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Risk factors for severe outcomes of COVID-19: a rapid review

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Title: Risk factors for severe outcomes of COVID-19: a rapid review

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ABSTRACT: 300 words

Background: Identification of high-risk groups is needed to inform COVID-19 vaccine prioritization strategies in Canada. A rapid review was conducted to determine the magnitude of association between potential risk factors and severe outcomes of COVID-19.

Methods: Ovid MEDLINE(R) ALL, Epistemonikos COVID-19 in L·OVE Platform, McMaster COVID-19 Evidence Alerts, and select websites were searched to 15 June 2020. Studies needed to be conducted in high-income countries and have used multivariate analyses. After piloting, screening, data extraction, and quality appraisal were performed by a single reviewer. Authors synthesized the findings narratively and appraised the certainty of the evidence for each risk factor-outcome association.

Results: Of 3,740 records identified, 34 studies were included that reported on median 596 (range 44-418,794) participants, aged 42 to 84 years. 17/34 (50%) were conducted in the United States. 19/34 (56%) were good quality. There was low or moderate certainty evidence for a large (≥2-fold) association with risk of hospitalization in people with COVID-19, for the following risk factors: obesity class III, heart failure, diabetes, chronic kidney disease, dementia, age >45 years, male gender, Black race/ethnicity (vs. non-Hispanic white), homelessness, and low income. Age >60 and >70 years may be associated with large increases in the rate of mechanical ventilation and severe disease, respectively. For mortality, a large association with increased risk may exist for liver disease, Bangladeshi ethnicity (vs. British white), age >45 years, age >80 years (vs. 65-69 years), and male gender among 20-64 year-olds (but not older). Associations with hospitalization and mortality may be very large (≥5-fold increased risk) for those aged >60 years.

Conclusion: Increasing age (especially >60 years) may be the most important risk factor for severe COVID-19. High-quality primary research (accounting for multiple confounders) is needed to better understand the level of risk potentially associated with other risk factors.

PROSPERO registration: CRD42020198001

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Strengths and limitations of this study

- This rapid review is a comprehensive synthesis of high-quality primary research on risk factors associated with severe COVID-19 outcomes that is most applicable to high-income countries.
- The findings indicate that advancing age (≥45 years and especially ≥60 years) may be the most important risk factor for hospitalization and mortality from COVID-19.
- Other important risk factors for severe disease include several pre-existing chronic conditions (class III obesity, heart failure, diabetes, chronic kidney disease, liver disease, dementia), male gender, Black race/ethnicity (vs. non-Hispanic white), Bangladeshi ethnicity (vs. British white), low income (vs. high), and homelessness.
- The conclusions of this rapid review should be interpreted cautiously in light of multiple unmeasured confounders.
- There is a need for high quality primary research to better understand the level of risk that may be associated with several understudied risk factors.

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INTRODUCTION

Novel coronavirus disease 2019 (COVID-19) is an infectious respiratory disease caused by the newly identified Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2),[1] which reached worldwide pandemic status in early March 2020.[2] As of August 24, there were over 23 million confirmed cases worldwide and 800,000 deaths attributed to the virus.[3] Most people who develop COVID-19 will experience mild-to-moderate illness primarily affecting the respiratory system and recover at home.[4] In more severe cases, patients may require specialized care (e.g., admission to hospital and/or intensive care unit [ICU], assisted ventilation)[5] as the disease can progress to respiratory failure and/or affect multiple organ systems.[4] Though new primary research is emerging rapidly, the evidence is fragmented and consensus on who might be at increased risk of severe outcomes from COVID-19 has not been established.

Given the rapid spread of COVID-19 since its first emergence in late 2019, and potential for severe illness (including death), the development of a preventive vaccine has become a global priority.[6] COVID-19 vaccine development has been progressing at an unprecedented pace. Once a successful COVID-19 vaccine candidate becomes available, the initial vaccine supply is not expected to be sufficient to cover the entire population right away. Therefore, there is an urgent need to plan for the efficient, effective, and equitable allocation of eventual COVID-19 vaccines when limited initial vaccine supply will necessitate recommendations for the vaccination of certain groups earlier than others. Due to the novel nature of COVID-19, these groups for early vaccination have not yet been established.[7]

The National Advisory Committee on Immunization (NACI) is an expert advisory body that provides advice on the use of vaccines in Canada.[8] At the time of writing, NACI is developing interim guidance on priority pandemic immunization strategies for COVID-19 vaccination when initial vaccine supply is limited.[7] To inform this guidance, NACI is using its recently published Ethics, Equity, Feasibility and Acceptability (EEFA) Framework[9] to ensure these factors are systematically and comprehensively considered. One of the evidence informed tools that make up this framework is the "Equity Matrix" which has adapted the PROGRESS-Plus model of health determinants and outcomes[10] to ensure important vaccine-specific equity factors are explicitly included. The resulting "P^{2}ROGRESS And Other Factors" framework includes a range of biological and social factors that likely contribute to inequities in health outcomes across population groups, but it is not yet clear how each factor might apply to COVID-19 outcomes. A discussion on the use of this Equity Matrix, with evidence from this rapid review, as a critical tool to guide the ethically just allocation of scarce resources is published elsewhere.[11]

With the aim of providing timely, evidence-informed guidance on pandemic vaccine prioritization, NACI required a rigorous and expedited synthesis of the available evidence on population groups who are at increased risk of severe illness and mortality as a result of COVID-19. Responding to this need, we conducted a rapid review to determine the magnitude of association between "P^{2}ROGRESS And Other Factors" and risk of severe outcomes of COVID-19.

METHODS

Review Approach

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The urgent need for empiric evidence to inform the prioritization of pandemic immunization strategies in Canada necessitated a rapid but rigorous approach to synthesizing the currently available data. Therefore, we performed a rapid review informed by traditional systematic review methodology,[12] with several modifications to allow for the evidence to be synthesized on an expedited timeline (e.g., single reviewer for study selection, data extraction, and assessment of risk of bias) and focusing on studies having high applicability to Canada (e.g., countries with universal health care system)

NACI's High Consequence Infectious Disease Vaccine Working Group was consulted to develop and refine the scope of the review (i.e., priority population(s), risk condition(s)/factor(s), and outcomes of interest), but was not involved in the conduct of the review. The working group was not involved in selection of studies nor the synthesis of findings.

