COVID-19" [All Fields] OR "Severe Acute Respiratory Syndrome Coronavirus 2" [Supplementary Concept] OR "Severe Acute Respiratory Syndrome Coronavirus 2" [All Fields] OR "2019-nCoV" [All Fields] OR "SARS-CoV-2" [All Fields]) OR "Pandemics" [MeSH Terms]). **#3** (("COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 testing" [All Fields] OR "2019 novel coronavirus disease testing" [All Fields] OR "COVID19 antibody testing" [All Fields] OR "SARS2 testing" [All Fields] OR "2019-nCoV testing" [All Fields] OR "COVID-19 antibody testing" [All Fields] OR "COVID-19 blood antibody testing" OR "SARS-CoV-2 infection antibody testing" [All Fields] OR "COVID-19 serological testing" [All Fields] OR "COVID19 serological testing" [All Fields] OR "Serology Testing for COVID-19" [All Fields] OR "COVID-19 serological testing" [All Fields] OR "Serology Testing for COVID-19" [All Fields] OR "SARS-CoV-2 infection serological testing" [All Fields] OR "LAMP assay" [Supplementary Concept] OR "LAMP assay COVID-19" [All Fields] OR LAMP assay SARS-CoV-2" [All Fields] OR LAMP assay Coronavirus Infections/*diagnosis [All Fields] OR "2019-novel coronavirus real-time reverse transcriptase diagnostic panel" [All Fields] OR "2019-nCoV RT-PCR diagnostic panel" [All Fields] OR "COVID-19 nucleic acid testing" [All Fields] OR "SARS-CoV-2 infection nucleic acid testing" [All Fields] OR "COVID19 nucleic acid testing" [All Fields] OR)). **#4** #1 AND #2 AND #3

Abbreviations: MEDLINE, Medical Literature Analysis and Retrieval System Online; CENTRAL, Cochrane Central Register of Controlled Trials; EMBASE, Excerpta Medica dataBASE; LILACS, Latin American and Caribbean Health Sciences Literature; PsycINFO, Psychology Information; CNKI, Chinese National Knowledge Infrastructure.

Study Selection

The PICO strategy [Population (P), Interventions/Exposure (I), Comparators (C) and Outcomes (O)] is detailed in Table 2.

Table 2 Inclusion and exclusion criteria

PICO component [23]	Inclusion criteria	Exclusion criteria
P – Population	Infant, Child, Adolescents, Young Adult, Adult and Aged (according to MeSH terms)* of all exes, of any ethnicity, and symptomatic and/or suspect for COVID-19.	–
I – Intervention/Exposure	Testing for COVID-19.	Testing for other previous pandemics.
C – Comparison	Individuals symptomatic for COVID-19 who have not been tested.	–
O – Outcome	The primary outcomes include the sensitivity as well as the specificity of the tests.	–

Abbreviations: MeSH, Medical Subject Headings; COVID-19, Coronavirus Disease 2019.
* In this systematic review, we will use definitions in accordance with the MeSH term indexing, such as "Infant" - a child between 1 and 23 months of age; "Child, Preschool"- a child between the ages of 2 and 5; "Child"- a person 6 to 12 years of age; "Adolescent"- a person 13 to 18 years of age; "Young Adult"- a person between 19 and 24 years of age; "Adult"- a person having attained full growth or maturity. Adults are 19 through 64 years of age; "Aged"- a person 65 through 79 years of age; "Aged, 80 and over"- a person 80 years of age and older.

Regarding the study design, we will include all studies with quantitative approaches (descriptive, observational and experimental studies), as well as the gray literature (editorials, opinion articles, reviews, clinical guidelines, conference proceedings, abstracts, book chapters, etc.) as recommended by the Cochrane Handbook.[26] Thus, studies that have investigated epidemiological and clinical aspects of testing capacity for symptomatic and suspected COVID-19 patients will be included in this systematic review. Nevertheless, studies evaluating mass testing for severe acute respiratory syndromes (SARSs) other than COVID-19 will be excluded. With regard to population characteristics, people living in the community and in nursing homes, outpatients and hospitalized people will be included.

