



2023

High-Risk COVID-19 Populations

IDENTIFYING VULNERABLE POPULATIONS IN DIFFERENT
PRACTICE ENVIRONMENTS

RESPIPLUS™

March 2023

Contents

About the Project.....	2
Scientific Panel & RESPIPLUS Team members	3
Scientific Panel	3
RESPIPLUS team members.....	3
Executive Summary.....	4
Introduction	5
Part 1: Scientific Committee works and Specialist Interviews regarding current COVID-19 landscape.....	6
Family Care.....	7
Respirology.....	8
Nephrology.....	9
Endocrinology	9
Cardiology	11
Immunology	13
Neurology.....	14
International - General.....	15
Part 2: Systematic Literature Review	17
List of Tables	17
List of Figures	17
Introduction	18
Methodology.....	18
Literature search strategy:.....	18
Study eligibility and selection	18
Data extraction	19
Statistical analysis	19
Results.....	20
Male gender, age, and BMI increased risk of hospitalization.....	20
Immune deficiency, coronary artery disease, and dyslipidemia increased hospitalization risk.....	21
Male gender and age increased risk of mortality	23
Summary and Discussion	24
Recommendations	26
Next Steps: Recommendations by the Scientific Committee	27
References	28
Appendix	30

About the Project

This report addresses the subject of identifying high-risk populations and COVID-19. It describes our investigation carried out between June and December 2022 and overseen by a panel of physicians composed of specialists in neurology, nephrology, respiratory, endocrinology, immunology, cardiology, as well as a family physician. Our goal is to explore the challenges associated in identifying the vulnerable populations in the different practice environments. The report has been prepared and published by RESPIPLUS, a non-profit organization with more than 20 years of expertise in developing educational programs for healthcare professionals and their patients in the field of respiratory medicine.

The development of this report was supported financially by Moderna. The investigation and content of the report have been created by an independent Scientific Panel.

Prepared on March 16th, 2023.

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Executive Summary

COVID-19 continues to evolve in its status and has now become endemic. This is a new reality, posing long-term challenges, that our already overloaded healthcare system is facing. Despite the high rates of vaccination achieved in Canada in 2021, work will need to be continuously done to ensure vulnerable populations are protected. These individuals, when exposed to the SARS-CoV2 virus, are at an increased risk of severe illness resulting in hospital admissions, intensive care unit stays, mechanical ventilation – associated with impaired quality of life – or having an increased risk of dying. Therefore, we must continue to identify, prioritize, and care for them.

Two main reasons for continued prioritization exercises:

- Within Canada, there was no homogeneity between provincial recommendations.
- With evolving literature, it makes it difficult to keep up with new findings and make sure we're not missing any important populations.

This report has been prepared by RESPIPLUS. Under the direction of a Scientific panel of leading physicians and specialists in a variety of medical fields, RESPIPLUS has developed this report to raise awareness about the dangers of COVID-19 in high-risk populations and identify what continued research is still needed.

This investigation, carried between June 2022 and March 2023, is presented in 2 parts:

- Part 1: Individual interviews and expert opinion by each of the members of the Scientific Committee
- Part 2: Systematic review of the literature

This Scientific panel objective is to close the gaps in the provincial definitions across Canada and ensure a complete approach and meaningful discussion related to the identification of COVID-19 vulnerable populations.

Introduction

As of November 2022, the U.S. [Center for Disease Control](#) has categorized COVID-19 high-risk populations in these groups:

- Older adults (+60): at higher risk of getting very sick or dying from COVID-19
- People with medical conditions such as: cancer, chronic kidney, liver and lung disease, dementia or neurological conditions, diabetes (type 1 & 2), heart conditions, HIV, overweight or obese, physical inactivity, sickle cell disease or thalassemia, smoking (current or former), stroke, substance abuse and tuberculosis
- Being immunocompromised or having a weakened immune system, or taking medications that lower the immune system response
- Pregnant and recently pregnant people: at higher risk of severe COVID-19 and of complications affecting the pregnancy, developing baby and the newborn infant.

RESPIPLUS has conducted a systematic review (presented in Part 2 of this report) to determine more precisely who falls into the high-risk populations for negative COVID-19 infection outcomes based on age, gender and all comorbidities. Our systematic literature search identified 440 articles documenting clinical outcomes of COVID-19 in relation to comorbid conditions. Following abstract and full-text screening, 29 studies were selected for data analysis. The detailed results are described in “Systematic Literature Review” section of this report.

Once identified, these populations need to be prioritized for education, vaccination, medications, and preventative treatments. Clear, concise materials with simple language can be developed to educate people on the risks they face. Oftentimes high-risk populations fall into marginalized groups, who lack trust in the healthcare system, do not understand their risk factors, and are vaccine hesitant.

Part 1: Scientific Committee works and Specialist Interviews regarding current COVID-19 landscape

An initial meeting between Dr. Jean Bourbeau (respirologist) and Dr. Peter Lin (Family Doctor) allowed for the identification of the expert panelists to be included. RESPIPLUS proceeded to invite specialists representing multiple therapeutic areas to participate to this Scientific Panel. Twenty-seven different physicians across Canada were invited to be part of this committee, and we succeeded to have representation from the following areas:

- Family Medicine
- Respiriology
- Nephrology
- Endocrinology
- Cardiology
- Immunology
- Neurology
- An international expert with experience in COVID-19, Geriatrics and Diabetes

Over multiple meetings, the Scientific Committee guided the works for the systematic review presented in Part 2 of this report.

To complement the research completed, and the large amount of data collected, RESPIPLUS wanted to determine if real-life clinical experience matched our results. We proceeded to interview each member of the Scientific Committee to hear first-hand how COVID-19 has affected their specific clientele and what could be done to better prioritize them in the future. It is important to know how to better identify this clientele, especially those who may not know or understand why they are at risk.

The Scientific Committee determined to explore the following topics during the individual interviews:

1. What is the patient clientele observed by each member?
2. Is this clientele currently recognized and targeted as being high-risk for severe outcomes of COVID-19?
 - a. If yes, what are the main reasons they are high-risk?
 - b. If no, should they be considered high-risk?
3. Panelist perspective in terms of challenges experienced by this clientele in the following areas:
 - a. Prioritization for vaccines
 - b. Prioritization for prevention measures
 - c. Access to adequate care and treatment when needed
 - d. Patient education for COVID-19
4. For the list above, what needs to be done to overcome these challenges?

Here are the results of the individual interviews. Please note the following is direct dialogue recorded from the interviewee (healthcare professional) and therefore represents their unique personal thoughts and opinions.

Family Care

Dr. Peter Lin | Family Physician, Toronto

Director, Primary Care Initiatives, Canadian Heart Research Centre

What is your patient clientele?

I'm in primary care, meaning we look after all patients, from babies to geriatric patients. All the patients at high risk for poor outcomes from COVID-19 at some point have a primary care doctor. It's a bit of a challenge, because you're looking after everybody and, in your mind, you have to tease out all the high-risk people. In the beginning, when there were restrictions as to who could get the COVID vaccine, we would use our electronic medical record to compile a list of high-risk patients so we could offer the vaccines to them. However, because the vaccination process was not handled by family physicians but in vaccination clinics, sometimes we didn't even know whether our high-risk patients had received the vaccine or not. Now it's up to us and every time we see a patient, we need to ask them, if they have been vaccinated?

What would you suggest we do to focus on the prioritization of vaccines for high-risk patients?