The review was conducted following an *a-priori* protocol (PROSPERO #CRD42020198001). Because there is not yet formal guidance on the reporting of rapid reviews, reporting adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[13]

Literature Search

A health sciences librarian searched Ovid MEDLINE(R) ALL on 15 June 2020 using concepts related to COVID-19, P^{2}ROGRESS And Other Factors, and severe outcomes (Supplemental File). The search was limited to studies published in English or French in 2020. Additionally, the search was limited to populations in countries that are members of the Organisation for Economic Cooperation and Development (OECD),[14] in an effort to include studies of highest relevance to the Canadian context. Editorials and letters were excluded. We supplemented the Medline search by hand-searching Epistemonikos COVID-19 in L·OVE Platform (https://app.iloveevidence.com/topics) and McMaster COVID-19 Evidence Alerts (https://plus.mcmaster.ca/COVID-19/) for relevant prognosis or aetiology studies up to 12 June 2020. A hand-search of relevant websites recommended by the NACI working group was also undertaken, as well as continual surveillance for publication of eligible pre-prints located by the search. Searches were exported to an Endnote Library (X9, Clarivate Analytics, Philadelphia, PA) and duplicates removed.

Eligibility Criteria

We included studies published in English or French since 1 January 2020 that reported on the magnitude of association between potential P^{2}ROGRESS And Other Factors and severe outcomes of COVID-19 (Supplement File). Eligible populations, in order of priority, were people (a) from a general/community sample, (b) with COVID-19 confirmed (by laboratory testing or epidemiologic linkage), (c) hospitalized with COVID-19, and d) with a risk factor of interest. To ensure relevance to the Canadian context, studies had to be conducted in OECD countries;[14] we included studies from countries that do not provide universal (or near universal) coverage for core medical services (i.e., Chile, Greece, Mexico, Poland, the Slovak Republic, and the United States)[15] but considered these to be less applicable to the Canadian context when interpreting the findings.

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The exposures of interest were any P²ROGRESS And Other Factors believed to be associated with differential health outcomes across population groups (i.e., pre-existing conditions, place or state of residence, race/ethnicity/culture/language, immigration, refugee status, occupation, gender identity or sex, religion or belief system, education or literacy level, socioeconomic status, social capital, age, and other factors).[16, 17] Eligible comparators were population groups that did not have the P²ROGRESS And Other Factor, or experienced a P²ROGRESS And Other Factor to a different degree (e.g., older vs. younger). Factors could be present among a population with or without COVID-19. The infection must have been confirmed by laboratory testing or linked epidemiologically (e.g., household contact). Studies including populations with other pandemic-related infections (e.g., Severe Acute Respiratory Syndrome, Middle East Respiratory Syndrome) were excluded if data specific to COVID-19 cases could not be isolated. We also excluded studies of interventions and where the entire study population had severe disease (e.g., ICU settings).

Any length of follow-up for outcomes of interest was acceptable. Eligible studies reported on at least one primary outcome (i.e., rate of hospitalization, hospital length of stay, severe disease [as defined by study authors; for example, composite outcome of ICU transfer or death], ICU admission and length of stay, need for mechanical ventilation [MV], and mortality [case fatality or all-cause]). In order to prioritize the most rigorous and applicable evidence, we included only prospective and retrospective cohort studies that employed a multivariate analysis and provided results of the independent contribution of P²ROGRESS And Other Factors to severe outcomes, while accounting for potential confounders (minimally age and sex). Pre-prints were included only if they were accepted by a peer-reviewed journal; pre-prints that were later published (between the date of the search and manuscript submission) were included. Government reports from hand-searched websites were eligible.

Study Selection

All records retrieved by the searches were exported to a Microsoft Office Excel (Microsoft Corporation, Redmond, WA) spreadsheet for screening. After piloting the eligibility criteria on a sample of 70 records, one reviewer independently screened records for inclusion by title/abstract, and those deemed to be potentially relevant were assessed by full text. Uncertainties about the inclusion of any full text study were resolved through consultation with a second reviewer.

Data Extraction

Following a pilot round, one reviewer independently extracted data from each included study into an Excel workbook. We extracted data on (a) population size and demographics, (b) setting, (c) dates of data collection, (d) COVID-19 ascertainment method, (e) co-infections, (f) outcomes reported with definitions for composite outcomes (e.g., severe disease), (f) number of participants analysed, (h) relevant outcome data related to P²ROGRESS factors of interest. For both continuous and dichotomous outcomes, we extracted adjusted relative effect sizes (i.e., odds ratio [OR], risk ratio [RR], hazard ratio [HR]) and measures of variability (95% confidence interval [CI]). A second reviewer was consulted in the event of uncertainty about any of the extracted data. Given the expedited approach, we extracted only data that were reported within the included studies and made no attempt to contact authors for missing or unclear data.

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Quality Assessments

To expedite quality assessments, we did not use a formal tool; instead we focused on key variables that were considered to be most relevant to the topic, and that would allow for meaningful stratification of studies by quality. The key variables that we used to assess the quality of the included studies were (a) the extent of adjustment for relevant covariates (i.e., basic adjustment for age and sex, versus more extensive adjustment for numerous potential confounders including comorbidities), (b) follow-up duration and extent of censorship for some outcomes (e.g., $\geq$2 weeks for mortality), and (c) inappropriate or large exclusions from the study and/or analysis (e.g., missing data on risk factor status or analytical variables). Following assessment of these key variables by a single reviewer, studies without concerns for all three criteria were rated good while others were rated fair. A second reviewer was consulted in the case of uncertainty about the assessment of any individual study.

Synthesis

Given substantial clinical (e.g., risk factors and/or comparators examined, outcome definitions) and methodological (varying covariates included in the adjusted analyses, different measures of association) heterogeneity, it was not appropriate to pool the studies statistically. Instead, we present a narrative summary of the results across studies for each risk factor. When making conclusions about the association between a P^{2}ROGRESS And Other Factor and an outcome, we focused primarily on the magnitude of effect rather than statistical significance, which is heavily dependent on sample size. We categorized associations to be small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70), moderate (1.71 to 1.99), large (≥2.00), or very large (≥5.00).[18] When determining the magnitude, we compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies.

Certainty of Evidence

The expedited approach to evidence synthesis did not allow for a formal appraisal of the certainty of evidence across studies for each P^{2}ROGRESS And Other Factor-Outcome association. Instead, a single reviewer assessed the certainty of the evidence for each association considering relevant components of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach:[19, 20] (a) directness in terms of country (presence of universal healthcare) and source population (community sample vs. hospitalized patients), (b) sample size (n<500 considered small) and magnitude of association, (c) study quality, and (d) consistency of associations (in direction and magnitude) across studies. Bodies of evidence started at high certainty[21] and were rated down for weaknesses in any of the aforementioned characteristics. The level of certainty in associations are referred to using the terms 'uncertain' (no or very low certainty), 'may' (low or some certainty), and 'probably' (moderate certainty).[22] At least two other reviewers confirmed the certainty of evidence appraisals, with disagreements resolved by discussion.