The primary outcomes of this systematic review include the sensitivity as well as the specificity of the tests for COVID-19. The sensitivity of a test corresponds to the probability of "true positive". In other words, it indicates the percentage of people with the disease that correctly tested positive. Therefore, a test is highly sensitive if it identifies the actual positive cases which are clinically identified as such.[27] The specificity of a test corresponds to the probability of a "true negative". It indicates the true percentage of people who did not have the disease that correctly tested negative. [27] These terms describe the performance characteristics of a test and can be used to gauge the effectiveness and validity of a test result. [28]

The screening and selection of studies will be carried out by two reviewers (LCLJ and EB) independently and blindly. After this selection, a third reviewer (RAGL) will be responsible for analyzing and deciding on the inclusion or exclusion of each article, especially in relation to those about which there is a conflicting decision. The Rayyan™ application, developed by the *Qatar Computing Research Institute*, [24] will be used as an auxiliary tool for data management.

Screening

After importing documents retrieved from the initial searches, duplicates will be removed, and two reviewers (LCLJ and EB) will independently screen the studies based on their titles and abstracts. If good agreement is achieved between reviewers (at least 80%), then each will proceed to full article screening. If there is less than 80% agreement, the articles will be reevaluated, and the disagreements will be discussed and resolved by consensus; if a disagreement persists, a third reviewer (RAGL) will make a final decision using the Rayyan™ app.

Data Extraction

Full-text screening will be performed by the same independent investigators. To measure intercoder agreement during each screening phase, Cohen's kappa will be performed. Once consensus is reached on the selected studies, a standardized form based on previous studies [29 30 31 32 33 34] will be used for data extraction. The information to be extracted includes four domains: I) identification of the study (article title; journal title; impact factor; authors; country of the study; language; sources of funding; publication year; host institution of the study [hospital; university; research center; single institution; multicenter study]; conflicts of interest; and study sponsorship); ii) methodological characteristics (study design; study objective or research question or hypothesis; sample characteristics, e.g., sample size, age, eligibility criteria, ethnicity, baseline characteristics; groups and controls; recruitment methods and study completion rates; comparator group; timeframe for follow-up; cointerventions; validated measures; costs and/or remuneration related to participation; statistical analyses; and adjustments); iii) main findings and implications for clinical practice; and iv) conclusions. The same two reviewers will independently perform the data extraction. Discrepancies between the reviewers will be resolved either by discussion or, in the lack of agreement, by a third reviewer (RAGL).

Methodological appraisal

The internal validity and risk of bias for RCTs will be assessed with the appraisal tool from the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0, [26] which assesses

the following seven domains: I) Randomization sequence allocation; II) Allocation concealment; III) Blinding of participants and team involved; IV) Blindness of outcome evaluators; V) Incomplete outcomes; VI) Report of selective outcome; and VII) Other sources of bias. Based on the evaluation of these domains, studies are classified as at risk of low, high or uncertain bias. For assessing nonrandomized controlled trials, the Methodological Index for Non-Randomized Studies (MINORS) [35] will be used. This MINORS instrument contains eight items for noncomparative studies: 1) A clearly stated aim; 2) Inclusion of consecutive patients; 3) Prospective collection of data; 4) Endpoints appropriate to the aim of the study; 5) Unbiased assessment of the study endpoint; 6) Follow-up period appropriate to the aim of the study; 7) Loss to follow-up less than 5%; and 8) Prospective calculation of the study size. [35] With regard to the case-control or cohort studies, we will use the Newcastle-Ottawa Scale to evaluate the methodological quality of the studies. [36] Using the Newcastle-Ottawa Scale, the case–control and cohort studies will be given star ratings in 3 categories—Selection (maximum 4 stars), Comparability (maximum 2 stars), and Outcome (maximum 3 stars)—with a maximum score of 9 stars. [36] The same two reviewers (LCLJ and EB) will conduct the quality assessment independently. Disagreements will be resolved by a third reviewer (RAGL).