We need better information because often family physicians do not have a record of whether their high-risk patients have been vaccinated or whether they have tested positive for COVID-19. What we've been doing is asking patients whether they have contracted COVID since we last saw them or whether they have been vaccinated since their last visit. If they previously had COVID, it puts them in a higher risk category because people that have COVID seem to have more complications later. And for those patients with conditions that puts them at high-risk for poor outcomes, if they haven't had COVID, but have not been vaccinated that puts them at higher risk. For patients whose health is at risk from heart disease, high blood pressure, diabetes, or other conditions, a bigger risk to their health is getting COVID. If they get COVID their risk of dying is very high compared to the risk of death from their heart disease, high blood pressure or elevated cholesterol.

Do you feel that high-risk patients are aware of what to do if they get COVID?

No. Unfortunately, what happens is that patients get COVID, figure there's nothing to do and just hunker down at home and try and ride it out. Right now, I have so many people who get sick, and then they finally contact me two days or three days later, saying "I'm terribly ill, my fever is really like 40." They're in a panic and if they can't get a hold of me, they just don't know what to do. They end up clogging up the emergency department. We need to make people high-risk aware they are high-risk and show them what to do when they get sick, so they receive the proper treatment, promptly.

What about the level of knowledge among health-care providers about managing high-risk patients?

I think they've given up because the patients don't care anymore and think getting COVID is no big deal. That's why I think physicians are going back to treating other diseases. COVID is no longer top of mind, and we assume everybody knows everything about managing it. That's why things are falling apart. High-risk patients with COVID are not getting vaccinated or appropriately treated and they are ending up in

Emergency. We aren't making patients aware of basic preventive measures such as isolating at home which is why COVID is spreading through families now. Tools such as TikTok videos can be useful if they have more than general statements and give people specific information on what to do if they get sick.

Respirology

Dr. Jean Bourbeau | Senior Scientist, [Translational Research in Respiratory Diseases Program](#), McGill University Health Centre

Professor of Respirology, Department of Medicine, Faculty of Medicine and Health Sciences, McGill University

What is the patient clientele that you care for?

I am a respirologist and I see patients with respiratory conditions; mainly chronic obstructive lung disease (COPD) but also those with asthma, interstitial lung disease and lung cancer. While there is relatively little information about this population, we know those with asthma and lung cancer are at higher risk for poorer outcomes from COVID-19 infection. Patients with COPD may not be at higher risk of getting COVID, but they also can have more complications after being infected. Those with lung cancer may be immunocompromised because of their cancer or treatment and as a result may also be at higher risk of both catching COVID-19 and having more complications from COVID. Much of this information comes from the early phase of the pandemic and we still don't have a clear answer on the impact of chronic respiratory diseases on outcomes after COVID infection. This is troublesome because it is still not clear which respiratory patients should be prioritized for treatment. Co-morbidities can also make the situation more complex.

What are the main challenges facing this patient population in dealing with COVID?

Making sure those in the respiratory patient population who are at high risk are properly vaccinated against COVID-19 is the main challenge. With all respiratory patients we try and determine their vaccine status for COVID as well as making sure they are vaccinated for influenza. Because these patients have a chronic respiratory condition and tend to be older, we tell them they are at risk for COVID infection and complications and urge them to take preventive measures such as avoiding large groups in indoor settings and those who are sick as well as urging them to wear a mask.

Unless a patient has not been vaccinated or is immunocompromised, they do not have priority access to antivirals for treatment in the outpatient setting. If the patient is in hospital because of COVID infection, they will be treated with an anti-viral and if they are on oxygen or in the intensive care until they will also receive systemic corticosteroids which have been shown to reduce complications.

What about patient education for this population?

After three years we now have information about COVID-19 that should be presented to patients in a standardized format. I think it's time to tell patients what we know about COVID, what preventive measures they can take, and what to do if they are infected with COVID or develop long COVID. This

information should be developed by a third-party rather than those producing the vaccines or treatments and should be updated when appropriate. Unfortunately, there is currently no funding to do this.

What else can be done to better protect patients with respiratory diseases?

Vaccination is key. Education is key and having a formal program based on what we know. But the whole area of treatment has been a huge failure because after three years we have only a few treatments that are recognized as being effective. To me it is a sign that this area has not been properly funded.

Nephrology

Dr. Claire Harris | Clinical Assistant Professor of Medicine (Nephrology), University of British Columbia Medical Director, Vancouver General Hospital Hemodialysis Unit

Are nephrology patients currently recognized as being at high-risk for severe outcomes from COVID 19?

Nephrology patients are considered high risk because of impaired immune function from renal failure and also because they often have comorbidities such as diabetes, obesity, heart disease, and hypertension which are also known to be risk factors for poor outcomes after COVID-19 infection. They are also high-risk because they use immunosuppressive medications for transplant or autoimmune disease.

What is your perspective of challenges experienced by this clientele in prioritization for COVID vaccines and preventive measures against COVID infection?

While nephrology patients are high-risk for poor outcomes after COVID-19 infection many fall just short of being prioritized to receive COVID vaccines. Only those undergoing dialysis, those receiving certain immunosuppressive drugs, or patients who have undergone renal transplantation have been given priority to receive vaccines.

There has been poor communication to the renal community as a whole about being at high risk for poor outcomes from COVID-19. However, work has been done provincially and regionally here to develop communication strategies to better inform patients as these were lacking for both patients and medical staff. Work was done to create culturally appropriate and accessible documents that were translated into multiple languages as many of our patient population do not speak English.

Endocrinology

Dr. Akshay Jain
Clinical and Research Endocrinologist, Surrey, BC
Co-Chair, Primary Care Interest Group - Diabetes Canada

Are the patients you care for recognized and targeted as being high-risk for severe outcomes of COVID-19?

People living with diabetes and obesity are at a significantly high risk of worse outcomes with COVID-19.

Several studies have reported that pre-existing diabetes as well as newly diagnosed diabetes with a first glucose measurement on hospital admission are both associated with an increased risk of all-cause mortality in hospitalized patients with COVID-19. Several studies have reported new-onset diabetes (either type 1 or type 2) is associated with the presence of COVID-19. For obesity, multiple studies have revealed a strong correlation between ICU admission and BMI, independent of other (metabolic) risk factors.

What is your perspective in terms of challenges experienced by your at-risk patients?

Patients with obesity and diabetes would definitely benefit from prioritization for COVID vaccines and prevention measures, especially if they also have other comorbidities or complications related to severe forms of these conditions.

Patients with obesity or diabetes would benefit from close monitoring and follow-up in the outpatient setting to ensure that cases of mild Covid 19 do not progress to significant severity.

Apart from sporadic reports in the lay media, not much emphasis has been given on the increased complication risk in these populations and so both patients and healthcare providers would benefit better education about COVID-19 and the benefits of vaccination and preventive measures.

What is needed to change or overcome these challenges?

Increasing awareness to the general public as well as healthcare professionals is of paramount importance in raising awareness that people with diabetes or obesity are at a significantly increased risk of developing complications due to Covid 19. At the same time, research has shown those with even mild Covid 19 are at an increased risk of developing diabetes mellitus in the ensuing months. So primary care providers should be aware that appropriate screening is indicated in these individuals, especially if they also have other comorbid conditions such as obesity.

Cardiology

Dr. Kim Connelly

Staff cardiologist, St. Michael's Hospital, Toronto.

Which patients with cardiovascular conditions are at higher risk for complications from COVID-19 infection?

Many patients with cardiovascular issues have risk factors that we know are risk factors for adverse outcomes from COVID-19 – conditions such as chronic kidney disease, diabetes, hypertension, concomitant coronary artery disease, or cerebral vascular disease. Cardiovascular patients who also have complications as a result of diabetes are certainly at much higher risk of adverse outcomes from COVID-19, be it ICU admission, death or sequelae from COVID.

My patient population is essentially divided between older relatively well-off patients and those from inner city communities with lower socio-economic status.

Have your patients been identified as high-risk and prioritized for vaccination?