Patient and Public Involvement

This research was conducted without patient and public involvement.

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RESULTS

Characteristics of Studies

Of 3,740 unique records identified by the searches, 949 were screened at full text, and 34 studies that reported on 32 unique populations were included in the review (Figure 1; Supplemental File shows studies excluded by full text, with reasons).[23-56] Three studies conducted in the United Kingdom (UK)[39, 44, 47] used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study[56] is likely to also be overlapping with these populations, but the degree of overlap is not known.

Table 1 shows the characteristics of the included studies (full details about individual studies in Supplemental File). Briefly, all of the included studies were prospective or retrospective cohorts. The studies were published between 23 April and 6 July 2020, and half (17/34, 50%) reported on populations in the United States.[23, 24, 31, 32, 36-38, 40-43, 45, 46, 49, 51, 53, 54] The remaining countries represented (Italy,[25, 27-30, 35, 50, 55] Spain,[26] UK[33, 39, 44, 47, 48, 52, 56]) all have universal or universal-like healthcare (one study used data from 17 countries). All studies reported on adults, and the overall median was 596 participants (range 44 to 418,794). The mean or median age of the populations studied ranged from 42 to 84 years (32/34 [94%] 54 to 71 years). Most studies (16/34, 47%) examined the association between risk factors and outcomes in a hospitalized population. Studies most commonly reported on the independent association of pre-existing conditions (n=27 studies), gender identity or sex (n=18), and race or ethnicity (n=12) with severe outcomes (most commonly hospitalization, n=9). P^2ROGRESS And Other Factors not examined in the included studies were immigration or refugee status, religion or belief system, social capital, and substance use disorders. There were also no data specific to pregnant women, indigenous populations, people with disabilities, nor different ages in children.

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Table 1. Included studies overview (n=34)

Study design & country (no. of studies)	P²ROGRESS risk factors (no. of studies*)	COVID-19 (no. of studies)	Primary outcomes (no. of studies*)	Risk of bias (no. of studies)
Study design: • Retrospective cohort (25) • Prospective cohort (9) Country: • USA (17) • Italy (8) • UK (7 studies in 5 populations) • Spain (1) • Multi-country§ (1)	❖ Pre-existing disease/disability: ○ Any comorbidity or number of comorbidities (4) ○ Underweight, overweight or obesity (12 studies of 10 populations) ○ Cardiovascular (chronic cardiac disease/heart disease, congestive heart failure, coronary artery disease, hyperlipidemia, hypertension) (10 studies of 9 populations) ○ Endocrinologic (diabetes, hyperglycemia) (8) ○ Respiratory (asthma, COPD, chronic bronchitis, lung disease, previous pneumonia) (8 studies of 7 populations) ○ Renal (chronic kidney disease) (5) ○ Malignancy (cancer) (5) ○ Neurological (Alzheimer's, dementia, chronic neurological disorder) (4) ○ Hepatic (liver disease, with or without cirrhosis) (3) ○ Immunocompromised (rheumatic disease, HIV/AIDS) (2) ○ Mental health (2) ○ Gastrointestinal (irritable bowel disease) (1) ❖ Place of residence (4) ❖ Race or ethnicity (11 studies of 10 populations) ❖ Occupation (1) ❖ Gender identity or sex (18 studies of 17 populations) ❖ Education (1) ❖ Socioeconomic status (5 studies of 4 populations) ❖ Age (17 studies of 16 populations) ❖ Other factors: ○ Smoking status (7 studies of 5 populations) ○ Alcohol consumption (3 studies of 1 population) ○ Physical activity (2 studies of 1 population)	Diagnosis: • RT-PCR/PCR (25) • Lab-confirmed (5) • ICD codes (1) • Lab-confirmed or ICD codes (2) • Lab-confirmed or symptoms (1)	• Rate of hospitalization (9) • Hospitalization/self-isolation (composite) (1) • Hospital length of stay (0) • Severe disease (4) • ICU admission (3) • ICU length of stay (0) • ICU or MV (1) • Non-invasive ventilation or MV (1) • MV (4) • ICU or mortality (composite) (3) • MV or mortality (composite) (1) • Mortality (19)	Good (19) Fair (15)

* a study may contribute to more than one risk group, or outcome

§ study of healthcare workers includes data from Australia, Canada, Chile, China, Germany, India, Ireland, Italy, Netherlands, New Zealand, Pakistan, Poland, Singapore, South Africa, Sweden, UK, and USA

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BMI: body mass index; COVID-19: novel coronavirus; HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome; ICD: International Classification of Diseases; ICU: intensive care unit; MV: mechanical ventilation; No: number; NR: not reported; RT-PCR; reverse transcription polymerase chain reaction; UK: United Kingdom; USA: United States of America

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Study Quality

The majority of studies (19/34, 56%) were rated as good quality[23, 24, 29, 31, 33-36, 40, 42, 45, 46, 48-53, 55] because they adjusted for age, sex, and pre-existing disease in their analysis, had adequate follow-up of outcomes, and few or no missing data. The remaining studies had flaws in one or more of the three domains that we considered to be most important for this review.

Association Between Risk Factors and Outcomes

Table 2 shows a summary of findings for associations between each reported risk factor and outcomes of interest; all contributing data are shown in the Supplemental File.

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Table 2. Summary of evidence for associations between risk factors and severe outcomes of COVID-19

Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Pre-existing conditions						
Body mass index(kg/m²)[d]						
Underweight (<18.5) vs. normal (18.5-24.9)	Hospitalized		- (low)	- (low)		- (low)
Overweight (25.0-29.9) vs. normal	Community sample or positive for COVID-19	- (low)	uncertain	uncertain	- (low)	- (low)
Obesity class I and II (≥30.0) vs. normal	Community sample or positive for COVID-19	+ (low)	+ (low)	+ (low)	- (low)	- (moderate)
Obesity class III (≥40.0) vs. normal	Positive for COVID-19	++ (low)		uncertain	+ (low)	- to + (low)
Respiratory conditions						
Chronic, varied (e.g., asthma, COPD)	Community sample or positive for COVID-19	- (moderate)	uncertain	uncertain	- (moderate)	- (moderate)
Prior pneumonia	Community sample	- (low)				
Cardiovascular disease						
Heart failure	Community sample	- (low)				
	Positive for COVID-19	++ (low)			+ (low)	- (low)
Coronary artery disease, hypertension, hyperlipidemia, composite outcomes	Community sample or positive for COVID-19	- (moderate)	uncertain	uncertain	- (low)	- (low)
Diabetes	Community sample	- (low)				
	Positive for COVID-19	++ (low)	uncertain	- (low)	- (low)	- (moderate)
Liver disease	Positive for COVID-19	- (low)				++ (low)
	Hospitalized					- (low)
Chronic kidney disease	Community sample or positive for COVID-19	++ (moderate)			- (moderate)	- (moderate)
Inflammatory bowel disease	Positive for COVID-19	- (low)			- (low)	
Dementia/chronic neurologic disorders						

