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Identification of important clinical variables for the severe course of COVID-19 in hospitals: A systematic review

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Rachel Guimarães[1], Flávio Augusto Pereira Terra[2], Estael Luzia Coelho da Cruz-Cazarim[3], Fábio da Costa Carbogim[4], Maurílio de Souza Cazarim[5], Layla Kamenny Coelho de Sousa[6] and Karen Cristina coelho de Sousa[7].

ABSTRACT

Infection with the new coronavirus transformed the world from 2019 onwards. The severity of this respiratory syndrome caused by SARS-Cov-2 has divergent opinions on the causes of injuries and deaths. The objective of this study was to identify factors in the sociodemographic and clinical profile that are possibly related to COVID-19 cases that lead to hospitalization. This is a systematic review, in which the search strategy was defined by the acronym PECOS. The search was carried out in the scientific reference databases: MEDLINE via PubMed, Cochrane Library of Cochrane and; in specific databases: EMBASE via Elsevier and LILACS. Observational studies of the prospective cohort type without the use of filters were included. Exposure was considered as hospitalization for COVID-19 with a positive test and the individuals not exposed were those hospitalized with unconfirmed suspicion. The monitoring of the cohorts carried out by the studies lasted an average of 77.6±54.8 days. The mean time of infection of the patients was 9.5±22.32 days with a mean isolation period of 9.5±4.81 days. The symptoms commonly presented by the exposure group were: fever 787 (2.84%) cases, headache 658 (2.37%) cases, cough, sore throat, decreased appetite, headache, diarrhea. Factors such as age, 41.16±11.27 years; Non-essential occupation (79.79%) and medium and low education were evident in the exposure group. Respiratory diseases (0.22%), p= 0.045 and chronic kidney disease (0.08%), p= 0.038 were characteristics of the clinical profile for the exposed individuals. It is concluded that individuals with characteristic flu-like symptoms and diarrhea, with a profile of non-elderly adulthood, lower education, with non-essential occupation and who have characteristics of respiratory diseases and chronic kidney disease are more likely to be hospitalized for COVID-19.

Keywords: Comorbidities, Tertiary Care Centers, COVID-19.

[1] Graduate Program in Nursing, Federal University of Juiz de Fora, Brazil
[2] Department of Pharmaceutical Sciences, School of Pharmacy, Federal University of Juiz de Fora, Brazil
[3] Graduate Program in Pharmaceutical Sciences, Federal University of Juiz de Fora, Brazil.
[4] Graduate Program in Nursing, Federal University of Juiz de Fora, Brazil
[5] Graduate Program in Nursing, Federal University of Juiz de Fora, Brazil
Department of Pharmaceutical Sciences, School of Pharmacy, Federal University of Juiz de Fora, Brazil
E-mail: maurilio.cazarim@ufjf.br
[6] Medical
Uniceuma
[7] Medical
Uniceuma

INTRODUCTION

COVID-19 was a pandemic disease that became a public health emergency in 2020, as infection by the Sars-Cov-2 pathogen was unprecedented and was associated with mass mortality. Since then, numerous studies have been initiated on the subject to investigate the origin, characteristics of the pathogen, the disease, conducts, and treatments (Giacomelli et al., 2022; Cordeiro et al., 2022). As of March 2024, the number of accumulated cases in Brazil was 38,592,310, according to the coronavirus dashboard of the Health and Environment Surveillance Secretariat (SVSA) (Brasil, 2024a).

Clinical manifestations can be classified according to the COVID Guidelines Manual (2023) as: MILD: presence of non-specific symptoms, cough, sore throat or runny nose, followed or not by anosmia, ageusia, diarrhea, abdominal pain, fever, chills, myalgia, fatigue and/or headache. MODERATE: the most frequent symptoms range from mild signs of the disease, persistent cough and daily persistent fever, to signs of progressive worsening of another symptom related to COVID-19 (adynamia, prostration, hyporexia, diarrhea), in addition to the presence of pneumonia without signs or symptoms of severity. SEVERE: severe acute respiratory syndrome (flu-like syndrome presenting dyspnea/respiratory distress or persistent pressure in the chest or O2 saturation less than 94% on room air or bluish color of the lips or face). CRITICAL: these are sepsis, septic shock, acute respiratory distress syndrome, severe respiratory failure, multiple organ dysfunction, severe pneumonia, need for respiratory support, and admissions to intensive care units (Brasil, 2023a; Brazil, 2023b; Freitas et al., 2022).

In attention to the severe form of the disease, which has an unbalanced multisystem immune and inflammatory response, with cardiovascular, respiratory, neurological, intestinal, hepatic, pancreatic, renal, cutaneous and hematological involvement. Due to the response, it is mediated by activity without virus deviations, with endothelial disorder, inflammation and thrombosis of the microcirculation of the organs, with cases resulting from bilateral interstitial pneumonia, multiple organ failure, ARDS, sepsis, and disseminated intravascular coagulation (DIC), which can lead to death. Blood coagulation stimulates the prothrombotic state with an increase in fibrin, which is the breakdown product of fibrin (D-dimer) and fibrinogen, called COVID-19-related coagulopathy (Lima et al., 2021; Escosteguy et al., 2020).

COVID-19-related coagulopathy comprises an increase in cytokines, and will stimulate endothelial cells and damage to the pulmonary microvascular that will culminate in microthrombosis in the region and in the middle of hypercoagulability, which can occur thrombosis of wide vessels. Then, the procoagulant process, which is formed by COVID-19 coagulation factors correlated with risk causes, such as immobility, mechanical ventilation, and infection, the patient is prone to thromboembolic disorders, such as arterial thrombosis, pulmonary embolism (PE), pulmonary thrombosis, deep vein thrombosis (DVT), unusual thrombosis of arterial catheters or central lines,

extracorporeal membrane oxygenation (ECMO) cannulas, and early thromboses of hemodialysis filters extrarenal. The vascular alteration related to COVID-19 infection and the accuracy of deciding how to satisfactorily proceed with tromprophylaxis, it is important to verify the reason for complications in the various ways of performing interpellations in therapy (Escosteguy et al., 2020).

In the COVID-19 guidelines manual (2023), it explains that the SARS-CoV-2 virus, the virus has undergone numerous mutations, dividing into genetic groups or clades. These mutations are normal in the biological cycle of viruses, but some can lead to the emergence of variants that have a significant impact on public health, increasing transmissibility or disease severity. To identify and study these mutations and variants, it is necessary to use molecular techniques such as RT-PCR, which allows obtaining suitable material for genetic sequencing (Brasil, 2023b).

The rapid development of vaccines was a significant achievement, the Ministry of Health initially made available among the Federative Units the amount of 47 million doses of COVID-19 vaccine until April 2021 for application in priority groups and later continued to contract more doses for the population. The monitoring of the disease continued so that the outbreak of the pandemic could be controlled through a network of central laboratories, emergency response teams, a strategic information center for health surveillance, a national network for hospital epidemiological surveillance and surveillance of respiratory syndromes, and the death verification service, as reported by the National Health Fund (2021) (Souza et al., 2021; Brazil, 2022).

In the population-based study, among people over 20 years of age hospitalized for SARS-COVID carried out on vaccine effectiveness in preventing deaths attributed to severe acute respiratory syndrome due to COVID-19 (SARS-COVID), in Blumenau, Santa Catarina, Brazil, 2021, each death due to SARS-COVID was indicated as "case", and "control", the survivor; the combination between vaccination status and the conclusion "death" by logistic return and good vaccination result were evaluated by (1-OR)*100. Where it was concluded that vaccinated individuals decreased the lethality by SARS-COVID in individuals aged ≥ 20 years (Renck et al, 2024).

Even after the start of vaccination, efforts were concentrated on the execution of protocols to reduce the transmission of the SARS-CoV-2 virus both in the professional environment and at home. Thus, Primary Health Care acted strongly in the collective mobilization of professionals, due to the concern with safety in the care of patients with COVID-19 in some countries (Brasil, 2022). Such actions are linked to the provision of quality information, both for society and for the family of the patient undergoing treatment. However, the lack of knowledge of factors related to the severity of the disease, as well as risk factors that can be controlled to avoid aggravations and, consequently, overload of the health system and increase in the number of deaths, is a public health problem in many countries (Rodrigues, et al, 2022).