Those with comorbidities in association with pre-existing cardiovascular disease have been prioritized. As have those identified by postal code who are living in areas where there were clusters of COVID-19 cases.

However, some patients from marginalized backgrounds or lower socio-economic groups had vaccine hesitancy and did not want to come to hospital or were worried about perceived side-effects of vaccines. About three quarters of my patients are vaccinated but about one quarter remain unvaccinated and are unlikely to do so despite discussing the issues with them.

Unfortunately, those folks that have the worst outcomes from any condition are exactly that group that are much less likely to be vaccinated. There are clear associations. And they're also the folks that have all the comorbidities, heavy smoking, lung disease, CKD, diabetes, hypertension, coronary artery disease. So, it all clustered together.

Are the vaccine-hesitant seeking advice or making up their own minds?

Many of these people live in social housing and do not have good access to medical information. Also, the sort of medical system that I represent, is often the same sort of government run system that in the countries of their origin, did not treat them well. So, there's always this distrust. Over time, I think we can see that people are starting to listen a bit more. But it takes quite a lot of work and time and building up that relationship. No-one cares about a pamphlet or an ad, they want someone that they trust.

Is there any sub-group of patients with cardiovascular disease who are at higher risk for poor COVID-19 outcomes?

The people who are at the highest risk are less likely to have a primary care doctor and that means they're less likely to enter the healthcare system. We must create a system whereby we can have people who are

appropriately screened and address the risk factors, because all those risk factors are preventable. That, to me, starts with primary care.

Are patients with cardiovascular disease prioritized for COVID-19 treatments such as antivirals?

Absolutely, yes.

In terms of prevention, drug therapy is good, but basically hand washing, isolation, and masking are the public health prevention measures that we need because I think they're cheap and effective.

When it comes to access to drug therapies for COVID-19, equity and access issues remain. It's going to be selected populations who are always going to get access to better care and are more likely to be more aggressively treated and more likely to have had therapy for their risk factors and so on. And the same issues resulting in vaccine hesitancy are also an issue with new COVID-19 therapies as there is still a lot of the same mistrust.

Do patients have good access to information programs about COVID-19?

Doctors are the worst at doing this. We are not mass educators of the population. We are taught in this model where it's one on one, you sit down and have a discussion. On big issues such as COVID-19 instead of saying 'it's a bad virus, there is something that's very safe and effective, you should take it and you should wash your hands and do this', it becomes 'well there is this and you should consider this. And what about this?' And what that means is for the person sitting in front of you, all they hear is 'bad, bad, bad' right?

It's extremely important that folks who are experts in understanding messaging take control of this. The medical profession needs to have the right people through scientific advisors to make certain that the information is vetted, but ultimately, it's got to be done at the right education level.

It's got to be done in a number of different ways. I would strongly suggest we have experts come up with simple messaging that is clear and consistent.

The other thing that we've learned from dealing with indigenous groups is that you need to pick key opinion leaders who are a trusted voice within each of the various communities.

Immunology

**Dr. Bruce Mazer | Professor of Pediatrics, Faculty of Medicine and Health Sciences, McGill University
Senior Scientist, Research Institute of the McGill University Health Centre
Associate Scientific Director, COVID-19 Immunity Task Force, Public Health Agency of Canada**

Do you care for patients who are at high risk for COVID-19 complications?

I care for children with asthma and allergies, and they are not considered a high-risk population. But I also care for children with immune deficiency, who don't make antibodies and who don't have good T cells, and children who are on high end immunosuppressants, because of their underlying disease. These children are very high risk.

In pediatrics, the kids who are high risk for sure are the cancer patients who are immune compromised and the nephrology patients. Children in chronic renal failure have very inadequate vaccine responses and they need boosters more frequently. Rheumatology patients who we see who are on specific drugs that are immune suppressants are the more high-risk kids.

What is your perspective of children with asthma regarding COVID-19?

So far, we have not seen a variant of COVID that creates problems in your average asthmatic child. In fact, it's clear, I think that if you are an average asthmatic and you're taking your inhaled steroids, you may have some protection against the severe pulmonary complications. We tell our patients you had better stay on your meds because if you get COVID, you could get really sick. But if you stay on your meds, it seems to be protective.

Was your patient population prioritized for vaccines and other preventive measures against COVID-19?

Children who were immune deficient and kids on immune suppressants were absolutely prioritized. And they were the first group of kids to get it (the COVID vaccine).

As an immunologist and as somebody who really thinks that vaccination is important, not just for the individual, but for the community, I've been very proactive about kids getting vaccinated. I think that if you have children who are in school, and you want to keep them in school, every little bit helps. When it comes to vaccination, I think that the pediatric group and the allergists in Quebec have been very, very proactive for children.

What is your perspective on the challenges of access to COVID-19 testing and treatments?

If you're sick, we can tell you come to the emergency room, and we test our kids. There's always access through the emergency room, but I think it's a travesty that we don't have sufficient PCR tests in the community.

As we speak, our emergency room is going crazy. It can't keep up with the demand as people are coming in to get their kids checked constantly. And there's lots of testing going on. There's less hesitancy among

new immigrants or other cultural communities to bring your child to the emergency room than if you were an adult.

Is patient education about COVID-19 sufficient for the populations you serve?

With children, I think to be effective, you need to target schools, and debunk some of the myths that are going on and give them proper guidelines about care. In addition to proper education about the importance of masking, we must create conditions to reinforce the lessons learned early in the pandemic, about hygiene and hand washing and having safe spaces.

Neurology

Dr. Gustavo Saposnik

Associate Professor of Medicine (Neurology), University of Toronto.

Staff Neurologist, St. Michael's Hospital, Toronto.

Which patients with neurologic conditions are at higher risk for complications from COVID-19 infection?

COVID-19 infection is associated with a pro-thrombotic state, so for patients who have had a stroke or a minor stroke (TIA) the risk of having a recurrent stroke is much higher if they develop COVID-19 and could be more severe.

Patients who have well-established risk factors for developing a stroke such high blood pressure, being overweight, having diabetes, or being a smoker are at higher risk for having a stroke if they also have COVID-19, irrespective of age.

Are high-risk neurology patients given priority for vaccination or treatment?

Those patients who have had a stroke or who are taking immunosuppressive therapy for other neurologic conditions such as multiple sclerosis are characterized as high-risk in Canada and are prioritized for vaccination. However, those who have not had a stroke but may be at risk usually are not. There is a knowledge and knowledge-to action gap there.

What are the treatment options for patients with neurologic conditions when it comes to COVID-19?

For patients at increased risk of thrombosis who develop COVID-19, antiviral treatments are available and accessible. However, reduced access to PCR tests to confirm infection now makes it more difficult to determine who may need treatment and when. Many physicians are also not well-aware of who is eligible for antiviral therapy and to whom it should be offered.

With many family physicians still not seeing patients in-person telehealth is a good option for obtaining timely care and advice.

Are people aware of their options?

It depends. Some patients are very aware of the options available while others are not. In some cases, resources are available to assist patients but physicians may not be aware of them and this is a problem when physicians are the first point of contact patients have with the healthcare system.

Are stroke patients or those at-risk and physicians who treat them receiving the education they need about health issues?

Information overload is contributing to misinformation. We are overloaded with information we don't have time to read. What is needed is more clear and concise information that people will take time to read.

International - General

Dr. David Strain

Senior Clinical Lecturer, University of Exeter Medical School, UK

What patient clientele do you care for?