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Alzheimer's disease or dementia	Community sample	++ (low)				- (low)
Chronic neurologic disorders	Hospitalized					- (low)
Cancer						
Any cancer	Positive for COVID-19	- (moderate)			- (moderate)	- (moderate)
Hematological malignancy	Positive for COVID-19					+ (low)
Immunocompromised						
Rheumatic disease	Positive for COVID-19	uncertain	uncertain			uncertain
Human immunodeficiency virus	Hospitalized					uncertain
Mental health						
Depression	Positive for COVID-19	- (low)				
Ever visited a psychiatrist	Community sample	- (low)				
Other factors						
Age[d]						
45-54 vs. ≤45 years old	Positive for COVID-19	++ (moderate)			- (low)	++ (low)
50-64 vs. ≤45 years old	Positive for COVID-19	++ (moderate)			- (low)	++ (moderate)
>60 vs. ≤45 years old	Positive for COVID-19	++/+++ (moderate/low)		++ (low)	+ (low)	++/+++ (moderate/low)
>70 or 75 vs. ≤45 years old	Positive for COVID-19	+++ (moderate)			++ (low)	+++ (moderate)
>80 vs. ≤45 years old	Positive for COVID-19	+++ (low)				+++ (low)
70-79 vs. 65-69 years old	Hospitalized					- (moderate)
>80 vs. 65-69 years old	Hospitalized					++ (low)
Increased age (continuous/incremental)[e]	Community sample or positive for COVID-19	Approximately 2-6% relative increase per year (moderate)	- (low)	- (low)	- (low)	Approximately 5-10% relative increase per year

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
						(moderate)
Gender or sex						
Male vs. female (all ages, mean 54 to 73)	Community sample	- (low)				
	Positive for COVID-19	++ (moderate)	uncertain	+ (low)	- (low)	- (moderate)
Male vs. female (20-64 years)[f]	Hospitalized					++ (low)
Race/ethnicity						
Black vs. non-Hispanic white	Community sample or positive for COVID-19	++ (low)	- (moderate)	- (moderate)	- (moderate)	- (moderate)
Hispanic vs. non-Hispanic white	Positive for COVID-19	- (low)	uncertain	- (low)	- (low)	
Asian vs. white	Community sample or positive for COVID-19	- (moderate)	- (low)	- (low)	- (low)	- (moderate)
Asian (Bangladeshi) vs. British white	Hospitalized					++ (low)
Culture/language/immigrant/refugee status						
Place of residence/household size						
Living in a low income area	Positive for COVID-19	- (low)				
Homeless vs. has a home	Positive for COVID-19	++ (low)				
Suburban vs. urban hospital	Hospitalized			uncertain		
1, 3, or 4 vs. 2 household members	Community sample	- (low)				
Occupation						
Laryngologist or intubator vs. assistant	Healthcare workers for COVID-19 patients	- (low)				
Education level						
Lower education vs. university degree	Community sample	- (low)				
Socioeconomic status						

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Highest vs. lowest quintile of social deprivation	Community sample	+ (low)				- (moderate)
Income ≤25th vs. >50th or 75th percentile	Positive for COVID-19	++ (low)				
≥Average vs. below average income	Community sample	- (low)				
Smoking						
Current or former vs. never	Community sample or positive for COVID-19	- (moderate)		uncertain	- (low)	- (low)
Alcohol consumption						
Above vs. within guidelines	Community sample or positive for COVID-19	- (low)				
Physical activity level						
Below vs. within guidelines	Community sample or positive for COVID-19	- (low)				

COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; OR: odds ratio; RR: risk ratio

[a] When not listed, the reference group are those without the risk factor.

[b] Outcomes of severe disease (as defined by authors), ICU admission, mechanical ventilation, and mortality are all in a hospitalized population, except for Liver Disease, where findings differed depending on the population denominator used.

[c] A formal assessment of the quality/confidence of the evidence was not performed but was informed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. We determined our confidence in the magnitude of the associations by considering primarily study limitations (risk of bias), consistency in findings across studies, and precision (sample size). Very low confidence indicates that were have no/very low confidence about possible associations; low means that the evidence indicates that there ***may*** be an association; moderate means that the evidence indicates that there ***probably*** is an association. High certainty evidence as not found for any association.

[d] For categorical data for age, and BMI, the reference group differed slightly across studies.

[e] For continuous or incremental data for age, the rate of hospitalization and mortality outcomes, approximately half of the studies analyzed data on a continuum (with the remainder reporting in incremental categories, e.g., 5-year units)

[f] Subgroup data from one study that analyzed the younger population separately

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There was low or moderate certainty of evidence for important/large associations with increased risk of hospitalization in people having confirmed COVID-19, for the following risk factors: obesity class III (body mass index ≥40 kg/m^2; 1 study, n=5,297),[49] heart failure (2 studies, n=6,331),[23, 49] diabetes (2 studies, n=6,331),[23, 49] chronic kidney disease (confirmed COVID-19 or community sample; 2 studies, n=424,073),[47, 49] dementia (1 study, n=418,794),[47] age over 45 years (vs. 45 or younger; 2 studies, n=6,331),[23, 49] male gender (3 studies, n=3,812),[23, 49, 51] black race/ethnicity (vs. non-Hispanic white; confirmed COVID-19 and community samples, 5 studies in 4 populations, n=428,606),[23, 44, 47, 49, 51] homelessness (1 study, n=1,052),[23] and low income (<25th vs. >50th percentile; 1 study, n=1,052).[23] Age over 60 and over 70 years may be associated with important increases in the rate of mechanical ventilation (1 study, n=486)[40] and severe disease (1 study, n=2,725),[49] respectively.