Data synthesis

A qualitative synthesis on the RCT risk of bias will be made for the included and analyzed studies. The studies will be classified according to the risk of bias as follows: "low" if all the main domains were classified as "low risk"; "uncertain" if one or two main domains were classified as "uncertain risk"; and "high" if more than two main domains have been classified as "uncertain" or "high risk". When no information is available, we will assign "uncertain risk". [37] For assessing the nonrandomized studies, each item from the MINORS will be rated from 0 to 2, which means that a score of 0 indicates that the information was not reported, 1 indicates that the information was inadequately reported, and 2 indicates that the information was adequately reported. [35] Regarding the case–control and cohort studies assessed by the Newcastle-Ottawa Scale, the quality of these studies will be adjudicated based on a previous study [38]: good quality: Selection ≥3 stars AND Comparability ≥1 stars AND Outcome ≥2 stars; fair quality: Selection 2 stars AND Comparability ≥1 stars AND Outcome ≥2 stars; poor quality: Selection ≤1 star OR Comparability 0 stars OR ≤1 star. [38]

In addition, we will complete a narrative synthesis, providing a comprehensive descriptive summary around the type of COVID-19 test, the study design, and the target population characteristics, that is focused on the primary outcome (the sensitivity as well as

the specificity of the tests for COVID-19). In text and table formats, the methodological characteristics of the studies, subpopulation characteristics, test characteristics, and sensitivity and specificity of the tests will also be presented. The assessment of the certainty of the evidence will take into consideration the precision of the synthesis findings (i.e., confidence interval if available), the number of studies and participants, the consistency of effects across studies, the risk-of-bias of the studies, how directly the included studies address the planned question (directness), and the risk of publication bias. [39]

Study findings will be presented in tables or graphs in the same way as the syntheses are reported in order to facilitate the comparison of similarities and differences in designs and outcomes among studies. Key characteristics, such as study design, sample size, risk of bias, sensitivity and specificity, which may affect interpretation of the data, will also be presented. Outcomes will be analyzed according to sex, population (children, adolescents, young adults, adults and aged), and the type of COVID-19 test and according to the income classification of the countries (high, upper-middle, lower-middle, and low), based on The World Bank Classification using the Gross National Income (GNI) per capita. [40]

Meta-analyses will be conducted if there is sufficient homogeneity in study design and study subjects among the selected articles. Therefore, continuous and dichotomous outcomes will be pooled together for meta-analysis purposes. Quantitative data from each study will be extracted and inserted into an Excel sheet by two independent reviewers. Statistical analyses will be carried out using the Statistical Package for the Social Sciences - SPSS, version 18.0 (SPSS, Inc., Chicago, IL, USA).

Standardized mean differences (SMDs) and 95% CIs will be used to calculate the effect sizes; [41 42] studies included in our meta-analysis will have reported the differences in methods of testing for COVID-19. All effect sizes will be transformed into a common metric, i.e., the bias-corrected standardized difference in means (Hedges' g), to make them comparable across studies. For continuous outcome measures, standardized mean differences (SMDs) and risk ratios (RRs) for categorical outcomes from individual studies will be considered for the final assessment. The SMD was chosen as a measure of the pooled results considering the likely variability in the measuring scales for continuous outcomes. [42] The effect size will be interpreted by Cohen's proposal: 0.20 corresponds to a small effect size, 0.50 corresponds to a medium effect size, and 0.80 corresponds to a large effect size. [43]

A random effects model will be selected under the assumption that the studies included in the meta-analysis were carried out with heterogeneous populations. Heterogeneity will also be tested by the I^2 statistic, which can quantify the heterogeneity as ranging from 0%

(no heterogeneity) to 100% (the differences between the effect sizes can completely be explained by chance alone), and the interpretations of the percentages are as follows: 0%–40% indicates potentially unimportant heterogeneity, 30%–60% indicates moderate heterogeneity, 50%–90% indicates substantial heterogeneity, and 75%–100% indicates considerable heterogeneity. [42] To explore the heterogeneity across studies, subgroup analysis will be performed using a mixed effects model according to the following variables: sex, population (children, adolescents, young adults, adults and aged), COVID-19 test type, and country income classification (high, upper-middle, lower-middle, and low).