I am the clinical lead for COVID services in our Trust and responsible for all patients with COVID, and the program to prevent COVID locally. The population taking up most energy is the vulnerable elderly and those that have been identified as high risk from adverse outcomes of a COVID infection. The latter group are then further sub-divided into those that are unlikely to have mounted a sufficient response to their vaccination (e.g., those with major immunosuppression pharmacologically (e.g. transplant recipients) or pathologically (e.g. blood borne cancers,) or those who would likely suffer poor outcomes if they were to develop COVID despite appropriate vaccination (e.g. those with solid cancers, neurological disorders, etc.).

Is this clientele currently recognized and targeted as being high-risk for severe outcomes of COVID-19?

While the population described above has been identified as high-risk there is a growing appreciation that there are other groups who should be included; specifically, people living with obesity, those with poorly controlled type 2 diabetes, and those with heart failure etc. Other patient populations such as those with long COVID and ME/CFS* should also be seen as high-risk because they could be harmed by recurrent COVID infections.

*Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a disabling and complex illness.

What is your perspective in terms of the challenges experienced by this clientele?

The biggest problem with ensuring all patients are properly vaccinated at the moment is vaccine hesitancy. Access to preventive medicine is variable around the UK. In well-established centres a daily service operates in which people are contacted by a trained Physician Associate and receive their anti-virals/monoclonal antibodies within 24 hours of a positive test. There are other regions in the country

that only offer services from Monday to Friday and just offer Molnupiravir despite evidence of better alternatives.

In your view is patient education about COVID-19 adequate?

Patient education is an ongoing deficiency – for that matter HCP education for those who are caring for patients could also do with a boost. There is a growing rhetoric that “COVID is over”, however this is clearly not the case, particularly given the current rise in COVID cases in the UK, which is also likely to occur in Canada over the next few weeks. An educational program about which treatments are available, when they should be used, and how to access them would be very useful.

Of the challenges we face, education of both at-risk individuals and health care providers is the most immediate deficiency. Educational material should be accessible and presented in a language that will be understood rather than the medical terminology that is often used.

Vaccine fatigue is another challenge, and it will be a more difficult problem to address. Perhaps reminding people that COVID hasn't gone away would a good strategy.

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Part 2: Systematic Literature Review

List of Tables

Table 1. Demographic characteristics of hospitalized and non-hospitalized patients	20
Table 2. Association of characteristics and hospitalization	20
Table 3. Association of selected comorbidities with at least 2 studies available and hospitalization	21
Table 4. Association of selected comorbidities with at least 10 studies available and hospitalization	23
Table 5. Demographic characteristics of deceased and alive patients.....	23
Table 6. Association of characteristics of deceased and alive patients.....	23
Table 7. Association of some selected comorbidities with at least 2 studies available and death	24
Table A1. Literature Search Strategy	30
Table A2. Included Studies.....	32

List of Figures

Figure 1. Flowchart diagram for abstract and full-text screening	19
Figure 2. Magnitude of association of comorbidities	25

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Introduction

The objective of this study is to determine the population who is at high-risk of death or hospitalization from COVID-19 based on age, gender and underlying comorbid conditions. We conducted a systematic literature search which identified 440 articles documenting clinical outcomes of COVID-19 in relation to comorbidities. Following abstract and full-text screening, 29 studies were selected for data analysis. Using random-effect model, we found that several comorbidities increased hospitalization and mortality risks including cardiac diseases, COPD, diabetes, and CKD.

Methodology

Literature search strategy:

A systematic literature search was conducted using Ovid MEDLINE(R) and Epub databases to identify manuscripts specific to COVID-19 and high-risk populations, published between 1946 and March 13, 2023. The key words “coronavirus”, “COVID-19”, “vulnerable populations”, “high risk”, “death”, “ICU” and “comorbid” were used in various combinations. Manuscripts ahead of print, in-process, in-data-review, and other non-indexed citations were all searched and collected if deemed eligible. Articles relevant to other members of the coronavirus family such as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Middle East respiratory syndrome (MERS) were excluded from the final list of selected articles for screening, which included 440 eligible articles. The literature search strategy is summarized in Table A1 in appendix.

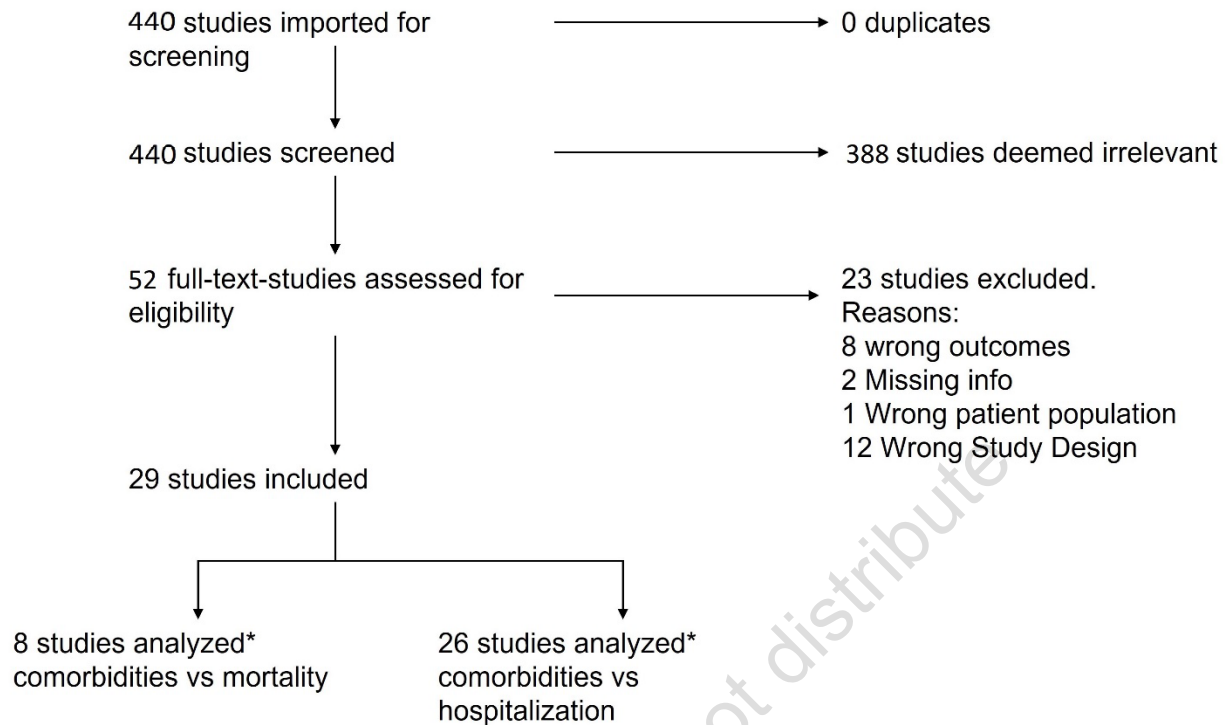
Study eligibility and selection

Using Covidence, the abstracts of 440 articles were first screened according to the following inclusion criteria:

- 1- The studies should be in the English language.
- 2- The studies should be adult patients with COVID-19. Studies with pediatric population were included only if the pediatric proportion does not exceed 10%.
- 3- The studies should be observational which includes retrospective, prospective. Meta-analysis studies were excluded. Interventional studies such as clinical trials and drug treatments were excluded. Furthermore, studies investigating prognostic factors, gender differences, socioeconomic factors, pathogenesis and mechanisms of action, impact of COVID-19 on disease severity and overall well-being were excluded.

Following the initial abstract screening, 52 studies were found eligible for full-text screening assessment, which focused on studies that documented clinical outcomes of COVID-19. A total of 23 studies were excluded because of wrong outcomes reported (n=8), missing information that prohibit data extraction and analysis (n=2), wrong patient population where the pediatric portion was more than 10% (n=1), and wrong study design where the studies investigated COVID-19 clinical outcomes for select comorbidity (n=12). 29 full-text studies were then used for data extraction, of which 8 studies reported mortality rates for COVID-19 positive cases and 26 studies documented hospitalization rates including intensive care unit (ICU) admission, intubation, and oxygen therapy. 17% of the full-text studies reported both mortality and hospitalization rates (Figure 1).