For mortality, important associations with increased risk may exist for liver disease (2 studies, n=20,597),[33, 53] Bangladeshi ethnicity (vs. British white; 1 study, n=130,091),[56] and age over 45 years (vs. <45 years; 3 studies, n=87,819).[33, 49, 56] The data were somewhat inconsistent for gender, with most studies showing moderate certainty of no important effect, but one large fair quality study (n=130,091)[56] from the UK that stratified its analysis by age showed that hospitalized males aged 20-64 years (but not older) may be at about two-fold increased risk of mortality compared to females. Associations with hospitalization and mortality may be very large for those aged over 60 years (2 studies, n=6,331 for hospitalization;[23, 49] 3 studies, n=24,163 for mortality[33, 41, 49]) and are probably very large for those over 70 years (2 studies, n=6,331 for hospitalization;[23, 49] 2 studies, n=22,858 for mortality[33, 49]). One study (n=63,094)[56] directly compared subgroups of older adults, showing that compared to those aged 65-69 years, there may be no important increased risk of mortality among hospitalized adults aged 70-79 years, but risk may increase about 2-fold for those 80 years and older. Studies treating age on a continuum or across small increments consistently found that risks for hospitalization and mortality increased with increasing age (e.g., approximately 2-6% and 5-10% relative increase in risk per year) (3 studies in 2 populations, n=422,275 for hospitalization;[44, 47, 51] 11 studies, n=6,877 for mortality).[25-27, 31, 35, 38, 45, 46, 48, 51, 55]

Moderate associations may exist for increased risk of mechanical ventilation (4 studies, n=1,559)[38, 40, 42, 46] and ICU admission (2 studies, n=873),[38, 42] and severe disease (1 study, n=2,725)[49] with obesity (body mass index ≥30 or 40 kg/m^2); severe disease with heart failure (1 study, n=2,725);[49] mortality with haematological malignancy (1 study, n=1,183);[52] mechanical ventilation with male gender (4 studies, n=881);[27, 40, 42, 46] and hospitalization with social deprivation (highest vs. lowest quintile; 1 study, n=340,996).[44]

There was moderate certainty evidence for no important increase in risk of hospitalization with chronic respiratory conditions (4 studies in 3 populations, n=425,125),[23, 44, 47, 49] cardiovascular disease apart from heart failure (i.e., coronary artery disease, hypertension, hyperlipidaemia; 4 studies in 3 populations, n=425,125),[23, 44, 47, 49] non-specific cancer (2 studies, n=6,331),[23, 49] Asian race/ethnicity other than Bangladeshi (vs. non-Hispanic white; 3 studies in 2 populations, n=424,073),[44, 47, 49] and current or former smoking (5 studies in 3 populations, n=425,125).[23, 39, 44, 47, 49] Additionally, there was moderate certainty evidence for no important increase in severe

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disease with chronic respiratory conditions (1 study, n=2,725),[49] chronic kidney disease (2 studies, n=2,922),[24, 49] nonspecific cancer (2 studies, n=2,769),[29, 49] and Black race/ethnicity (vs. non-Hispanic white; 2 studies, n=3,030);[36, 49] and no important increase in risk of mortality with obesity (body mass index ≥30 kg/m^2; 6 studies, n=8,716),[35, 38, 43, 46, 49, 51] chronic respiratory conditions (4 studies, n=23,315),[31, 33, 46, 49] diabetes (4 studies, n=23,315), [31, 33, 46, 49] chronic kidney disease (3 studies, n=23,058), nonspecific cancer (3 studies, n=24,041),[33, 49, 52] male gender (9 studies, n=27,875),[25-27, 31, 33, 35, 46, 49, 51] Black (5 studies, n=135,418)[38, 48, 49, 51, 56] or Asian race/ethnicity (vs. non-Hispanic white; 3 studies, n=4,015),[38, 48, 49] and social deprivation (lowest vs. highest quintile; 1 study, n=130,091).[56] Overall, there were few data for the ICU and mechanical ventilation outcomes.

DISCUSSION

Responding to an urgent need for empiric evidence to inform decision-making on Canada's immunization strategies,[7] in this rapid review we synthesized studies employing a multivariate analysis to ascertain potential independent associations between "P^{2}ROGRESS And Other Factors" and severe outcomes of COVID-19. Among 22 potential risk factors examined across the included studies, the most important risk factors (i.e., those associated with large/important increased risk; OR or RR ≥2.0) for hospitalization among those with confirmed COVID-19 were several pre-existing chronic health conditions (obesity class III, heart failure, diabetes, chronic kidney disease [community sample or with COVID-19], dementia [community sample]), older age (>45 years vs. younger), male gender, Black race/ethnicity (community sample or with COVID-19), homelessness, and low income (≤25th vs. >50th percentile). Liver disease may be associated with a large increased risk of mortality among people with COVID-19 and advancing age (>45 years vs. younger) and Bangladeshi ethnicity (vs. British white) are likely to be associated with a large increased risk of mortality among hospitalized patients. There is evidence to suggest that male gender may increase risk of mortality among younger (20-64 years), but not older men.

Among the factors identified as increasing risk of severe outcomes, age seemed to be the most influential; adults older than 60 years may have at least 5 times increased odds of hospitalization and mortality from COVID-19 compared to those aged less than 45 years. This increased risk appears to magnify at least to some degree even for those older than 60 years, with those aged over 80 years having double the mortality risk of those aged 65-69 years. Though we focused the review on better quality studies that minimally controlled for age and sex, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for. For example, studies reporting on associations between outcomes and age did not adjust for nursing home residency, and studies examining race did not account for occupation, which may be an important confounder influencing susceptibility to the infection.[56] In addition, it is important to be aware that criteria for COVID-19 testing and hospitalization may differ by place and time, but it is difficult to predict how this may have impacted the findings. In general, many studies conducted testing based on symptoms and the evidence is likely most applicable to these populations. The evidence for mechanical ventilation, ICU admission, and severe disease outcomes was relatively sparse, and we located no evidence meeting our publication date and inclusion criteria to inform the

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impact of immigration or refugee status, religion or belief system, social capital, substance abuse disorders, pregnancy, Indigenous identity, living with a disability, nor differing levels of risk among children in various age groups.

The findings of this rapid review will be used to populate the Equity Matrix of NACI's Ethics, Equity, Feasibility, and Acceptability Framework,[9] which will be a part of a suite of considerations for informing the development of NACI recommendations on priority pandemic immunization strategies when initial COVID-19 vaccine supply is limited. NACI will be using the results of this rapid review and their current understanding of the epidemiology of COVID-19 in Canada to identify distinct inequities associated with COVID-19, potential reasons for these inequities, and suggested interventions to reduce inequities and improve access to vaccine when it becomes available. The Equity Matrix applied to COVID-19 with evidence to-date can be found elsewhere.[11]

Strengths and Limitations

The expedited methods used in this review allowed for a rapid but comprehensive synthesis of the highest quality evidence available on multiple risk factors associated with severe COVID-19 outcomes that is applicable to OECD countries. Generalizations to other countries should be made with caution, as high risk groups in these populations may differ. We excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore our findings for mechanical ventilation and mortality are applicable to people with COVID-19 or in general populations, but not necessarily all those with severe infection. Most studies of patients in the ICU setting that we located were relatively small and descriptive in nature, such that many would have been excluded due to lack of adjustment or only have been able to provide low or very low certainty evidence due to their lack of precision. As described previously, many available studies do not control for any important confounding variables which limited the number of studies and risk factors included in this review. Given the rapid emergence of new evidence on the topic, potential associations (or lack of association) for which only low or very low certainty of evidence is available should continue to be reviewed as new primary research is published. There is a need for high quality primary research (accounting for multiple confounders) to better understand the level of risk that might be associated with immigration or refugee status, religion or belief system, social capital, substance abuse disorders, pregnancy, indigenous identity, living with a disability, and differing levels of risk among children in various age groups.