Patient and public involvement

Since this is a systematic review protocol, no patients or public will be involved.

Ethics and dissemination

Due to the characteristics of this study design, ethical approval was not required. The findings of this systematic review will be disseminated through peer-reviewed publication as well as via different media, such as symposia and conferences related to this field. Moreover, any amendments to this protocol will be documented with reference to the saved searches and analysis methods, which will be recorded in bibliographic databases, for data collection and synthesis.

DISCUSSION

In this systematic review protocol, we clearly describe the studies' designs, participants, interventions and outcomes that will be considered in line with the research question and the data sources, search strategy, data extraction, methodological quality of the studies, and data synthesis approach. [35] In addition, with this protocol study, we reinforce the clarity of the search strategy and minimize the risk of bias. [44] These results will provide evidence to inform and customize shared decision making to the healthcare providers, stakeholders, and government personnel.

Since the sensitivity and specificity of the tests for COVID-19 vary widely by test, this might be the main limitation of this systematic review, followed by the publication bias of the original studies and the methodological appraisal of the studies, which may influence the external validity.

The testing of all symptomatic patients, according to the Imperial College study and the Chinese experience, [45] is essential to contain the epidemic. In a clinical context, although positive tests for COVID-19 are extremely useful, due caution must be taken while interpreting negative tests. Particularly, it must be taken into account the pretest probability of

disease. This has important implications for health care professionals who interpret tests and policymakers who design diagnostic algorithms for COVID-19. [10] The Chinese handbook of COVID-19 prevention and treatment states "*if the nucleic acid test is negative at the beginning, samples should continue to be collected and tested in the following days*". [46] False negatives carry substantial risks; for instance, patients can be transferred to wards not affected by COVID-19, leading to the spread of hospital-acquired COVID-19 infection, and caregivers can also spread the infection to vulnerable dependents. [10 28 47] Therefore, guidelines on repeated testing are needed to reduce the risk of false negatives. Finally, physicians must ensure that patients are informed about the limitations of the tests. Patients with a single negative test, but with symptoms that are suggestive of COVID-19, should be advised to isolate themselves according to the guidelines for suspected COVID-19, since no test is 100% accurate. [10 28 47]

Hence, this systematic review will deliver relevant evidence on the influence of the testing capacity for symptomatic individuals. Ultimately, we will provide evidence to help the health sector achieve better identification, control, and timely monitoring of COVID-19 cases and to guide important strategies and health policy decision-makers in several countries.

REFERENCES

1 Zhu N, Zhang D, Wang W, *et al*. A novel Coronavirus from patients with pneumonia in China, 2019. *N Eng J Med* 2020;**382**:727-733. doi: 10.1056/NEJMoa2001017 pmid: https://pubmed.ncbi.nlm.nih.gov/31978945/

2 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol* 2019;**17**:181-92. doi: 10.1038/s41579-018-0118-9 pmid: https://pubmed.ncbi.nlm.nih.gov/30531947/

3 Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. *BMJ* 2020;**368**:m1036. doi: 10.1136/bmj.m1036 pmid: https://pubmed.ncbi.nlm.nih.gov/32165426/

4 Wang C, Horby, PW, Hayden FG, *et al*. A novel coronavirus outbreak of global health concern. *Lancet* 2020;**395**:470–473. doi: 10.1016/S0140-6736(20)30185-9 pmid: https://pubmed.ncbi.nlm.nih.gov/31986257/

5 Li R, Pei S, Chen B, *et al*. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science* 2020;**16**:eabb3221. doi: 10.1126/science.abb3221 pmid: https://pubmed.ncbi.nlm.nih.gov/32179701/

6 Roser M, Ritchie H, Ortiz-Ospina E & Hasell J. Coronavirus Pandemic (COVID-19) Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource]

7 The Lancet. COVID-19 in Brazil: "So what?". *Lancet.* 2020;**395**:1461. doi: S0140-6736(20)31095-3

8 Turci MA, Holliday JB, de Oliveira NCVC. A Vigilância Epidemiológica diante do Sars-Cov-2: desafios para o SUS e a Atenção Primária à Saúde. *APS em Revista* 2020;**2**:44-55. doi:10.14295/aps.v2i1.70

9 De Oliveira WK, *et al.* Guia de Vigilância Epidemiológica: Emergência de Saúde Pública de Importância Nacional pela Doença pelo Coronavírus 2019. 3 ed. Brasília: Ministério da Saúde; 2020.