Figure 1. Flowchart diagram for abstract and full-text screening



**Note: Some studies documented both mortality and hospitalization outcomes.*

Data extraction

The data extracted included study type, number of patients, age, body mass index (BMI), gender, smoking, comorbidities, mortality, hospitalization, ICU admission, oxygen therapy, and intubation. The age extracted from the studies were grouped based onto 2 cut-offs older than 60 years old or 65 years old, based on the reported ages per study. BMI was grouped into 2 categories: less than 30kg/m² or above 30kg/m².

Statistical analysis

We used a random-effects (random intercept) generalised logistic mixed effects model (PROC GLIMMIX in SAS) to estimate odds ratios (ORs) and 95% CIs of hospitalization (versus non-hospitalization) or death (versus alive) associated with some selected comorbidities among COVID population. Estimates were calculated if there were at least 2 studies with the reported comorbidities. The missing mean values were replaced with median values if available. The pooled results and p-value were obtained by random-effect mixed model with random intercept for study. All analysis was performed using SAS, version 9.4 (SAS Institute, Carey, N.C.).

Results

Male gender, age, and BMI increased risk of hospitalization

We collected and analyzed data from 29 studies investigating hospitalization rates which includes ICU admission, intubation, and non-invasive ventilation support. Demographically, a higher proportion of hospitalized patients were male: 56.78% hospitalized versus 46.16% non-hospitalized (Table 1). Hospitalized patients were on average older than non-hospitalized patients and tended to be active smokers.

Using a random-effect model to estimate odd ratios (OR) and 95% confidence interval (CI), we then examined whether gender increases the risk of hospitalization (Table 2). Being male markedly increased hospitalization odds. COVID-19 positive patients who are older, particularly those who are above 65 years, and have high BMI (>30kg/m²) were significantly at risk of being hospitalized. No statistical significance was found when comparing the impact of smoking on hospitalization. (Table 2).

Table 1. Demographic characteristics of hospitalized and non-hospitalized patients

Characteristics	Hospitalized		Non-Hospitalized		p-value
	Number of studies	Pooled mean/cumulative percent (95% CI)	Number of studies	Pooled mean/percent (95% CI)	
Male, pooled cumulative percent %	22	56.78 (49.43, 64.14)	21	46.16 (38.72, 53.59)	<0.001*
Age, mean	17	57.68 (52.20, 63.16)	18	47.93 (42.52, 53.34)	<0.001*
BMI, mean	4	29.39 (26.22, 32.56)	6	27.06 (24.01, 30.12)	0.054
Smoking (active smoking), pooled cumulative percent %	8	9.02 (4.76, 13.28)	7	5.83 (1.54, 10.13)	0.020*

The missing mean values were replaced with median values if available.

The pooled results and p-value were obtained by random-effect mixed model with random intercept for study.

Table 2. Association of characteristics and hospitalization

	Number of studies	Proportion on hospitalized	Proportion on non-hospitalized	I ²	Random-effect model	
					OR (95% CI)	p-value
Male vs. female	21	0.54	0.44	21.77	1.40 (1.32, 1.48)	<0.001*
Age > 60 vs. <60	4	0.76	0.71	98.83	2.18 (1.91, 2.50)	<0.001*
Age > 65 vs. <65	5	0.96	0.90	90.38	8.77 (7.57, 10.17)	<0.001*
BMI > 30 vs. <30	5	0.29	0.29	99.16	1.15 (1.11, 1.19)	<0.001*
Smoking, yes vs. no	5	0.05	0.04	30.15	1.25 (0.90, 1.74)	0.129

We were interested in exploring other age cut-offs, especially younger populations such as 50 yrs and older. However, this data was not available: the majority of studies reported age only as a continuous variable, and those who reported age brackets used 60 or 65 yrs old as a cut-off.

Immune deficiency, coronary artery disease, and dyslipidemia increased hospitalization risk

When comparing the odds ratio of hospitalized to non-hospitalized COVID-19 positive patients, a number of comorbidities were associated with higher likelihood of hospitalization (Table 3):

- Immune deficiency, dementia and coronary artery disease were identified as the top comorbidities to increase hospitalization risk among the medical conditions listed in Table 3.
- Immune deficiency disease significantly increased hospitalization risk up to 15.23 (4.83, 48.01).
- Patients with dementia are at a significantly higher risk of being hospitalized by 7.20 (1.83, 28.27).
- Heart conditions increased the odds of a patient being hospitalized with the main associations being coronary artery disease by 7.06 (5.56, 8.98) and congestive heart failure by 5.46 (4.07, 7.32).
- COVID-19 positive patients with dyslipidemia are more likely to be admitted to the hospital by 6.07 (4.58, 8.05). Studies only collected dyslipidemia as a comorbidity for patients hospitalized, but did not report whether these patients were stable on their treatment or uncontrolled at the time of the event
- Patients with any renal disease were at higher risk of being hospitalized, particularly patients with chronic kidney disease (CKD) by 4.61 (4.10, 5.19)
- Overall, respiratory conditions augmented the hospitalization particularly if the patient suffers from chronic obstructive pulmonary disease (COPD), by 3.33 (2.87, 3.86).

Table 3. Association of some selected comorbidities with at least 2 studies available and hospitalization

Comorbidities	Number of studies	Proportion on hospitalized	Proportion on non-hospitalized	I ²	Random-effect model	
					OR (95% CI)	p-value
Any Renal disease	3	0.23	0.18	82.97	1.42 (1.33, 1.53)	0.002*
CKD	10	0.06	0.01	97.74	4.61 (4.10, 5.19)	<0.001*
Hypertension	20	0.37	0.14	96.43	3.55 (3.40, 3.71)	<0.001*
CVD	9	0.59	0.69	91.1	1.46 (1.40, 1.53)	<0.001*
Coronary Artery Disease	6	0.19	0.03	96.38	7.06 (5.56, 8.98)	<0.001*
Congestive Heart Failure	5	0.16	0.03	83.89	5.46 (4.07, 7.32)	<0.001*
Other Heart Disease	4	0.51	0.33	93.66	2.85 (2.57, 3.15)	<0.001*
Obesity	7	0.24	0.15	15.83	1.46 (1.38, 1.55)	<0.001*
Diabetes	19	0.38	0.26	98.99	1.94 (1.90, 1.99)	<0.001*
Dyslipidemia	3	0.40	0.10	95.83	6.07 (4.58, 8.05)	0.001*
Cerebrovascular Disease	4	0.078	0.05	45.7	1.72 (1.25, 2.38)	0.013*