The scenario of hospital care capacity in overload in the pandemic is something undesirable and eminent due to possible new outbreaks of COVID-19. This may again imply a lack of beds, especially in Intensive Care Units (ICUs), lack of personal protective equipment (PPE), stress and exhaustion of health professionals at extreme levels due to the increased workload and the imminent risk of infection. In this context, the adoption of some measures in the areas of Management, Teaching and Research in some University Hospitals after the beginning of the pandemic is emphasized. Such measures, aimed at the safety, quality of life, and training of professionals and students that have contributed significantly to the prevention of COVID-19 transmission, as well as to a better understanding of this disease (Rodrigues et al., 2022; Brazil, 2024b).

Therefore, even with the control of the disease and the development of the vaccine, having knowledge of variables that can be characterized as risk factors for the aggravation of COVID-19 is essential for planning and assistance in the face of persistent cases of the disease and the risk of outbreaks. In this context, the objective of this study was to identify the clinical variables that may be associated with the progression of severe COVID-19 in the hospital environment.

METHOD

A systematic review was conducted following the Cochrane criteria (Higgins et al., 2022), in which it started from the following study question: What is the clinical and sociodemographic profile of individuals hospitalized for COVID-19? For this, individuals exposed and not exposed to infection were considered, Exposure was considered as hospitalization for COVID-19 with a positive test for SARS-Cov-2 and individuals not exposed were those hospitalized with unconfirmed suspicion. The search strategy was defined by the acronym PECOS; scientific reference bases: MEDLINE via PubMed, Cochrane Library of Cochrane and; in specific databases: EMBASE via Elsevier and LILACS. Prospective observational cohort studies were included. Two independent researchers selected publications, assessed the quality of included studies, and extracted data on standardized forms. The criteria for characteristics and definitions are as shown in the table below (Table 1).

Table 1 - Table with key terms for structuring the PECOS search.

-	-	**Feature and Definition**
P	**Population**	COVID-19 patients seen in tertiary care
E	**Exposure**	Variables (characteristics) of COVID-19 patients treated in tertiary care
C	**Comparison**	Supportive/symptomatic therapy or non-intervention
O	***Outcomes (Outcomes)***	Not applied.
S	***Studies***	Prospective Cohort Studies.

In the search strategy, the Boolean operators to be used are: intracategory "OR" for word combination and inter category "AND" for word combination, population, and intervention. No search filters were used. It should be noted that the search groups were divided according to PECS, and when combining the "OR" the terms/words should always be in parentheses, as unlinking the "OR" in the search can find off-target results and provide a broad view, inaccurate search. Descriptors and keywords were extracted from controlled vocabularies, thesaurus for the strategies gathered in EMBASE, Health Sciences Descriptors (DeCS) in Portuguese/Spanish/English for LILACS; MeSH (Medical Subject Headings) for PubMed, Cochrane and Scopus. The search was carried out on December 13, 2023, in English, Portuguese and Spanish. The search strategies were adapted to each search base according to the peculiarities of each database (Appendix 1).

The studies were selected in the following order: Reading of the title, the abstract and the full text. After reading, the data were tabulated in order to know the main variables of patients affected by COVID-19 at the tertiary health level, and thus extract the sociodemographic characteristics, description of the intervention and control groups, if any, as well as the indicators analyzed.

Data extraction began after the reading and beginning of data collection of the articles, such as: references, year of publication, country of origin, type of study design, patient sample planning, eligible patients, duration of study days, gender, number of days of hospitalization, comorbidities, body mass index, groups with exposure, groups without exposure, schooling, essential occupation, disease progression, medication use, and mortality.

SELECTION AND ELIGIBILITY CRITERIA

Search strategies were executed for each database. The studies were retrieved and the file was generated for inclusion in the Rayyan systematic review database (https://www.rayyan.ai). Looking ahead, the duplicates were removed and two researchers were selected for blind analysis. Initially, the first stage of the system consisted of analyzing the title and abstract of the studies. Those who did not include according to our protocol criteria were not eligible and were removed if there was consensus between the two researchers. The articles selected after reading the title and abstract were analyzed in full to include those studies that responded to the question of the systematic review and that met the inclusion, exclusion and eligibility criteria. Conflicts in the selection of articles were

mutually resolved, when there was no agreement between the authors, a third researcher had the power of decision. The following inclusion and exclusion criteria are listed (Higgins, 2022; Ouzzani, 2016).

INCLUSION CRITERIA

Cohort comparison studies with hospitalized patients with suspected COVID-19, with clinical management for the disease at the hospital level. Studies that divided the cohort into exposure and non-exposure, considering exposure as the confirmed cases of SARS-Cov-2 infection.

EXCLUSION CRITERIA

Studies published in the form of narrative or integrative reviews, dissertations or theses, editorials, news, comments, letters to the editor, abstracts published in scientific journal channels or congresses and guidelines; studies that did not include the PECOS strategy, those that also did not consider the treatment of patients diagnosed with COVID-19; that analyzed non-reproducible variables for interventions in the clinical management of COVID-19; that did not pointed out variables related to the care of patients with COVID-19; and those whose variables described in the clinical management were not clear as to their correlation with the disease. Randomized or non-randomized clinical trials were also excluded, because unlike observational studies, in these studies the researcher plans and actively intervenes in the factors that influence the sample and because COVID-19 is an emerging disease, it is not possible to consider some type of outcome due to the lack of knowledge about the disease. Similarly, studies with patient populations with disease-specific conditions such as patients with myasthenia gravis, cancer, migraine, inflammatory bowel disease, hemodialysis patients, and pediatric patients were not considered.

DATA EXTRACTION

The extraction of data from its study in order to prioritize groups of information about the studies, such as: author, year of publication, country, study design, age, gender, occupation, education, comorbidities, signs, symptoms, monitoring time, days of hospitalization, duration of study days, clinical variables, number of non-infected, number of infected, number of deaths, smoking, obesity, disease progression and medication consumption.

ANALYSIS

The analysis of the results was performed using classical statistics to obtain summary measures, dispersion and percentages. The MINITAB v17 software was used to perform some statistical analyses. For the contingency analyses between groups, the chi-square and Fisher's exact

tests were used to test the hypothesis that the exposure and control groups diverged in clinical and sociodemographic factors. The *Student's t-test* was used to test the hypothesis of divergence between the groups regarding continuous variables, such as age, for example. In addition, the agreement between researchers was analyzed, before the moment of consensus among them, by the Kappa coefficient. For this, a value above 0.70 was considered acceptable, which was developed for consensus quality scoring. Otherwise, there would be a need to restructure a new search strategy. The Kappa coefficient was interpreted by the classification of Landis and Koch, according to Cordeiro et al. (2022) (Table 2).

Table 2 – Classification of the Kappa coefficient.

Kappa Value	**Meaning**
<0	No agreement
0.00 – 0.20	Practically no agreement
0.21 – 0.40	Weak agreement
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 0.95	Almost perfect agreement
0.95 – 1.00	Perfect Concordance

Source: Classification Landis and Koch (1977) cited by Cordeiro et al. (2022).

The evaluation of the quality of the studies was based on the criteria of *Downs and Black* (1998), which comprises a *checklist* of 28 items, which, after being answered, generates a score, used to classify the quality of the studies. The scores calculated by the instrument were measured in percentages from 0 to 100%. The interpretation of the scores was summarized as: up to 50% considered studies to be flawed or irrelevant; those between 50% and 69% considered themselves to have weak evidence; 70–79% considered good evidence; and 80-100% considered to have high scientific evidence. Based on this classification, an assessment based on the Cochrane risk criteria was applied to the *Downs and Black instrument*, for a quali-quantitative assessment of the quality of the studies retrieved in the review. In this classification, it was possible to predict the domain that is most prone to bias and its percentage of risk of bias (Downs & Black, 1998; Higgins, 2022).