10 Beeching NJ, Fletcher TE, Beadsworth MBJ. Covid-19: testing times. *BMJ* 2020;**369**:1403. doi: 10.1136/bmj.m1433

11 World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. WHO: 2020.

12 Peto J. Covid-19 mass testing facilities could end the epidemic rapidly. *BMJ* 2020;**368**:1163. doi: 10.1136/bmj.m1163

13 Rocha, C. A dificuldade do Brasil de aplicar testes em massa na pandemia. [atualizado em 10 de abril de 2020; acesso em 11 de abril de 2020]. Disponível em: https://www.nexojornal.com.br/expresso/2020/04/10/A-dificuldade-do-Brasil-de aplicar-testes-em-massa-na-pandemia

14 Zhang W, Du RH, Li B, *et al.* Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 2020;**9**:386-389. doi: 10.1080/22221751.2020.1729071

15 Wang W, Xu Y, Gao R, *et al.* Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA,* 2020. doi:10.1001/jama.2020.3786

16 Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections—the state of the art. *Emerg Microbes Infect* 2020;**9**:747-56. doi: 10.1080/22221751.2020.1745095

17 Carver C, Nick J. Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. *Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford* (2020).

18 Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, *et al.* SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med 2020;***382**:1177-9. doi: 10.1056/NEJMc2001737

19 Sheridan C. Fast, portable tests come online to curb coronavirus pandemic. *Nat Biotechnol* 2020;**38**:515-518. doi:10.1038/d41587-020-00010-2.

20 Moore SC, Penrice-Randal R, Alruwaili M, Dong X, Pullan ST, Carter D, *et al.* Amplicon based MinION sequencing of SARS-CoV-2 and metagenomic characterisation of nasopharyngeal swabs from patients with COVID-19. *MedRxiv* 2020. doi: 0.1101/2020.03.05.20032011.

21 Kim YJ, Sung, Heungsup S, Chang-Seok, Hur M. COVID-19 Testing in South Korea: Current Status and the Need for Faster Diagnostics. *Ann Lab Med* 2020;**40**:349-350.

22 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;**4**:1. doi: 10.1186/2046-4053-4-1

23 Methley AM, Campbell S, Chew-Graham C, *et al*. PICO, PICOS and SPIDER. A comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC Health Serv Res* 2014;**14**:579. doi: 10.1186/s12913-014-0579-0

24 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*2016;**5**(1):210.

25 Lopes-Júnior LC, Rosa MADRP, Lima RAG. Psychological and Psychiatric Outcomes Following PICU Admission: A Systematic Review of Cohort Studies. *Pediatr Crit Care Med* 2018;**19**:e58–e67.

26 Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. *The Cochrane Collaboration.* Chichester, UK: John Wiley & Sons 2011.

27 Trevethan R. Sensitivity, specificity, and predictive values: foundations, pliabilities, and pitfalls in research and practice. *Front Public Health.* 2017;**5**:307. doi: 10.3389/fpubh.2017.00307.