Other Lung Diseases	6	0.32	0.27	92.22	1.27 (1.22, 1.31)	<0.001*
Asthma	7	0.03	0.05	93.28	0.88 (0.78, 1.00)	0.052
Asthma/COPD	2	0.35	0.21	88.76	2.02 (1.36, 3.01)	0.028*
COPD	8	0.05	0.02	94.53	3.33 (2.87, 3.86)	<0.001*
Cirrhosis	3	0.045	0.01	79.67	4.82 (2.77, 8.38)	0.007*
Chronic Liver Disease	5	0.01	0.00	97.01	3.83 (2.50, 5.86)	<0.001*
Severe Depression	2	0.08	0.08	99.3	0.95 (0.70, 1.29)	0.291
Neurological (except epilepsy) or dementia	2	0.26	0.18	99.92	1.43 (1.19, 1.72)	0.025*
Dementia	2	0.19	0.03	97.22	7.20 (1.83, 28.27)	0.035*
Any Cancer	7	0.08	0.07	67.83	1.12 (1.05, 1.19)	0.004*
Hematologic cancer	2	0.01	0.00	27.95	3.43 (0.07, 167.01)	0.155
Solid Organ Cancer	3	0.11	0.04	0	3.06 (2.20, 4.26)	0.005*
HIV	6	0.01	0.00	0	2.47 (1.15, 5.30)	0.029*
Immune deficiency or suppression	3	0.01	0.00	97.16	15.23 (4.83, 48.01)	0.009*
Organ transplant	5	0.03	0.01	87.89	5.06 (2.84, 9.01)	0.001*
Autoimmune disease	2	0.03	0.02	81.76	0.78 (0.00, 4937.31)	0.775
Other*	9	0.06	0.04	97.03	2.07 (1.87, 2.29)	<0.001*

*Other = Sleep Apnea + Connective Tissue Disease + Peripheral Vascular Disease + Hemiplegia + Urinary System Disease + Anemia + Coagulopathy + Bone Marrow Dysfunction

Pooled ORs were estimated using random-effects models and heterogeneity of studies was assessed using the I^2 statistics, and I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than chance. I^2 is calculated as $(Q-df)/Q \times 100\%$, where Q is the Cochran's homogeneity test statistic and df is the degrees of freedom. $I^2 = 25\%$: low heterogeneity, $I^2 = 50\%$: moderate heterogeneity, $I^2 = 75\%$: substantial heterogeneity.

Table 3 presents a univariate analysis, not adjusted for age, sex, or other variables. We were unable to conduct an adjusted analysis due to the low number of studies available, except for CKD, HTN, and diabetes. Table 4 depicts these three comorbidities with an adjusted OR for age and sex.

Table 4. Association of some selected comorbidities with at least 10 studies available and hospitalization

Comorbidities	Number of studies	Proportion on hospitalized	Proportion on non-Hospitalized	I ²	Random-effect model	
					Adj. OR (95% CI)	p-value
CKD	7	0.06	0.02	97.74	3.33 (1.71, 6.52)	0.008*
Hypertension	14	0.37	0.14	96.43	1.49 (1.16, 1.92)	0.005*
Diabetes	13	0.39	0.26	98.99	2.51 (1.79, 3.54)	<0.001*

Male gender and age increased risk of mortality

We then extracted and analyzed data from the 8 selected studies documenting mortality rates and comorbidities. Demographically, the proportion of male gender reported by studies on mortality was higher than in studies reporting an alive outcome, though not a significantly significant difference. The average age of deceased patients was 72 years compared to 57 years for recovered patients (Table 5). Using the random-effect model, we determined that, similar to the hospitalization outcome, male patients are significantly at higher risk of death than females. Age higher than 60 years further increases the odds of death (Table 6).

Table 5. Demographic characteristics of deceased and alive patients

Characteristics	Deceased		Alive		P-value
	Number of studies	Pooled mean/cumulative percent (95% CI)	Number of studies	Pooled mean/percent (95% CI)	
Male, pooled cumulative percent %	5	58.63 (47.89, 69.38)	5	48.4 (37.65, 59.15)	0.098
Age, mean	4	72.25 (62.30, 82.20)	3	57.4 (46.56, 68.24)	0.259

The missing mean values were replaced with median values if available.

The pooled results and p-value were obtained by random-effect mixed model with random intercept for study.

Table 6. Association of characteristics of deceased and alive patients

	Number of studies	Proportion on deceased	Proportion on alive	I ²	Random-effect model	
					OR (95% CI)	p-value
Male vs. female	5	0.42	0.42	96.9	1.37 (1.33, 1.42)	<0.001*
Age> 60 vs. <60	3	0.99	0.52	99.68	73.25 (55.38, 96.88)	<0.001*

Increased mortality risk

We then investigated the impact of documented comorbidities on mortality risk (Table 7). The odds of death for patients with COPD was 25.31 (23.08, 27.76) and for patients with asthma was 12.55 (8.71, 18.07), indicating that these two respiratory conditions significantly augment the risk of dying from COVID-19. CKD increased mortality risk by 8.45 (7.71, 9.27). Hypertension markedly increased the odds of death by 6.67 (6.25, 7.11). Similarly, patients with cardiovascular disease were ~2-fold more likely to succumb to COVID-19. Moreover, diabetes and cancer increased mortality risk by 1.53 (1.48, 1.58) and 1.80 (1.64, 1.98), respectively. Obesity further elevated the risk of mortality by 1.61 (1.00, 2.60), though only 2 studies reported on obesity. Among the above-mentioned comorbidities, COPD was found to increase mortality risk the most by an odds ratio of 25.31 (23.08, 27.76).

Table 7. Association of some selected comorbidities with at least 2 studies available and death

Comorbidities	Number of studies	Proportion on deceased	Proportion on alive	I ²	Random-effect model	
					OR (95% CI)	p-value
Asthma	2	0.47	0.14	99.93	12.55 (8.71, 18.07)	0.007*
COPD	4	0.40	0.05	99.75	25.31 (23.08, 27.76)	<0.001*
CKD	5	0.16	0.03	98.18	8.45 (7.71, 9.27)	<0.001*
Hypertension	5	0.64	0.23	99.62	6.67 (6.25, 7.11)	<0.001*
CVD	4	0.70	0.33	99.94	1.90 (1.78, 2.03)	<0.001*
Other Heart Disease	2	0.40	0.13	56.49	3.52 (0.54, 23.18)	0.075
Obesity	2	0.29	0.20	15.23	1.61 (1.00, 2.60)	0.049*
Diabetes	6	0.39	0.22	99.84	1.53 (1.48, 1.58)	<0.001*
Cancer	3	0.10	0.05	99.88	1.80 (1.64, 1.98)	0.001*

Pooled ORs were estimated using random-effects models and heterogeneity of studies was assessed using the I² statistics, and I² describes the percentage of total variation across studies that is due to heterogeneity rather than chance. I² is calculated as $(Q-df)/Q \times 100\%$, where Q is the Cochran's homogeneity test statistic and df is the degrees of freedom. I² = 25%: low heterogeneity, I² = 50%: moderate heterogeneity, I² = 75%: substantial heterogeneity.