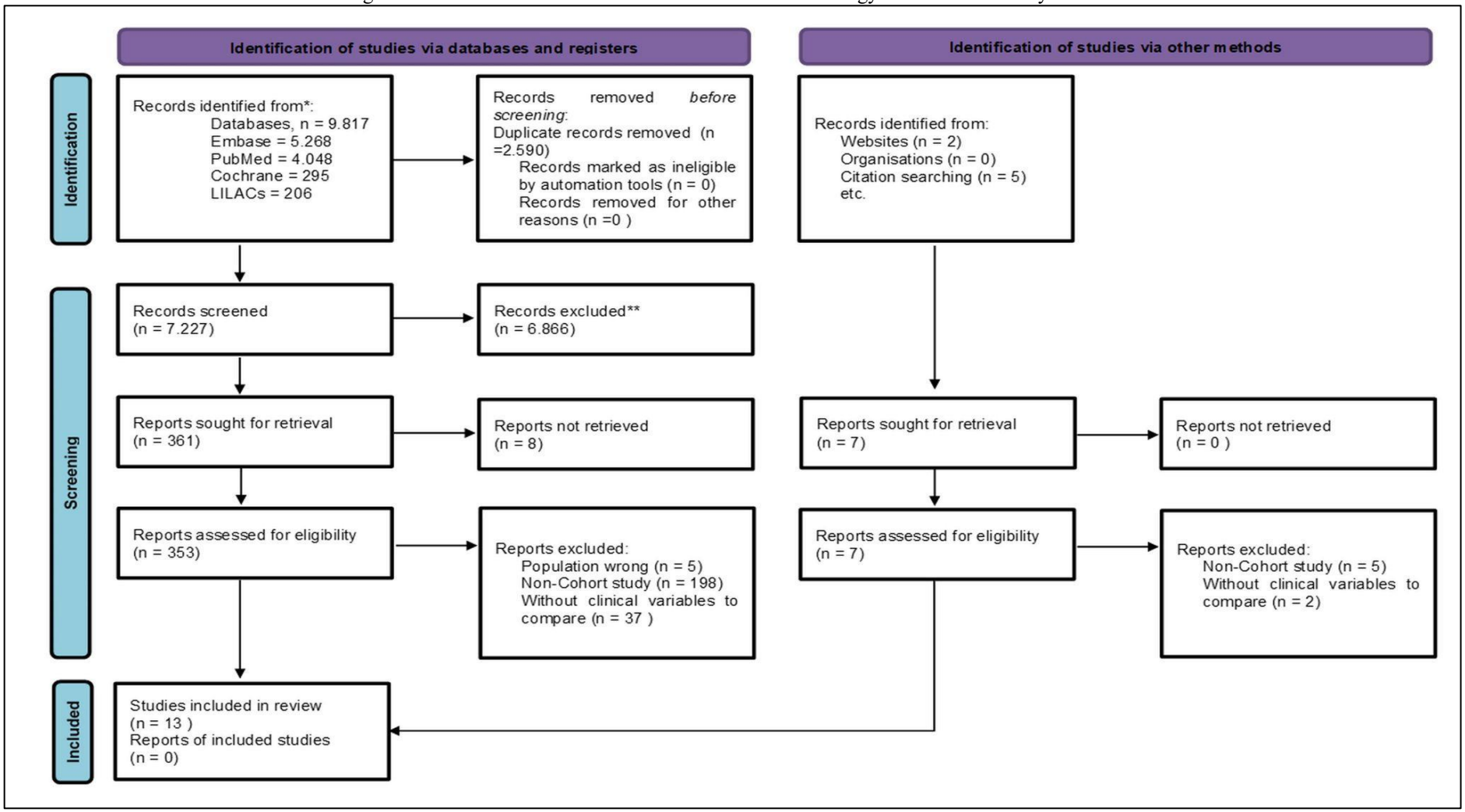
STUDY PROTOCOL

This review was guided by a protocol (https://www.cientperiodique.com/article/CPQME-11-6-323.pdf) registered in the PROSPERO database - International Prospective Registry of Systematic Reviews - for systematic review, number ID 256450. This was structured and organized in the PECOS format (Population / Exposure / Comparison / Results / Study Design), which was used to prepare the review questions, to ensure a systematic search of the scientific literature.

RESULTS

The search strategy used for the systematic review was according to the Prisma flowchart in agreement in peer review, which initially for the identification of the records of the articles were collected the following: databases n=9,817, embase=5,268, pubmed=4,048, Cochrane=295, lilacs= 206; After this identification, these articles were sorted, where duplicate articles were excluded in a total of 2,590; In the screening process, the selected records were n= 7,227, where 6,866 records were excluded, 8 records were not recovered, the reports for eligibility evaluation were n=353, according to the exclusion reports, n=5 were erroneously selected, n= 198 study without cohort study and n=37, the studies were without comparison variables. In the phase of studies included in the review, in n= 13 studies were included in the systematic review (Figure 1).

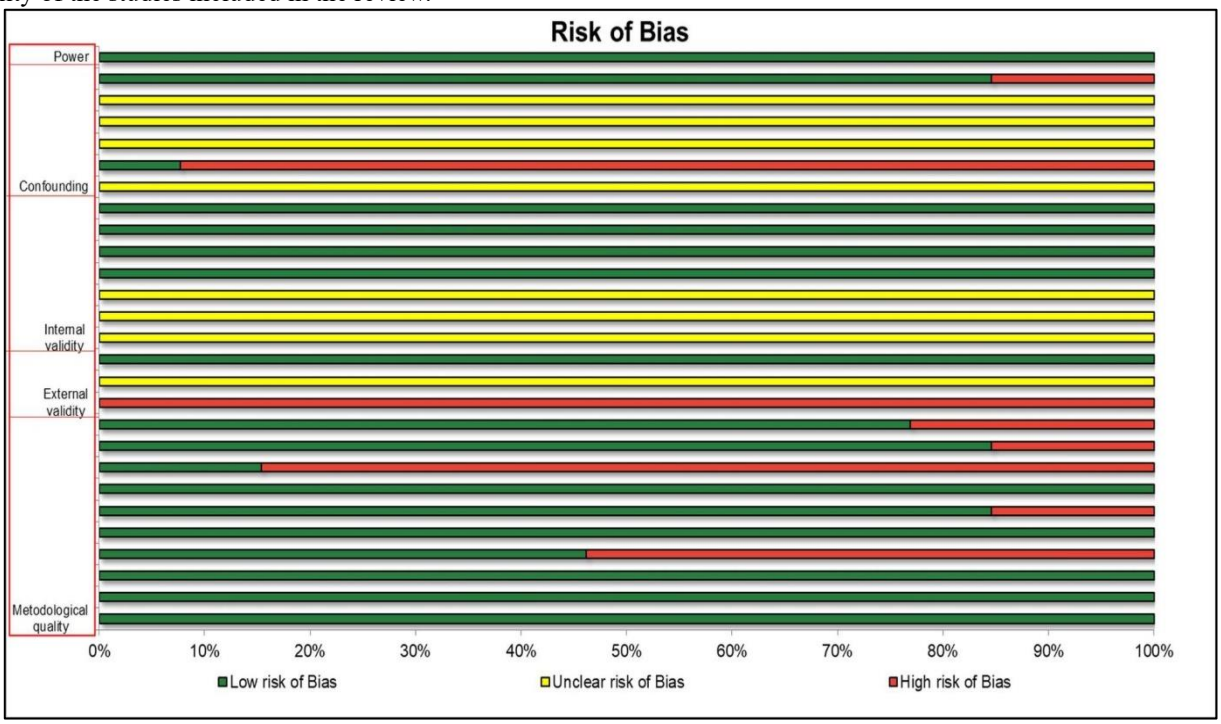
Figure 1 - Prisma flowchart for the search and selection strategy carried out in the systematic review.



Caption: This flowchart is in English as directed by Cochrane.
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

After the quality assessment, it was found that the risk of bias was low because the studies complied with the methods with adequate robustness to achieve the results presented. Of all twenty-seven questions, eleven had a low risk of bias for all studies and another five questions had a medium risk of bias. Regarding strength, all studies showed a low risk of bias. Regarding internal validity and the confounding domain, of thirteen questions, five presented low risk of bias and one question high risk, which was already predicted, since the studies did not differentiate between the intervention and randomization groups (Figure 2).

Figure 2 – Figure adapted from the *Downs and Black instrument* and the Cochrane risk of bias for the assessment of the quality of the studies included in the review.



Caption: The title was generated by the *software* is in the English language; Risk of bias = risk of bias; Power = statistical power; Confounding = confounding of variables in the results; internal validity= internal validity; external validity = external validity; methodological quality = methodological quality. Source: Prepared by the author (2023).

All studies included in this review were classified as good, with 4 classified as having high efficiency (30.80%) and 9 classified as having good efficiency (69.20%). There was no difference between the scores of the same classification, but the studies with good evidence had greater representativeness for the results, p=0.047 (Table 3).

Table 3 - Relationship between the quality score of the studies and the classification in contribution to the evidence generated in terms of biases.