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FIGURES

Figure 1 – PRISMA flow of study selection

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ABBREVIATIONS

COVID-19	Novel coronavirus disease 2019
ICU	Intensive care unit
NACI	National Advisory Committee on Immunization
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
P^{2}ROGRESS	Pre-existing disease or disability, place of residence, race, ethnicity, culture, language, immigrant/refugee status, occupation, gender, religion/belief system, education, socioeconomic status, social capital, age, and other factors
RR	Risk ratio

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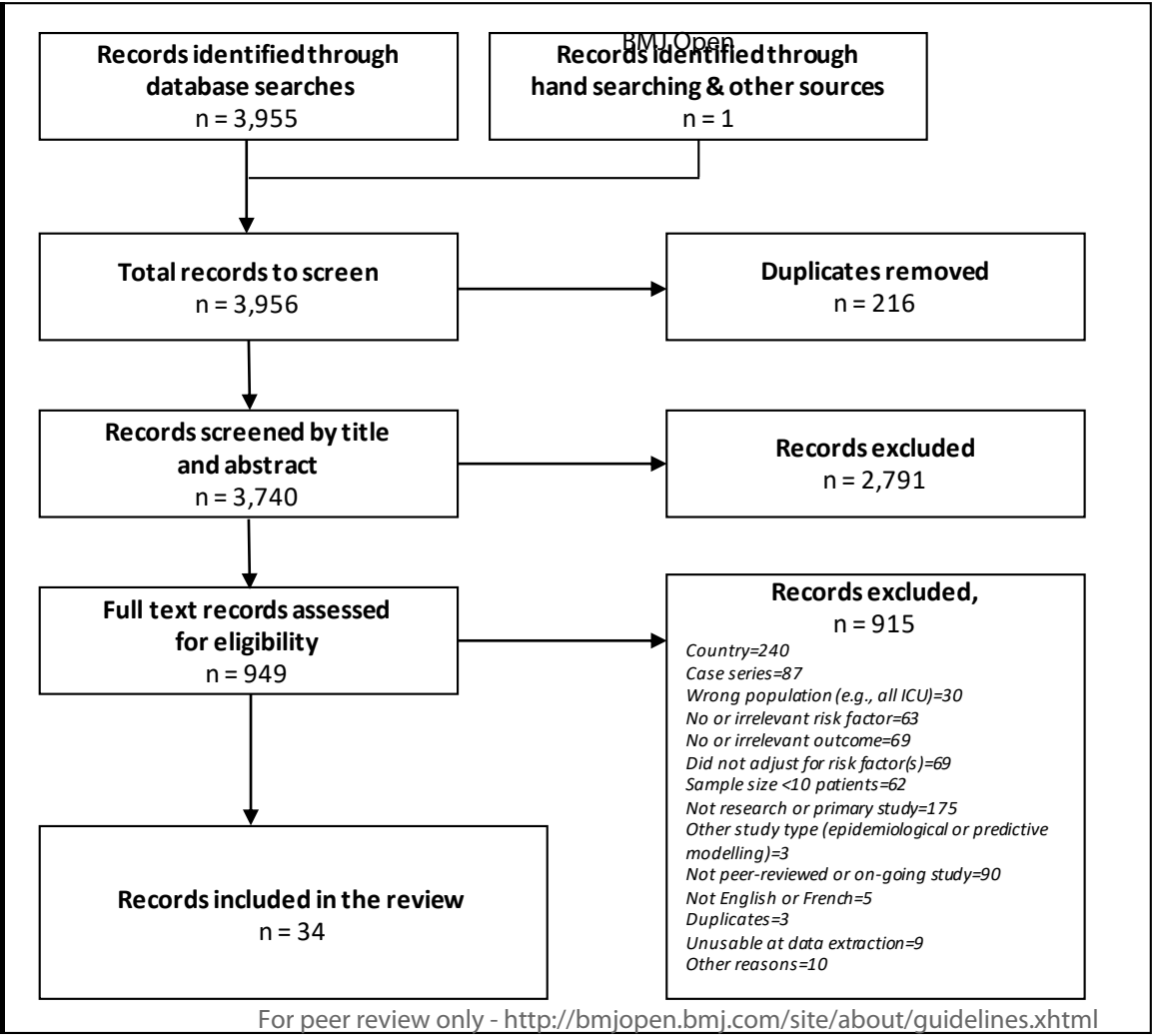

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Figure 1. PRISMA flow of study selection

Supplement File

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Supplement 1. Search strategy