Summary and Discussion

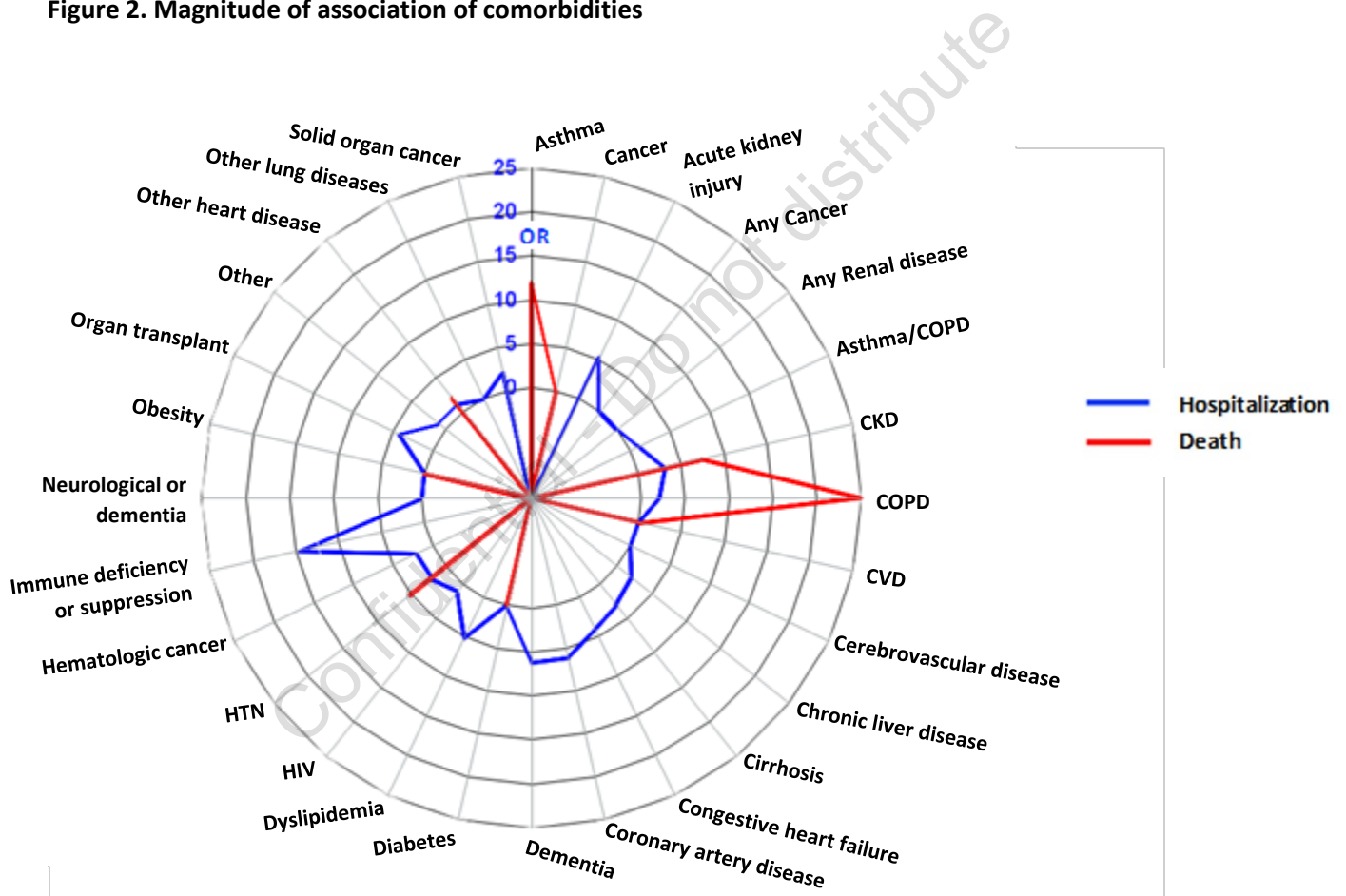
Between June and December 2022, we conducted a systematic literature search to identify the population who is at high-risk of death or hospitalization from COVID-19 based on age, gender and underlying comorbid conditions. Male patients and those older than 60 years old who are infected with COVID-19 were more likely to be hospitalized and die. High BMI increased hospitalization rates, but none of the selected studies reported on its impact on mortality rates. Hospitalization rates were found to be

significantly higher for COVID-19 positive patients with a wide range of comorbidities including immune deficiency, dementia, coronary artery disease and many others.

Similarly, multiple comorbidities were found to increase mortality risk, including respiratory diseases, cardiac conditions, CKD, diabetes, and cancer. Interestingly, COPD had the highest mortality risk. These results suggest that while COVID-19 positive patients with COPD had an elevated risk of being hospitalized, they are most likely to succumb to COVID-19 compared to patients with cardiac disease or any other conditions.

Figure 2 compares the magnitude of association of different comorbidities for both hospitalization and death.

Figure 2. Magnitude of association of comorbidities



An important shortcoming was evident during the systematic literature search. We noted that there was no consistency among all 29 studies in reporting demographics and comorbidities data. For one, some studies had detailed breakdown about the different types of a disease area, while others reported overall proportions. This was also the case for age and BMI. Second, because of the variation in reporting data, the number of studies used for data analysis was vastly different which may impact statistical significance.

Of the 29 studies that were analyzed, 10 were conducted in the United States, 7 were conducted in China and 12 were conducted in other countries including, Canada Denmark, England, Gabon, Indonesia, Japan, Korea, Malaysia, Mexico, Poland, and Scotland.

17 studies were published in 2021 and 12 in 2020. It would be tempting to associate a relevant COVID-19 variant with each study provided we know the year of publication; however, this may not be the case. Further investigation would need to be carried out regarding specific timings of data collection to provide this insight.

It is important to discuss our challenges in trying to analyse the effect of vaccines. Only 17 studies were published in 2021. In the selected articles for full read and data collection, it was not described whether vaccines were available (and if so, which type of vaccines) at the time of the outcome measurement reported. This issue highlights the need for a systematic way to report results in future COVID-19 studies, so that clinicians and researchers will have a complete set of information available. For the same reason (absence of data), additional efforts need to be rolled out in the area of vaccination and boosting from a vigilance standpoint, particularly for the populations that we have identified as high-risk.

Recommendations

Our results suggest that the hospitalization and mortality rates vary by comorbidity. While some comorbidities had a high hospitalization risk, they weren't necessarily increasing mortality rates.

This work also highlights the current gaps in the literature and serves as hypothesis generator to identify some groups at high-risk of hospitalization or death associated with COVID-19. Patients, family-members, HCP, and policymakers should be aware of these associations to develop strategies to ameliorate the effects of COVID-19 in the health care system

High-risk patients are advised to take and follow all necessary measures to limit their exposure to COVID-19. As recommended by medical and governmental authorities, staying up to date on vaccines, wearing masks in public places and regularly washing hands drastically reduce the risk of exposure to COVID-19. Of importance, medical and governmental officials need to put in place effective plans to protect vulnerable patients from death and increase their chance of recovery.

Next Steps: Recommendations by the Scientific Committee

Below is a list of requests by the scientific committee for future analysis of the initial data, as well as suggestions for publications:

- Two publications are necessary:
 - A first paper to discuss the results of the literature review described in Part 2 of this report.
 - A second paper to propose a standardized method for data collection, identifying and reporting high-risk populations in future studies relative to COVID-19. Looking at potential data systems that could be put in place to be able to follow-up data on a larger scale and minimum data requirements.
- Suggestions to be included on the 2nd paper (methodology) which will recommend how data should be reported in future COVID-19 publications:
 - Include data related to current variants during the time of the study, and vaccination and boosting rates in the region. Additionally, patient data should include vaccination and boosting information.
 - Reporting age as a mean is fine. However, studies should also present age brackets, and start at younger ages. Reporting on age categories would be more aligned with the main objective. In other words, metrics of central tendency (dispersion) do not contribute to identify subgroups of patients at higher risk of death or hospitalization
 - Report BMI, not only as a mean but also in categories.
 - Report co-morbidities, so that it facilitates confounding analysis.
 - Report concurrent medications for study participants (for example, if a participant is on biologics, or immune suppressant medications such as B-cell inhibitors).
 - Report whether patients are stable on their current medications or unstable at the time of COVID-19 events (e.g. hospitalization).
 - For diabetic patients, report HbA1c control.
 - Documenting long-term outcomes of COVID.