Study	Quality Score	Percentage (%)	Classification	Representativeness	Comparison of intracategory scores	Comparison of scores between classifications
(ABRAHIM *et al*., 2020)	14	73,70%	Good evidence	69,20%	p=0.617	
(BRENDISH et al., 2020)	14	73,70%	Good evidence			
(continued) (BURREL et al., 2020)	14	73,70%	Good evidence			
(YACONITTI *et al*., 2020)	14	73,70%	Good evidence			
(CHEW et al., 2021)	15	79,00%	Good evidence			
(LAAKE et al., 2021)	15	79,00%	Good evidence			
(RODRÍGUEZ et al., 2020)	15	79,00%	Good evidence			
(TELLE et al., 2020)	15	79,00%	Good evidence			
(THOMSON et al., 2020)	15	79,00%	Good evidence			p= 0.047
(CORTES et al., 2020)	16	84,20%	High evidence	30,80%		
(GIACOMELLI et al., 2020)	16	84,20%	High evidence		p=0.999	
(HUANG et al., 2020)	16	84,20%	High evidence			
(VIAL et al., 2020)	16	84,20%	High evidence			

Legend: ¥ = the Student's t-test was run; ł = Fisher's exact statistical test was run.

Most of the studies retrieved and selected in this review were published in 2020 and 2021, respectively, in Italy, the United Kingdom, Australia, Sweden, Mexico, China, Norway, Chile, and Argentina. The mean follow-up of the research participants in the studies was 77.6±54.8 (Table 4).

Table 4 - Table with the primary extractions of the articles.

Reference	Anus	Country	Study design	Study duration (days)
(ABRAHIM *et al*., 2020)	2020	Italy	Prospective cohort	101
(BRENDISH *et al*., 2020)	2020	United Kingdom	Prospective cohort	40
(BURREL *et al*., 2020)	2020	Australia	Prospective cohort	124
(continued) (CHEW *et al*., 2021)	2021	Sweden	Prospective cohort	30
(CORTES *et al*., 2020)	2020	Mexico	Prospective cohort	95
(GIACOMELLI *et al*., 2020)	2020	Italy	Prospective cohort	47
(HUANG *et al*., 2020)	2020	China	Prospective cohort	18
(LAAKE *et al*., 2021)	2021	Norway	Prospective cohort	102
(RODRÍGUEZ *et al*., 2020)	2020	Not informed	Prospective cohort	34
(TELLE *et al*., 2020)	2020	Norway	Prospective cohort	183
(THOMSON *et al*., 2020)	2020	United Kingdom	Prospective cohort	28
(VIAL *et al*., 2020)	2020	Chile	Prospective cohort	31

(YACONITTI *et al*., 2020)	2020	Argentina	Prospective cohort	176

For divergence between the groups without exposure and exposure in terms of sociodemographic data, age was evident, 45.89±13.98 years and 41.16±11.27 years; non-essential occupation in greater proportion to those exposed (79.79%) and medium and low education also in greater proportion for these individuals (Table 5).

Table 5 - Table with the sociodemographic profile of the infected people.

Variables	**No exposure group (n= 389,369)**	**Group with exposure (n= 27,702)**	**p-value**
Mean age (SD)	45,89 ± 13,98	41,16 ± 11,27	p=0.042
Gender (%)			
Men	81.608 (50,17%)	2.433,8 (43,85%)	
Women	81.044 (49,83%)	3.117 (56,15%)	p= 0.156
Essential occupation (%)	221 (40,11%)	407 (20,21%)	
Non-essential occupation (%)	330 (59,89%)	1.607 (79,79%)	p=0.009
Schooling			
Loud	301 (52,35%)	180 (36,36%)	p=0.046
Average	218 (37,91%)	233 (47,07%)	-
Low	56 (9,74%)	82 (16,57%)	-
Disease progression (%)	-	729 (18,90%)	-
No disease progression (%)	-	3.129 (81,10%)	-
Comorbidities (%)	-	1.318 (47,38%)	-
Absence of comorbidities (%)	-	1.464 (52,62%)	-

Legend: -= absence of participants with such characteristics.

The mean time of infection of the patients was 9.5 ± 22.32 days with a mean isolation period of 9.5 ± 4.81 days. The symptoms most commonly presented by the patients were: Fever 787 (2.84%) cases, respiratory symptoms 2,583 (9.32%) cases, headache 658 (2.37%) cases, cough, sore throat, decreased appetite, headache, diarrhea, loss of smell, and in more severe cases the need for mechanical respiration. Respiratory diseases (0.22%), p= 0.045, and chronic kidney disease (0.08%), p= 0.038 were characteristics of the clinical profile for the exposed individuals (Table 6).

Table 6 - Table with variables of the clinical profile.

Clinical profile variables	No exposure group (n= 389,369)	Group with exposure (n=27,702)	p-value
Risk factors			
Smoking (%)	46659 (11,98%)	3857 (13,92%)	p= 0.241
Obesity			
Obese (%)	64.472 (16,56%)	5.303 (19,14%)	p= 0.202
Morbidities			
Heart failure (%)	74.862 (19,23%)	6.135 (22,15%)	p= 0.185
Ischemic Heart Disease (%)	8.122 (2,09%)	632 (2,28%)	p= 0.798
Peripheral arterial disease (%)	-	1 (0,004%)	-
Cerebrovascular disease (%)	1658 (0,43%)	176 (0,64%)	p= 0.664
Stroke (%)	-	2 (0,01%)	-
Diabetes (%)	27.418 (7,04%)	2.400 (8,66%)	p= 0.518
COPD (%)	8.247 (2,11%)	779 (2,81%)	p= 0.114
Asthma (%)	-	67 (0,24%)	-
Respiratory disease (%)	79 (0,02%)	62 (0,22%)	p= 0.045
Dislipidemia (%)	66.675 (17,12%)	4.769 (17,21%)	p= 0.817
Cancer (%)	21.785 (5,59%)	1.778 (6,41%)	p= 0.377
Chronic Kidney Disease (%)	3 (0,001%)	22 (0,08%)	p= 0.038
Hypothyroidism (%)	-	13 (0,05%)	-
Chronic neurological disorder (%)	-	2 (0,007%)	-
Seizure (%)	-	3 (0,01%)	-
Rheumatoid arthritis (%)	-	2 (0,007%)	-
Kidney stone (%)	-	2 (0,007%)	-
Derrame cerebral (%)	-	2 (0,007%)	-
Hepatic steatosis (%)	-	1 (0,003%)	-
Benign prostatic hyperplasia (%)	-	1 (0,003%)	-
Hemiplegia (%)	-	1 (0,003%)	-
Hernia (%)	-	1 (0,003%)	-
HIV (%)	-	1 (0,003%)	-
Craniotomia (%)	-	1 (0,003%)	-
Neineih (%)	-	1 (0,003%)	-
Tuberculose (%)	-	1 (0,003%)	-
Symptoms			
Respiratory symptoms (%)	-	2.583 (9,32%)	-
Fever (%)	-	787 (2,84%)	-
Headache (%)	-	658 (2,37%)	-
Endpoint			
Medication consumption ± PD	-	1714 ± DP	

Legend: DP=Standard Deviation; COPD = Chronic Obstructive Pulmonary Disease; HIV= human immunodeficiency virus; - = there were no patients with these characteristics and it was not possible to test statistically.

DISCUSSION

The result of a quality research will be essential when the evidence is related to the ordered review research, minimizing risks of quality and bias of the methodology. The clinical outcomes of COVID-19 are many and can be presented differently in each individual. Thus, a probable infection is not rejected in the absence of clinical signs, just as a possible infection cannot be guaranteed with the presence of only one symptom. Despite the different symptoms, studies show that the most common symptoms are: headache, fever, cough, sputum production, sore throat, diarrhea, fatigue and myalgia. It is also notorious the perception that a greater number of infected people and subsequent aggravations of the disease are associated with the presence of some type of comorbidity, where the main ones are: hypertension, diabetes, obesity, smoking, cancer, and kidney disease (Lima, 2020).

There were no divergences in the main evidence manifested by individuals contaminated by the SARS-CoV-2 virus, both in the evidenced and non-evidenced groups. The main symptoms found included migraine, increased body temperature, decreased appetite, discomfort in the throat region, cough, digestive problems, respiratory symptoms, and the need for ventilatory assistance in severe cases (Li et al., 2020; Xaviers et al., 2020)

A relationship between the clinical profiles present in the two groups was investigated. The main profiles of infected individuals were overweight people and smokers. The main diseases identified were heart problems, high blood cholesterol levels, diabetes, cancer, circulation problems in the heart, cerebrovascular problems, and chronic kidney disease (Rodriguez et al., 2020; Xaviers et al., 2020; Rache et al., 2020).

The results shown in this in-depth analysis have characteristics equivalent to the existing information, making it easy to observe a correlation between the main symptoms presented by people infected with the SARS-CoV-2 virus, as well as the main concomitant diseases that are linked to an increase in the number of infections and worsening of clinical status (Grigonis et al., 2021; Cortés-Tellés et al., 2021).