Ovid MEDLINE(R) All 1946 to June 15, 2020

1	(Risk factor* or relative risk or odds ratio or between group* or Regression or multi-variate or multivaria* or covariate or univariate or co-variate or matching or ANOVA or Analysis of variance or ANCOVA or Correlation or Covariance or Principal Component Analysis or cohort* or follow-up or prognos* or predict*).mp.
2	exp cohort studies/ or cohort*.mp.
3	("Associated with" or "Association of" or "impact of" or "Correlated with" or "Impact* on" or characteristics or characterise or features or clinical findings or clinical outcomes or clinical manifestations or clinical course).ti.
4	(clinical data or (clinical adj5 (characteristics or features or manifestations))).tw,kf.
5	1 or 2 or 3 or 4
6	(Mortal* or fatal* or death* or died or discharged alive or poor prognos* or good prognos* or clinical outcome* or adverse outcome* or disease course or clinical course or ((severe* or serious* or critical*) adj4 (ill* or outcome* or course or case or cases or patient* or condition)) or Severity or ((ICU or hospital or intensive care) adj7 (admission* or admit*)) or Ventilator* or ventilation or Hospitaliz* or hospitalis* or (Length adj3 stay)).mp.
7	((pregnan* or maternal or perinatal or birth or neonat* or infant*) adj7 outcome*).mp.
8	6 or 7
9	5 and 8
10	(Coronavirus* or corona-virus* or betacoronavirus* or nCOV* or 2019nCoV or 2019-ncov or covid or covid19 or SARS-CoV*or SARSCov*).mp.
11	limit 10 to yr="2020 -Current"
12	limit 11 to abstracts
13	(11 not 12) and (1 or 2 or 3 or 4 or 6 or 7)
14	9 and 11
15	13 or 14
16	(exp China/ or Iran/ or exp Russia/) not (canada/ or exp united states/ or europe/ or austria/ or belgium/ or exp france/ or exp germany/ or exp united kingdom/ or exp italy/ or spain/ or netherlands/ or exp "scandinavian and nordic countries"/ or australia/ or new zealand/ or mexico/ or chile/ or colombia/ or exp japan/ or korea/ or exp "republic of korea"/ or baltimore/ or berlin/ or boston/ or chicago/ or "district of columbia"/ or london/ or los angeles/ or new orleans/ or new york city/ or paris/ or philadelphia/ or rome/ or san francisco/ or estonia/ or latvia/ or lithuania/ or czech republic/ or hungary/ or poland/ or slovakia/ or slovenia/ or greece/ or luxembourg/ or portugal/ or switzerland/ or israel/ or turkey/)
17	((China or wuhan or hubei or beijing).tw,kf. and china.in.) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle).tw,kf.

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18	((russia* or iran* or tehran or brazil*) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle)).tw,kf.
19	((china or russia or iran or tehran or Brazil) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle)).in.
20	15 not (16 or 17 or 18 or 19)
21	limit 20 to (english or french)
22	limit 21 to editorial
23	21 not 22
24	Remove duplicates from 23

Online databases, hand-searched up to June 12, 2020:

Epistimonikos COVID-19 in L*VE Platform (epidemiology, etiology and prognosis questions) at:
https://app.iloveevidence.com/loves/5e6fdb9669c00e4ac072701d?utm=epdb_en

McMaster COVID-19 Evidence Alerts (prognosis or etiology studies) at:
https://plus.mcmaster.ca/COVID-19/

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Supplement 2. Eligibility criteria

Criterion	Include	Exclude
Population/ Exposure	P²ROGRESS risk factors[1], with or without infection with COVID-19[2] [1]Risk factors include: – Pre-existing disease/condition, disability (e.g., chronic disease, immunocompromised, pregnancy) – Place/state of residence (e.g., remote, overcrowding, homeless, institutionalization) – Race/ethnicity/culture/language/immigrant/refugee status – Occupation – Gender identity/sex – Religion/belief system – Education/literacy level – Socio-economic status – Social capital (e.g., social support/networks/trust) – Age – Other (risk behaviours e.g., drug and alcohol use disorders, smoking) [2]COVID-19 infection may include lab-confirmed, or epidemiologically-linked cases (e.g., transmission/cases within households). Cases with co-infections (e.g., influenza such as H1N1) will be accepted, but may be analyzed separately from COVID-19-only infections.	Studies including populations with pandemic-related infections (e.g., SARS, MERS) without data isolated for COVID-19
Comparator	Staged, in the following order: i) The same P²ROGRESS factor experienced differently or to a different degree (e.g., higher or lower socioeconomic status, higher or lower literacy level) or the absence of a P²ROGRESS factor (e.g., non-refugee; no pre-existing disease). ii) None (in some circumstances such as pregnancy and immunocompromised)	Not applicable
Outcomes	Primary outcomes[3] – Hospitalization rate (including readmissions) – Hospital length of stay (binary or continuous) – Admission to ICU – ICU length of stay (binary or continuous) – Need for mechanical ventilation – Case fatality – All-cause fatality – Severe or critical infection (composite; as defined by authors) [3]Data may be extracted for outcomes listed above for the following population denominators, in order of priority: i) General population ii) Population positive for COVID-19 iii) Population hospitalized for COVID-19 iv) Population with a risk factor	COVID-19 infection requiring outpatient treatment (e.g., treatment at primary care office, attendance at ED) Hospitalization for an illness other than COVID-19 infection Outcomes post-hospital discharge (e.g., readmissions unrelated to index COVID-19 infection)
Timing	Any follow-up duration	Not applicable

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Criterion	Include	Exclude
Setting	OECD countries (https://www.oecd.org/about/document/list-oecd-member-countries.htm)	Non-OECD countries
Study design	Prospective and retrospective cohort studies	Studies of interventions/treatments
Language	Full text in English or French; pre-prints if accepted for publication in a peer-reviewer journal.	Language other than English or French

COVID-19: novel coronavirus 2019; ED: emergency department; ICU: intensive care unit; MERS: Middle East Respiratory Syndrome; MV: mechanical ventilation; OECD: Organisation for Economic Co-operation and Development; SARS: severe acute respiratory syndrome

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Supplement 3. Excluded studies

Excluded – case series (n=87)

1. Akdur A, Karakaya E, Ayvazoglu Soy EH, Alshalabi O, Kirnap M, Arslan H, et al. Coronavirus Disease (COVID-19) in Kidney and Liver Transplant Patients: A Single-Center Experience. Exp Clin Transplant. 2020;18(3):270-4.

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Supplement 4. Characteristics of included studies

Author, year; Publication date; Country; Study design; Study period & follow-up	**Enrolled cohort; Study sample; Mean age (SD), years[1] Male, proportion**	**COVID-19 diagnosis**	**P[2]ROGRESS risk factors, adjusted for in multivariate regression analysis[2]**	**Outcomes**	**Quality rating & concerns (if any)**
Azar K, 2020 May 21 (published) USA Retrospective cohort Jan 1-Apr 8	Patients ≥18 years old who had at least one encounter at a Sutter facility (integrated health system) during the study period for suspected or confirmed COVID-19 infection N=1,052 53 (95% CI 52-54) 49%	ICD codes or evidence in lab records (reports suspected cases but confirmed cases analyzed separately)	Pre-existing condition (asthma, cardiovascular disease, cancer, chronic pulmonary disease, congestive heart failure, type II diabetes, hypertension, depression); Place of residence (homeless); Race/ethnicity; Sex; SES (household income); Age; Other factors (smoking status)	Rate of hospitalization	Good; No major concerns
Bhargava A, 2020 May 30 (published) USA Retrospective cohort Mar 8-Apr 8	Adults admitted to a tertiary care urban academic medical center with COVID-19 N=197 61 (16) 52%	RT-PCR	Pre-existing condition (renal disease); Sex; Age	Severe disease	Good; No major concerns
Bianchetti A, 2020 May 11 (accepted) Italy Retrospective cohort Study period not reported	Adults admitted to acute medical wards with COVID-19 pneumonia in Brescia N=627 71 (13) 47%	RT-PCR	Pre-existing condition (dementia); Sex; Age	Mortality	Fair; Did not report follow-up duration or censorship for outcomes