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Appendix

Table A1. Literature Search Strategy

#	Query	Results from 13 Jun 2022
1	exp Coronavirus/	141,271
2	exp Coronavirus Infections/	177,528
3	(coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or "Kawasaki like paediatric inflammatory multisystem syndrome" or "Kawasaki like pediatric inflammatory multisystem syndrome" or "PIMS-TS" or "Kawa-COVID-19" or "MIS-C" or "multisystem inflammatory syndrome in children" or pediatric multisystem inflammatory disease).mp.	281,486
4	(or/1-3) and ((20191* or 202*).dp. or 20190101:20301231.(ep).) [this set is the sensitive/broad part of the search]	268,543
5	4 not (SARS or SARS-CoV or MERS or MERS-CoV or Middle East respiratory syndrome or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or influenza virus or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or avian influenza or H1N1 or H5N1 or H5N6 or IBV or murine corona*).mp. [line 5 removes SARS, MERS, and veterinary noise from the sensitive/broad search results]	96,501
6	((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp. [Early articles about the outbreak]	6,992

7	(2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or SARS-2-nCoV or SARS-2-Cov or SARS-COV-19 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS 2 coronavirus* or Severe Acute Respiratory Syndrome-CoV-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19 or SARS-CoV-2) and pandemic*2) or (coronavirus* and pneumonia)).mp. [specific to Covid-19, Covid pneumonia, Covid pandemic]	264,757
8	(2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or SARS-2-nCoV or SARS-2-Cov or SARS-COV-19 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS 2 coronavirus* or Severe Acute Respiratory Syndrome-CoV-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19 or SARS-CoV-2) and pandemic*2) or (coronavirus* and pneumonia)).mp. [specific to Covid-19, Covid pneumonia, Covid pandemic]	264,757
9	(COVID-19 or SARS-CoV-2).rx,px,ox,rn. or (COVID-19 or COVID-19 serotherapy or ORF7b protein, SARS-CoV-2 or ORF6 protein, SARS-CoV-2 or ORF8 protein, SARS-CoV-2 or pediatric multisystem inflammatory disease, COVID-19 related or envelope protein, SARS-CoV-2 or ORF7a protein, SARS-CoV-2 or spike protein, SARS-CoV-2 or ORF3a protein, SARS-CoV-2 or COVID-19 drug treatment or severe acute respiratory syndrome coronavirus 2 or membrane protein, SARS-CoV-2 or ORF1ab polyprotein, SARS-CoV-2 or nucleocapsid protein, Coronavirus or COVID-19 vaccine or COVID-19 diagnostic testing).os,ps,rn,rs. [Relevant Suppl. Concepts listed in MeSH 2021 Browser]	24,008
10	or/5-9 [Lines 5 to 9 are specific/relevant to the Covid-19 outbreak]	268,409
11	10 and 20191201:20301231.(dt). [only include records created for PubMed/MEDLINE from 1 December 2019 onwards]	266,254

12	*Vulnerable Populations/ or *Severity of Illness Index/ or exp *Risk Factors/ or ((exp *Risk/ or exp *Risk Factors/) and (*Hospital Mortality/ or exp *Death/ or exp *Intensive Care Units/))	31,174
13	((patient* or population* or group* or comorbid*) adj3 ((vulnerable or high-risk or "high risk") adj2 (disease sever* or death* or ICU or intensive care or mortality))).ti,kf. or ((patient* or population* or group* or comorbid*) adj3 ((vulnerable or high-risk or "high risk") adj3 (disease sever* or death* or ICU or intensive care or mortality))).ab. /freq=2	316
14	12 or 13	31,477
15	11 and 14	848
16	exp Epidemiologic Studies/	2,963,616
17	((case or cases) and (control or controls)) or cohort or "follow up study" or "follow-up study" or "observational study" or longitudinal or retrospective or "cross sectional" or compared or multivariate or epidemiologic study).tw,kf.	5,899,692
18	16 or 17	7,039,324
19	15 and 18	437
20	19 and 20220610:20230323.(dt). (Update to March 13, 2023)	3

Table A2. Included Studies

Study Date	Study Name	Location	Type	Total Number
2021	Association of pre-existing comorbidities with mortality and disease severity among 167,500 individuals with COVID-19 in Canada	Canada	Population-based case-control study	167,500
2021	Atrial Fibrillation as a Predictor of Mortality in High Risk COVID-19 Patients	United States	Multicenter study	171
2021	Comorbidities and clinical features related to severe outcomes among COVID-19 cases in Selangor, Malaysia	Malaysia	Retrospective	1,287
2020	Rapid Epidemiological Analysis of Comorbidities and Treatments as risk factors for COVID-19 in Scotland (REACT-SCOT)	Scotland	Population-based case-control study	41,220
2021	Predictors of severity and mortality among patients hospitalized with COVID-19 in Rhode Island	Rhode Island	Retrospective Cohort Study	259

2020	Association of Obesity with Disease Severity Among Patients with Coronavirus Disease 2019	United Sates	Retrospective Cohort Study	103
2021	Impact of overlapping risks of type 2 diabetes and obesity on coronavirus disease severity in the United States	United Sates	Cohort Study	28,093
2021	Associations between body-mass index and COVID-19 severity in 6.9 million people in England: a prospective, community-based, cohort study	England	Prospective Cohort Study	6,910,695
2020	Effect of Underlying Comorbidities on the Infection and Severity of COVID-19 in Korea: a Nationwide Case-Control Study	Korea	Retrospective case control Study	7,341
2020	Risk Factors for Poor Outcomes of Diabetes Patients With COVID-19: A Single-Center, Retrospective Study in Early Outbreak in China	China	Single Center Retrospective Study	52
2020	Obesity as a Potential Predictor of Disease Severity in Young COVID-19 Patients: A Retrospective Study	China	Retrospective Study	65
2021	A clinical profile and factors associated with severity of the disease among Polish patients hospitalized due to COVID-19 — an observational study	Poland	An observational study	100
2021	Chronic comorbidities and clinical outcomes in patients with and without COVID-19: a large population-based study using national administrative healthcare open data of Mexico	Mexico	Retrospective Study	38,324
2020	Clinical Course and Factors Associated With Hospitalization and Critical Illness Among COVID-19 Patients in Chicago, Illinois	United Sates	Retrospective, registry-based cohort study	8,673
2020	Predictors for Severe COVID-19 Infection	United Sates	Retrospective observational study	197
2021	Factors significantly associated with COVID-19 severity in symptomatic patients: A retrospective single-center study	Japan	Retrospective Study	61
2021	Patient Trajectories Among Persons Hospitalized for COVID-19_A Cohort Study	United Sates	Retrospective Cohort Study	832
2021	Adult COVID-19 Patients Cared for in a Pediatric ICU Embedded in a Regional Biothreat Center: Disease Severity and Outcomes	United Sates		37

2020	Risk factors for death in 1859 subjects with COVID-19	China		1,859
2021	Association between prognostic factors and the outcomes of patients infected with SARS-CoV-2 harboring multiple spike protein mutations	Indonesia	Retrospective Study	51
2020	A retrospective study of risk factors for severe acute respiratory syndrome coronavirus 2 infections in hospitalized adult patients	China	Retrospective Study	108
2020	From the American Epicenter: Coronavirus Disease 2019 in Patients with Inflammatory Bowel Disease in the New York City Metropolitan Area	United States		83
2020	Do underlying cardiovascular diseases have any impact on hospitalised patients with COVID-19?	China	Retrospective Study	541
2021	Demographic and Clinical Characteristics Associated With Severity, Clinical Outcomes, and Mortality of COVID-19 Infection in Gabon	Gabon	Retrospective Cross-sectional Study	313
2020	Early prediction and identification for severe patients during the pandemic of COVID-19: A severe COVID-19 risk model constructed by multivariate logistic regression analysis	China	Retrospective non-interventional study,	40
2021	Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State	United States	Multicenter retrospective cohort study	240
2021	Risk Factors Associated With SARS-CoV-2 Infections, Hospitalization, and Mortality Among US Nursing Home Residents	United States	Cohort Study	137,119
2021	Incidence and severeness of COVID-19 hospitalisation in patients with inflammatory rheumatic disease: a nationwide cohort study from Denmark	Denmark		47
2021	Risk factors for developing severe COVID-19 in China: an analysis of disease surveillance data	China		12,647

See full reference list on page 28-29.