Studies carried out reveal that most individuals contaminated by the coronavirus are people approximately 59 years of age, with low or medium academic education and, for the most part, not performing positions considered essential. This reason may be punctually linked to the suppression of public policies to satisfy the needy population, which needs these policies to have reach in health promotion and care. Individuals with a low level of education and without an essential occupation live in areas where life circumstances are more unstable, which indicates that the threats of contamination and worsening of the condition are more likely (Buffon et al., 2022; Teixeira et al., 2016).

There is similarity in the sociodemographic profiles between the contaminated individuals in the literature and the contaminated individuals in this systematic review. In the group without presentation, most of the participants were men, aged around 45 years, and most did not have any essential occupation. Other groups, in 90% had a medium to high level of education. The female group aged 41.16 years showed a higher number of representatives compared to groups without exposure to the virus (Teixeira et al., 2016). Therefore, individuals who did not have any essential activity (80%) had medium or low schooling. The description in the midst of the sociodemographic characteristic of the infected in the bibliography and the methodological review. It is identified that individuals who do not have a primary occupation, COVID-19 is more frequent in people over 41 years of age (Buffon et al., 2022; Cordeiro et al., 2022; Huang et al., 2020).

The results of this study allowed us to understand the essential variables that are related to COVID-19 and its fundamental symptoms, including the clinical representation, the

sociodemographic representative, and the period of contagion. Thus, it is likely to expand and promote innovations in therapeutic techniques and prevention of the disease, in order to offer an efficient treatment to all patients who are affected by the virus (Yacobitti et al., 2021; Khan et al., 2020).

To minimize the transmission of the coronavirus, several prevention and control measures have been adopted. These measures include effective public policies, cultural and behavioral adaptations, improvements in health, sanitation, and hygiene conditions. Some of the recommended practices include wearing masks, frequent hand hygiene with soap and water or alcohol gel, avoiding sharing objects, cleaning surfaces with 70% alcohol before and after use, and maintaining natural ventilation of environments (Malta et al., 2020; Rodrigues, 2022).

The SUS has implemented several actions to combat COVID-19 in the SUS, such as: monitoring the epidemiological situation, constantly monitoring the evolution of COVID-19 both in Brazil and internationally; the issuance of alerts and technical notes, with the publication of alerts on the increase in cases and deaths, as well as the identification of new variants, along with recommendations for control measures; case definitions, such as the continuous updating of the definitions of suspected, confirmed, and discarded cases as new knowledge about the disease emerges; the coordination of surveillance with the national coordination of surveillance of suspected and confirmed cases of COVID-19 (Brasil, 1990; Brazil, 2007; Brazil, 2021).

Data analysis with detailed analysis of data on COVID-19 cases and deaths; informative documentation, with the preparation of documents on the flow of collection of clinical samples for the detection of SARS-CoV-2; strengthening of the laboratory network with the improvement of the national network of laboratories for carrying out molecular tests and genomic sequencing; acquisition of supplies and training, with the purchase of supplies and training of professionals for laboratory diagnosis of the virus; the distribution of rapid tests with the distribution of rapid antigen tests to State Health Secretariats (SES); the update of Guidelines, with the update of the national guidelines for epidemiological surveillance of COVID-19 (Brasil, 2021); the information systems, with the maintenance and updating of the notification and information systems, in collaboration with Datasus, Sivep-Gripe, e-SUS Notifica, the Mortality Information System (SIM) and the Laboratory Environment Management System (GAL); risk communication with continuous risk communication for states, municipalities and the Federal District and sending support teams for local epidemiological surveillance; the strengthening of Integrated Surveillance, with the strengthening of the National System of Integrated Surveillance of COVID-19, Influenza and Other Respiratory Viruses through technical advice and training of epidemiological surveillance professionals (Brasil, 2008; Cavalcante et al., 2020.; Brazil 2020b)

Despite the end of the national and international health emergency, the pandemic character of the SARS-CoV-2 virus persists due to its widespread global transmission. Therefore, it is crucial to fully maintain the COVID-19 epidemiological surveillance model to respond effectively to new risks and variants.

CONCLUSION

The results of this review were based on studies at low risk of bias, with a higher propensity for good quality evidence. In this context, it is possible to identify the profile of patients hospitalized with COVID-19, which reveals the importance of sociodemographic factors such as adulthood, non-essential occupation, lower than average schooling as those more prone to the risk of health problems and hospitalization. Among other factors, classic flu-like symptoms such as headache, fever, cough, headache, sore throat, decreased appetite, plus diarrhea are present in most patients hospitalized for COVID-19, in exposure to SARS-Cov-2, consistent with a condition that can represent a greater risk to the severity of the disease. In addition, the existence of comorbidities such as underlying respiratory diseases and chronic kidney disease are factors that can influence the hospitalization of individuals with COVID-19 and possibly contribute to worsening of the disease.

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APPENDIX I - SEARCH STRATEGY ACRONYM PECOS

Primary care	
Databases	**Search items**
	MEDLINE/CENTRAL #1 ("COVID-19"[MeSH Terms]) OR ("COVID 19"[Text Word])) OR ("Disease, COVID-19 Virus"[Text Word])) OR ("Virus Disease, COVID-19"[Text Word])) OR ("COVID-19 Virus Infection"[Text Word])) OR ("COVID 19 Virus Infection"[Text Word])) OR ("COVID-19 Virus Infections"[Text Word])) OR ("Virus Infection, COVID-19"[Text Word])) OR ("2019-nCoV Infection"[Text Word])) OR ("2019 nCoV Infection"[Text Word])) OR ("2019-nCoV Infections"[Text Word])) OR ("Coronavirus Disease-19"[Text Word])) OR ("Coronavirus Disease 19"[Text Word])) OR ("2019 Novel Coronavirus Disease"[Text Word])) OR ("2019 Novel Coronavirus Infection"[Text Word])) OR ("2019-nCoV Disease"[Text Word])) OR ("2019 nCoV Disease"[Text Word])) OR ("2019-nCoV Diseases"[Text Word])) OR ("Disease, 2019-nCoV"[Text Word])) OR ("COVID19"[Text Word])) OR ("Coronavirus Disease 2019"[Text Word])) OR ("Disease 2019, Coronavirus"[Text Word])) OR ("SARS Coronavirus 2 Infection"[Text Word])) OR ("SARS-CoV-2 Infection"[Text Word])) OR ("Infection, SARS-CoV-2"[Text Word])) OR ("SARS CoV 2 Infection"[Text Word])) OR ("SARS-CoV-2 Infections"[Text Word])) OR ("COVID-19 Pandemic"[Text Word])) OR ("COVID 19 Pandemic"[Text Word])) OR ("COVID-19 Pandemics"[Text Word])) OR ("Pandemic, COVID-19"[Text Word])) OR ("SARS-CoV-2"[MeSH Terms])) OR ("Coronavirus Disease 2019 Virus"[Text Word])) OR ("2019 Novel Coronavirus"[Text Word])) OR ("2019 Novel Coronaviruses"[Text Word])) OR ("Coronavirus, 2019 Novel"[Text Word])) OR ("Novel Coronavirus, 2019"[Text Word])) OR ("Wuhan Seafood Market Pneumonia Virus"[Text Word])) OR ("SARS-CoV-2 Virus"[Text Word])) OR ("SARS CoV 2 Virus"[Text Word])) OR ("SARS-CoV-2 Viruses"[Text Word])) OR ("Virus, SARS-CoV-2"[Text Word])) OR ("2019-nCoV"[Text Word])) OR ("COVID-19 Virus"[Text Word])) OR ("COVID 19 Virus"[Text Word])) OR ("COVID-19 Viruses"[Text Word])) OR ("Virus, COVID-19"[Text Word])) OR ("Wuhan Coronavirus"[Text Word])) OR ("Coronavirus, Wuhan"[Text Word])) OR ("SARS Coronavirus 2"[Text Word])) OR ("Coronavirus 2, SARS"[Text Word])) OR ("Severe Acute Respiratory Syndrome Coronavirus 2"[Text Word]) #2 ("Therapeutics"[MeSH Terms]) OR ("Therapeutic"[Text Word])) OR ("Therapy"[Text Word])) OR ("Therapies"[Text Word])) OR ("Treatment"[Text Word])) OR ("Treatments"[Text Word])) OR ("Drug Therapy"[MeSH Terms])) OR ("Therapy, Drug"[Text Word])) OR ("Drug Therapies"[Text Word])) OR ("Therapies, Drug"[Text Word])) OR ("Chemotherapy"[Text Word])) OR ("Chemotherapies"[Text Word])) OR ("Pharmacotherapy"[Text Word])) OR ("Pharmacotherapies"[Text Word])) OR ("Disease Management"[MeSH Terms])) OR ("Disease Managements"[Text Word])) OR ("Management, Disease"[Text Word])) OR ("Standard of Care"[MeSH Terms])) OR ("Care Standard"[Text Word])) OR ("Care Standards"[Text Word])) OR ("Standards of Care"[Text Word])) OR ("Palliative Care"[MeSH Terms])) OR ("Care, Palliative"[Text Word])) OR ("Palliative Treatment"[Text Word])) OR ("Palliative Treatments"[Text Word])) OR ("Treatment, Palliative"[Text Word])) OR ("Treatments, Palliative"[Text Word])) OR ("Therapy, Palliative"[Text Word])) OR ("Palliative Therapy"[Text Word])) OR ("Palliative Supportive Care"[Text Word])) OR ("Supportive Care, Palliative"[Text Word])) OR ("Primary Health Care"[MeSH Terms])) OR ("Care Primary Health"[Text Word])) OR ("Primary Care"[Text Word])) OR ("Care Primary"[Text Word])) OR ("Primary Healthcare"[Text Word])) OR ("Healthcare Primary"[Text Word])) OR ("Health Care Comprehensive"[Text Word])) OR ("Comprehensive Healthcare"[Text Word])) OR ("Healthcare Comprehensive"[Text Word])) OR ("First Line Care"[Text Word])) OR ("Health Care Primary"[Text Word])) OR ("Community Health Services"[MeSH Terms])) OR ("Health Services, Community"[Text Word])) OR ("Community Health Service"[Text Word]))