28 Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. *BMJ.* 2020;**369**:m1808. doi:10.1136/bmj.m1808

29 Lopes-Júnior LC, Bomfim EO, Nascimento LC, *et al.* Non-pharmacological interventions to manage fatigue and psychological stress in children and adolescents with cancer: an integrative review. *Eur J Cancer Care* 2016;**25**:921–935. doi: 10.1111/ecc.12381

30 Carlos L Lopes-Júnior, Cruz LAP, Leopoldo VC, *et al*. Effectiveness of Traditional Chinese Acupuncture versus Sham Acupuncture: a Systematic Review. *Rev Lat Am Enferm* 2016;**24**:e2762. doi: 10.1590/1518-8345.0647.2762

31 Gonçalves CA, Lopes-Júnior LC, Nampo FK, *et al*. Safety, efficacy and immunogenicity of therapeutic vaccines in the treatment of patients with high-grade

cervical intraepithelial neoplasia associated with human papillomavirus: a systematic review protocol. *BMJ Open* 2019;**9**:e026975. doi: 10.1136/bmjopen-2018-026975

32 Lopes-Júnior LC, Lima RAG, Olson K, *et al*. Systematic review protocol examining the effectiveness of hospital clowns for symptom cluster management in pediatrics. *BMJ Open* 2019;**9**:e026524. doi: 10.1136/bmjopen-2018-026524

33 Nunes MDR, Bomfim E, Olson K, *et al.* Interventions minimizing fatigue in children/adolescents with cancer: An integrative review. *J Child Health Care*. 2018;**22**:186-204. doi:10.1177/1367493517752498

34 Rosa GS, Pessanha RM, Schuab SIPC, *et al.* Efficacy of the complementary therapies in the management of cancer pain in palliative cares: a systematic review. *Rev Lat Am Enferm* 2020;**28:**e3377. doi: 10.1590/1518-8345.4213.3377. *Ahead of print.*

35 Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003;**73**(9):712-6.

36 Wells GA, Shea B, O'Connell D, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 3 January 2019.

37 Laurant M, Biezen MVD, Wijers N, *et al*. Nurses as substitutes for doctors in primary care. *Cochrane Database Syst Rev* 2018;**7**:CD001271. doi: 10.1002/14651858.CD001271.pub3

38 Burnham JP, Fritz SA, Yaeger LH, Colditz GA. Telemedicine infectious diseases consultations and clinical outcomes: a systematic review. *Open Forum Infect Dis.* 2019;**6**. doi: 10.1093/ofid/ofz517.

39 Campbell M, McKenzie JE, Sowden A, *et al*. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ* 2020;**368**:l6890. doi: 10.1136/bmj.l6890

40 The World Bank. Classifying countries by income. IBRD.IDA. Available from: https://datatopics.worldbank.org/world-development-indicators/stories/the-classification-of-countries-by-income.html

41 Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, *et al.* Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;**34**:101623. doi:10.1016/j.tmaid.2020.101623

42 Silva Junior FJGD, Sales JCES, Monteiro CFS, *et al.* Impact of COVID-19 pandemic on mental health of young people and adults: a systematic review protocol of observational studies. *BMJ Open.* 2020;**10**(7):e039426.

43 Cohen J. *Statistical power analysis for the behavioral sciences*, 2nd. Lawrence Erlbaum Associates 1988.

44 Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. *JAMA* 2002;**287**:2831–4. doi: 10.1001/jama.287.21.2831

45 World Health Organization. *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19).* Geneva: World Health Organization; 2020. (WHO technical report).

46 First Affiliated Hospital of Zhejiang University School of Medicine. Handbook of COVID-19 Prevention and Treatment. 2020. https://gmcc.alibabadoctor.com/prevention-manual 21

47 Burki TK. Testing for COVID-19. *Lancet Respir Med*. 2020;**20**:30247-2. doi:10.1016/S2213-2600(20)30247-2

Reporting checklist for protocol of a systematic review.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-P reporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Identification	#1a	Identify the report as a protocol of a systematic review	1
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	1 and 2
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	1
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Sources	#5a	Indicate sources of financial or other support for the review	1

Sponsor	#5b	Provide name for the review funder and / or sponsor	1
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	1
Rationale	#6	Describe the rationale for the review in the context of what is already known	3 and 4
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5 and 6
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5 and 6
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5 and 7
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7 and 8
Data items	#12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study	8

		level, or both; state how this information will be used in data synthesis	
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	9
	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	9
	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9 and 10
	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	9 and 10
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a