	OR ("Health Service Community"[Text Word])) OR ("Service Community Health"[Text Word])) OR ("Services Community Health"[Text Word])) OR ("Community Health Care"[Text Word])) OR ("Care Community Health"[Text Word])) OR ("Health Care Community"[Text Word])) OR ("Community Healthcare"[Text Word])) OR ("Healthcare Community"[Text Word])) OR ("Community Health Services"[Text Word])) OR ("Community Care Service"[Text Word])) OR ("Community Care Services"[Text Word])) OR ("Preventive Health Care"[Text Word])) OR ("Preventive Medicine"[MeSH Terms])) OR ("Preventative Medicine"[Text Word])) OR ("Medicine Preventative"[Text Word])) OR ("Preventive Medicine"[Text Word])) OR ("Preventive Care"[Text Word])) OR ("Care Preventive"[Text Word])) OR ("Care Preventative"[Text Word])) OR ("Outpatients"[MeSH Terms]) #3 ("disease progression"[MeSH Terms]) OR ("Disease Progression"[MeSH Terms])) OR ("Prognosis"[MeSH Terms])) OR ("Severity of Illness Index"[MeSH Terms])) OR ("Time-to-Treatment"[MeSH Terms])) #4 ("mechanical ventilation"[Text Word]) OR ("fatal cases"[Text Word])) OR ("mortality"[MeSH Terms])) OR ("Severe Acute Respiratory Syndrome"[MeSH Terms])) OR ("critical care"[MeSH Terms])) OR ("severity"[Text Word])) OR ("intensive care"[Text Word])) OR ("Disease Exacerbation"[Text Word])) OR (("outpatient"[Text Word]) OR ("death"[Text Word]) #1 AND #2 AND #3 NOT #4
	EMBASE #1 ('covid 19'/exp OR 'covid 19' OR 'covid 19':ti,ab,kw OR '2019 novel coronavirus infection':ti,ab,kw OR covid19:ti,ab,kw OR 'coronavirus disease 2019':ti,ab,kw OR 'coronavirus disease-19':ti,ab,kw OR '2019-ncov disease':ti,ab,kw OR '2019 novel coronavirus disease':ti,ab,kw OR '2019-ncov infection': ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'severe acute respiratory syndrome coronavirus 2' OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'wuhan coronavirus':ti,ab,kw OR 'wuhan seafood market pneumonia virus':ti,ab,kw OR 'covid19 virus':ti,ab,kw OR 'covid-19 virus':ti,ab,kw OR 'coronavirus disease 2019 virus': ti,ab,kw OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR '2019 ncov':ti,ab,kw OR '2019 novel coronavirus':ti,ab,kw OR 'spike glycoprotein, covid-19 virus':ti,ab,kw OR 'covid-19 virus spike glycoprotein':ti,ab,kw OR '2019-ncov spike glycoprotein':ti,ab,kw) #2 ('drug therapy'/exp OR 'drug therapy' OR 'chemotherapy':ti,ab,kw OR 'pharmacotherapy':ti,ab,kw OR 'disease management'/exp OR 'disease management' OR 'standard of care'/exp OR 'standard of care' OR 'palliative therapy'/exp OR 'palliative therapy' OR 'palliative supportive care':ti,ab,kw OR 'primary health care'/exp OR 'primary health care' OR 'health care comprehensive': ti,ab,kw OR 'community care'/exp OR 'community care' OR 'preventive medicine':ti,ab,kw) #3 ('disease exacerbation'/exp OR 'disease exacerbation' OR 'disease exacerbation':ti,ab,kw OR 'prognosis'/exp OR 'prognosis' OR 'severity of illness index'/exp OR 'severity of illness index' OR 'time to treatment'/exp OR 'time to treatment' OR 'treatment outcome'/exp OR 'treatment outcome') #4 ('mechanical ventilation':ti,ab,kw OR 'fatal cases':ti,ab,kw OR 'mortality':ti,ab,kw OR 'severe acute respiratory syndrome':ti,ab,kw OR 'critical care':ti,ab,kw OR 'severity':ti,ab,kw OR 'intensive care':ti,ab,kw OR 'disease exacerbation':ti,ab,kw OR 'outpatient':ti,ab,kw OR 'death':ti, ab,kw) #1 AND #2 AND #3 NOT #4
	LILACS #1 ((Coronavirus AND Infections) OR (Infecções AND por AND Coronavirus) OR (Infecciones AND por AND Coronavirus) OR (Betacoronavirus) OR (2019-nCoV) OR (SARS-CoV-2) OR (Coronavírus AND da AND Síndrome AND Respiratória AND Aguda AND Grave AND 2) OR (Severe AND Acute AND Respiratory AND Syndrome AND Coronavirus AND 2) OR (SARS-CoV-2) OR (COVID-19) OR (2019-nCoV)) #2 ((Disease AND Progression) OR (Progressão AND da AND doença) OR (Progresión AND de AND la AND Enfermedad) OR (Survival AND analysis) OR (Análise AND de AND sobrevida) OR (Análisis AND de AND

	Supervivencia) OR (Prognosis) OR (Prognóstico) OR (Pronóstico) OR (Severity AND of AND Illness AND Index) OR (Índice AND de AND Gravidade AND de AND Doença) OR (Índice AND de AND Severidad AND de AND la AND Enfermedad) OR (Time-to-Treatment) OR (Tempo AND para AND o AND Tratamento) OR (Tiempo AND de AND Tratamiento) OR (Avanço AND da AND Doença) OR (Disease AND Exacerbation) OR(Progresión AND de AND Enfermedad) OR (Tempo AND até AND o AND Tratamento) OR (Análise AND de AND Sobrevivência) OR (Fatore$ Prognóstico$) OR (Prognostic Factor$) OR (Factore$ Pronostico$) OR (Índice AND de AND Severidade AND da AND Doença) OR (Índice AND de AND Gravedad AND de AND la AND Enfermedad) OR (Delay$ Treatment$) OR (Tiempo AND para AND el AND Tratamiento) OR (Primary AND Health AND Care) OR (Atención AND Primaria AND de AND Salud) OR (Atenção AND Primária AND à AND Saúde) OR (Primary AND Care) OR (Atención AND Primaria) OR (Atenção AND Primária) OR (Atenção AND Básica) OR (Community AND Health AND Service$) OR (Servicio$ AND de AND Salud AND Comunitaria) OR (Serviço$ AND de AND Saúde AND Comunitária) OR (Community AND Health AND Care) OR (Cuidado AND de AND Salud AND Comunitario) OR (Saúde AND Comunitária) OR (Preventive AND Medicine) OR (Medicina AND Preventiva) OR (Comprehensive AND Health AND Care) OR (Atención AND Integral AND de AND Salud) OR (Assistência AND Integral AND à AND Saúde)) #3 ((Drug AND Therapy) OR (Tratamento AND Farmacológico) OR (Quimioterapia) OR (Palliative AND Care) OR (Cuidados AND Paliativos) OR (Patient AND Care AND Planning) OR (Planejamento AND de AND Assistência AND ao AND Paciente) OR (Planificación AND de AND Atención AND al AND Paciente) OR (Tratamento AND Domiciliar) OR (Residential AND Treatment) OR (Tratamiento Domiciliario) OR (Therapeutics) OR (Terapêutica) OR (Terapéutica) OR (Disease AND Management) OR (Gerenciamento AND Clínico) OR (Manejo AND de AND la AND Enfermedad) OR (Drug AND therapy) OR (Treatment AND Outcome) OR (Treatment AND Failure) OR (Homebound AND Person) OR (Pacientes AND Domiciliares) OR (Personas AND Imposibilitadas) OR (Conservative AND Treatment) OR (Tratamento AND Conservador) OR (Tratamiento AND Conservador) OR (Tratamento AND com AND Fármacos) OR (Pharmacotherapy) OR (Terapia AND con AND Fármacos) OR (Tratamento AND com AND Medicamentos) OR (Terapia AND con AND Medicamentos) OR (Tratamento AND Paliativo) OR (Palliative AND Therapy) OR (Atención AND Paliativa) OR (Residential AND Treatment) OR (Procedimento AND de AND Tratamento) OR (Ações AND Terapêuticas) OR (Medida AND Terapêutica) OR (Acción AND Terapéutica) OR (Procedimiento AND Terapéutico) OR (Pessoa AND Confinada AND em AND Domicílio) OR (House-Bound AND Person) OR (Monitoramento AND Conservador) OR (Conservative AND Management) OR (Manejo AND Conservador)) #4 ((mechanical AND ventilation) OR (fatal AND cases) OR (mortality) OR (Severe AND Acute AND Respiratory AND Syndrome) OR (critical AND care) OR (severity) OR (intensive AND care) OR (Disease AND Exacerbation) OR (outpatient) OR (death)) #1 AND #2 AND #3 NOT #4
Secondary care	
Databases	**Search items**
	MEDLINE/CENTRAL #1 ("covid 19"[MeSH Terms] OR "covid 19"[Text Word] OR "disease covid 19 virus"[Text Word] OR "virus disease covid 19"[Text Word] OR "covid 19 virus infection"[Text Word] OR "covid 19 virus infection"[Text Word] OR "COVID-19 Virus Infections"[Text Word] OR "virus infection covid 19"[Text Word] OR "2019 ncov infection"[Text Word] OR "2019 ncov infection"[Text Word] OR "2019-nCoV Infections"[Text Word] OR "coronavirus disease 19"[Text Word] OR "coronavirus disease 19"[Text Word] OR "2019 Novel Coronavirus Disease"[Text Word] OR "2019 Novel Coronavirus Infection"[Text Word] OR "2019 ncov disease"[Text Word] OR "2019 ncov disease"[Text Word] OR "2019-nCoV Diseases"[Text Word] OR "disease

	2019 ncov"[Text Word] OR "COVID19"[Text Word] OR "Coronavirus Disease 2019"[Text Word] OR "disease 2019 coronavirus"[Text Word] OR "SARS Coronavirus 2 Infection"[Text Word] OR "sars cov 2 infection"[Text Word] OR " infection sars cov 2"[Text Word] OR "sars cov 2 infection"[Text Word] OR "SARS-CoV-2 Infections"[Text Word] OR "covid 19 pandemic"[Text Word] OR "covid 19 pandemic"[Text Word] OR "COVID-19 Pandemics"[Text Word] OR "pandemic covid 19"[Text Word] OR "SARS-CoV-2"[MeSH Terms] OR "Coronavirus Disease 2019 Virus"[Text Word] OR "2019 Novel Coronavirus"[Text Word] OR "2019 Novel Coronaviruses"[Text Word] OR "coronavirus 2019 novel"[Text Word] OR "novel coronavirus 2019"[Text Word] OR "Wuhan Seafood Market Pneumonia Virus"[Text Word] OR "sars cov 2 virus"[Text Word] OR "sars cov 2 virus"[Text Word] OR "SARS-CoV-2 Viruses"[Text Word] OR "virus sars cov 2"[Text Word] OR "2019-nCoV"[Text Word] OR "covid 19 virus"[Text Word] OR "covid 19 virus"[Text Word] OR "COVID-19 Viruses"[Text Word] OR "virus covid 19"[Text Word] OR "Wuhan Coronavirus"[Text Word] OR "coronavirus wuhan"[Text Word] OR "SARS Coronavirus 2"[Text Word] OR "coronavirus 2 sars"[Text Word] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Text Word]) #2 ("Secondary Care"[MeSH Terms]) OR ("Care, Secondary"[Text Word])) OR ("Secondary Cares"[Text Word])) OR ('secondary health care'[Text Word]) OR ('secondary healthcare'[Text Word]) OR ('secondary care center'[Text Word]) OR ('secondary health-care facilities'[Text Word]) #1 AND #2
	EMBASE #1 ('covid 19'/exp OR 'covid 19' OR 'covid 19':ti,ab,kw OR '2019 novel coronavirus infection':ti,ab,kw OR 'coronavirus disease 2019':ti,ab,kw OR 'coronavirus disease-19':ti,ab,kw OR '2019-ncov disease':ti,ab,kw OR '2019 novel coronavirus disease':ti,ab,kw OR '2019-ncov infection':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'severe acute respiratory syndrome coronavirus 2' OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'wuhan coronavirus':ti,ab,kw OR 'wuhan seafood market pneumonia virus':ti,ab,kw OR 'covid19 virus':ti,ab,kw OR 'covid-19 virus':ti,ab,kw OR 'coronavirus disease 2019 virus':ti,ab,kw OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR '2019 ncov': ti,ab,kw OR '2019 novel coronavirus':ti,ab,kw OR 'spike glycoprotein, covid-19 virus':ti,ab,kw OR 'covid-19 virus spike glycoprotein':ti,ab,kw OR '2019-ncov spike glycoprotein':ti,ab,kw) #2 ('drug therapy'/exp OR 'drug therapy' OR 'chemotherapy':ti,ab,kw OR 'pharmacotherapy':ti,ab,kw OR 'disease management'/exp OR 'disease management' OR 'standard of care'/exp OR 'standard of care' OR 'palliative therapy'/exp OR 'palliative therapy' OR 'palliative supportive care':ti,ab,kw) #3 ('secondary care'/exp OR 'secondary care' OR 'care, secondary':ti,ab,kw OR 'secondary cares':ti,ab,kw OR 'secondary health care':ti,ab,kw OR 'secondary healthcare':ti,ab,kw OR 'secondary care center':ti,ab,kw OR 'secondary health-care facilities':ti,ab,kw) #1 AND #2 AND #3
	LILACS #1 (Coronavirus AND Infections) OR (Infecções AND por AND Coronavirus) OR (Infecciones AND por AND Coronavirus) OR (Betacoronavirus) OR (2019-nCoV) OR (SARS-CoV-2) OR (Coronavírus AND da AND Síndrome AND Respiratória AND Aguda AND Grave AND 2) OR (Severe AND Acute AND Respiratory AND Syndrome AND Coronavirus AND 2) OR (SARS-CoV-2) OR (COVID-19) OR (2019-nCoV)) #2 ((Drug AND Therapy) OR (Tratamento AND Farmacológico) OR (Quimioterapia) OR (disease AND management) OR (Gerenciamento AND Clínico) OR (Manejo AND de AND la AND Enfermedad) OR (disease AND exacerbation) OR (Progressão AND da AND Doença) OR (Progresión AND de AND la AND Enfermedad) OR (prognosis) OR (Prognóstico) OR (Pronóstico) OR (severe AND acute AND respiratory AND syndrome) OR (Síndrome AND Respiratória AND Aguda AND Grave) OR (Síndrome AND Respiratorio AND Agudo AND Grave))

	#3 ((Outpatient AND Clinics AND Hospital) OR (Ambulatório AND Hospitalar) OR (Servicio AND Ambulatorio AND en AND Hospital) OR (Secondary AND Care) OR (Atención AND Secundaria AND de AND Salud) OR (Atenção AND Secundária AND à AND Saúde) OR (Secondary AND Health AND Care) OR (Cuidado AND de AND la AND Salud AND secundaria) OR (Cuidado$ AND de AND saúde AND secundário$) OR (Pulmonary Medicine) OR (Pneumologia) OR (Neumología)) #1 AND #2 AND #3
Terciary care	
Databases	**Search items**
	MEDLINE/CENTRAL #1 ("covid 19"[MeSH Terms] OR "2019 novel coronavirus infection"[Text Word] OR "covid19"[Text Word] OR "coronavirus disease 2019"[Text Word] OR "coronavirus disease-19"[Text Word] OR "2019-ncov disease"[Text Word] OR "2019 novel coronavirus disease"[Text Word] OR "2019-ncov infection"[Text Word] OR "wuhan coronavirus"[Text Word] OR "wuhan seafood market pneumonia virus"[Text Word] OR "covid19 virus"[Text Word] OR "covid-19 virus"[Text Word] OR "coronavirus disease 2019 virus"[Text Word] OR "sars cov 2"[Text Word] OR "sars2"[Text Word] OR "2019 ncov"[Text Word] OR "2019 novel coronavirus"[Text Word]) #2 ("clinical characteristics"[Text Word] OR "severity of illness index"[Text Word] OR "severe acute respiratory syndrome"[Text Word] OR "mechanical ventilation"[Text Word] OR "severity"[Text Word] OR "intensive care"[Text Word]) #3 ("inpatients"[Text Word] OR "hospitals"[MeSH Terms] OR "inpatient"[Text Word] OR "hospital"[Text Word]) #4 ("primary health care"[MeSH Terms] OR "preventive medicine"[MeSH Terms] OR "secondary health care" OR "mild"[Text Word] OR "milder"[Text Word] OR "primary care"[Text Word] OR "biomarkers"[Text Word] OR "protocol"[Text Word] OR "community healthcare"[Text Word] OR "healthcare community"[Text Word] OR "community health services"[Text Word] OR "preventive medicine"[Text Word] OR "medicine preventive"[Text Word] OR "preventive care"[Text Word] OR "care preventive"[Text Word] OR "preventative medicine"[Text Word] OR "preventative care"[Text Word] OR "care preventative"[Text Word] OR "health care comprehensive"[Text Word] OR "comprehensive healthcare"[Text Word] OR "healthcare comprehensive"[Text Word] OR "first line care"[Text Word] OR "health care primary"[Text Word] OR "community care service"[Text Word] OR "community care services"[Text Word] OR "preventive health care"[Text Word] OR "secondary health care"[Text Word] OR "secondary healthcare"[Text Word] OR "care secondary"[Text Word] OR "secondary care center"[Text Word] OR "mask"[Text Word] OR "genomic"[Text Word] OR "placental"[Text Word] OR "surgery"[Text Word] OR "systematic review"[Text Word] OR "lockdown"[Text Word] OR "swabs"[Text Word] OR "validation"[Text Word] OR "predict"[Text Word] OR "artificial intelligence"[Text Word] OR "machine learning"[Text Word]) #1 AND #2 AND #3 NOT #4
	EMBASE #1 ('covid 19'/exp OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'covid 19':ti,ab,kw OR '2019 novel coronavirus infection':ti,ab,kw OR 'covid19':ti,ab,kw OR 'coronavirus disease 2019':ti,ab,kw OR 'coronavirus disease-19':ti,ab,kw OR '2019-ncov disease':ti,ab,kw OR '2019 novel coronavirus disease': ti,ab,kw OR '2019-ncov infection':ti,ab,kw OR 'wuhan coronavirus':ti,ab,kw OR 'wuhan seafood market pneumonia virus':ti,ab,kw OR 'covid19 virus':ti,ab,kw OR 'covid-19 virus':ti,ab,kw OR 'coronavirus disease 2019 virus':ti,ab,kw OR 'sars cov 2':ti,ab,kw OR 'sars2':ti,ab, kw OR '2019 ncov':ti,ab,kw OR '2019 novel coronavirus':ti,ab,kw) #2 ('clinical characteristics':ti,ab,kw OR 'severity of illness index':ti,ab,kw OR 'severe acute respiratory syndrome':ti,ab,kw OR 'mechanical ventilation':ti,ab,kw OR 'severity':ti,ab,kw OR 'intensive care':ti,ab,kw) #3 ('inpatients':ti,ab,kw OR 'hospitals'/exp OR 'terciary care':ti,ab,kw OR 'inpatient':ti,ab,kw OR 'hospital':ti,ab,kw)

	#4 ('primary health care'/exp OR 'community care'/exp OR 'preventive medicine'/exp OR 'secondary health care'/exp OR 'mild':ti,ab,kw OR 'milder':ti,ab,kw OR 'primary care':ti,ab,kw OR 'biomarkers':ti,ab,kw OR 'protocol':ti,ab,kw OR 'community healthcare':ti,ab,kw OR 'healthcare community':ti,ab,kw OR 'community health services': ti,ab,kw OR 'preventive medicine':ti,ab,kw OR 'medicine preventive':ti,ab,kw OR 'preventive care':ti,ab,kw OR 'care preventive':ti,ab,kw OR 'preventative medicine':ti,ab,kw OR 'preventative care':ti,ab,kw OR 'care preventative':ti,ab,kw OR 'health care comprehensive':ti,ab,kw OR 'comprehensive healthcare':ti, ab,kw OR 'healthcare comprehensive':ti,ab,kw OR 'first line care':ti,ab,kw OR 'health care primary':ti,ab,kw OR 'community care service':ti,ab,kw OR 'community care services':ti,ab,kw OR 'preventive health care':ti,ab,kw OR 'secondary health care':ti,ab,kw OR 'secondary healthcare':ti,ab,kw OR 'care secondary': ti,ab,kw OR 'secondary care center':ti,ab,kw OR 'mask':ti,ab,kw OR 'genomic':ti,ab,kw OR 'placental':ti,ab,kw OR 'surgery':ti,ab,kw OR 'lockdown':ti,ab,kw OR 'swabs':ti,ab,kw OR 'validation':ti,ab,kw OR 'predict':ti,ab,kw OR 'artificial intelligence':ti,ab,kw OR 'machine learning': ti,ab,kw) #1 AND #2 AND #3 NOT #4
	LILACS #1 (Coronavirus AND Infections) OR (Infecções AND por AND Coronavirus) OR (Infecciones AND por AND Coronavirus) OR (Betacoronavirus) OR (2019-nCoV) OR (SARS-CoV-2) OR (Coronavírus AND da AND Síndrome AND Respiratória AND Aguda AND Grave AND 2) OR (Severe AND Acute AND Respiratory AND Syndrome AND Coronavirus AND 2) OR (SARS-CoV-2) OR (COVID-19) OR (2019-nCoV) #2 (Drug AND Therapy) OR (Tratamento AND Farmacológico) OR (Quimioterapia) OR (disease AND management) OR (Gerenciamento AND Clínico) OR (Manejo AND de AND la AND Enfermedad) OR (disease AND exacerbation) OR (Progressão AND da AND Doença) OR (Progresión AND de AND la AND Enfermedad) OR (prognosis) OR (Prognóstico) OR (Pronóstico) OR (severity AND of AND illness AND index) OR (Índice AND de AND Gravidade AND de AND Doença) OR (Índice AND de AND Severidad AND de AND la AND Enfermedad) OR (severe AND acute AND respiratory AND syndrome) OR (Síndrome AND Respiratória AND Aguda AND Grave) OR (Síndrome AND Respiratorio AND Agudo AND Grave) #3 (inpatients) OR (Pacientes AND Internados) OR (Pacientes Internos) OR (Outpatient AND Clinics AND Hospital) OR (Ambulatório AND Hospitalar) OR (Servicio AND Ambulatorio AND en AND Hospital) OR (Hospital AND Care) OR (Assistência AND Hospitalar) OR (Atención AND Hospitalaria) #4 (Primary AND Health AND Care) OR (Atenção AND Primária AND à AND Saúde) OR (Atención AND Primaria AND de AND Salud) OR (Community AND Health AND Services) OR (Serviços AND de AND Saúde AND Comunitária) OR (Servicios AND de AND Salud AND Comunitaria) OR (Preventive AND Medicine) OR (Medicina AND Preventiva) #1 AND #2 AND #3 NOT #4

Subtitle: MEDLINE, Medical Literature Analysis and Online Recovery System; CENTRAL, Cochrane Central Register of Controlled Trials; EMBASE, Excerpta Medica Database; LILACS, Latin American and Caribbean Literature in Health Sciences. For LILACS, DeCS should be used and, from these descriptions/keywords, the dictionary translation into Portuguese and Spanish should be used to search for words in the various fields.