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Borobia A, 2020 June 4 (published) Spain Retrospective cohort Feb 25-Apr 19; Follow-up to Apr 19	Adults >=18 years old hospitalized in wards or the ED at a university hospital with COVID-19 N=2,226 Median 61 (IQR 46-78) 48%	Lab-confirmed	Pre-existing condition (not clearly specified for multivariate analysis); Sex; Age	Mortality	Fair; No follow-up and censored to patients who died or were discharged by April 19
Busetto L, 2020 May 28 (accepted) Italy Retrospective cohort Mar 14-Apr 11	Adults hospitalized in a medical COVID-19 ward with SARS-CoV-2 related pneumonia N=92 71 (13) 62%	RT-PCR	Pre-existing condition (BMI/obesity, chronic respiratory disease, dementia, type II diabetes); Sex; Age	ICU admission; Noninvasive ventilation or MV (composite); Mortality (in-hospital)	Fair; Did not report follow-up duration or censorship for outcomes
Cecconi M, 2020 May 20 (published) Italy Retrospective cohort Feb 22-Mar 22	Adults ≥18 years old admitted to a hospital with COVID-19 N=239 64 (14) 71%	Positive assay	Pre-existing condition (coronary heart disease); Age	ICU admission or mortality (composite)	Fair; No adjustment for sex and patients were censored as of March 25 (inadequate for patients enrolled on March 22)
Colaneri M, 2020 Apr 23 (published) Italy Retrospective cohort Feb 21-28; Follow-up to Mar 4	Patients admitted to a hospital with COVID-19 N=44 Median 68 (IQR 29) 64%	RT-PCR	Pre-existing condition (tumor); Sex	Severe disease	Good; No major concerns

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Covino M, 2020 May 18 (accepted) Italy retrospective cohort Mar 1-31; Follow-up at 30 days from ED admission	Adults ≥80 years old admitted to ED of urban teaching hospital for suspected COVID-19 N=69 Median 84 (IQR 82-89) 54%	RT-PCR	Pre-existing condition (severe dementia)	Mortality	Fair; No adjustment for age or sex, or other pre-existing conditions
Cummings MJ, 2020 May 19 (published) USA Prospective cohort Mar 2-Apr 1; Follow-up to Apr 28	Adults admitted to high-dependency unit (O2) or ICU (MV) of two hospitals in New York with COVID-19 and were critically ill with acute hypoxaemic respiratory failure N=257 Median 62 (IQR 51-72) 67%	Lab-confirmed	Pre-existing condition (chronic cardiac disease [coronary artery disease or congestive heart failure], chronic pulmonary disease [chronic obstructive pulmonary disease/interstitial lung disease], diabetes, hypertension); Sex; Age	Mortality (in-hospital)	Good; No major concerns
Docherty AB, 2020 May 15 (accepted) UK Prospective cohort Feb 6-Apr 19; Follow-up at least 2 weeks to May 3	Children and adults admitted to 208 acute care hospitals with COVID-19 in England, Wales, and Scotland N=20,133 Median 73 (IQR 58-82) 60%	RT-PCR	Pre-existing condition (chronic cardiac disease, chronic pulmonary disease, asthma, CKD, DM, obesity, chronic neurological disorder, dementia, malignancy, moderate/severe liver disease, mild liver disease, chronic hematologic disease, rheumatologic disorder, HIV/AIDS, malnutrition); Sex; Age; Other factors (smoking status)	Mortality (in-hospital)	Good; No major concerns
D'Silva K, 2020 May 18 (accepted) USA Retrospective cohort	Patients seen at PHS who were ≥18 years of age and had a positive test result for SARS-CoV-2 by PCR clinical assay. *PHS is a large healthcare system that includes tertiary care hospitals (Massachusetts General Hospital	PCR	Pre-existing condition (rheumatic disease)	Rate of hospitalization; ICU admission/ or MV (all with MV); Mortality	Fair; No adjustment for sex, and mortality only adjusted for age and BMI

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Mar 1-Apr 8; Follow-up averaged 29 days	and Brigham and Women's Hospital), community hospitals and primary and specialty outpatient centres in the greater Boston N=156 63 (15) 31%				
El-Boghdadly K, 2020 June 9 (accepted) Multi-country Prospective cohort Mar 23-Jun 2	Healthcare workers from 503 hospitals in 17 countries who performed tracheal intubations, with data for new COVID-19 infection or new COVID-19 symptoms requiring self-isolation or hospitalization. N=1,718 42 (9) 60%	Lab-confirmed or symptoms	Occupation (intubator/laryngologist vs. assistant); Sex	Self-isolation/ hospitalization (composite)	Good; No major concerns
Giacomelli A, 2020 May 22 (published) Italy Prospective cohort Feb 21-Mar 19; Follow-up to Apr 20	Adults hospitalized at one hospital with COVID-19 N=233 Median 61 (IQR 50-72) 62%	RT-PCR	Pre-existing condition (age unadjusted Charlson Comorbidity Index, obesity, anemia); Sex; Age	Mortality	Good; No major concerns
Gold J, 2020 May 8 (published, MMWR weekly report) USA Prospective cohort Mar 1-30; Follow-up to Apr 28	Adults ≥18 years old hospitalized at eight hospitals with COVID-19 N=305 Median 60 (IQR 46-69) 49%	Lab-confirmed	Pre-existing condition (obesity, diabetes, cardiovascular disease, coronary artery disease, congenital heart disease, arrhythmia, chronic lung disease, asthma, chronic obstructive pulmonary disease, immunocompromising conditions/therapies, end-stage renal disease on dialysis, liver disease, hypertension,	MV or mortality (composite)	Good; No major concerns

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			neurologic disorder, chronic liver disease without dialysis, cancer, rheumatologic or autoimmune condition); Race/ethnicity; Sex; Age		
Hajifathalian K, 2020 (#163) May 29 (accepted) USA Retrospective cohort Mar 4-Apr 9; Follow-up to Apr 16	Adults ≥18 years old with and without obesity hospitalized in ED or inpatient wards with COVID-19 N=770 64 (17) 61%	RT-PCR	Pre-existing condition (obesity)	ICU admission; MV; Mortality (in-hospital)	Fair; No adjustment for sex, and 7-day follow-up inadequate for mortality
Hajifathalian K, 2020 (#1154) May 1 (accepted) USA Retrospective cohort Mar 4-Apr 9	Adults with SARS-CoV-2 N=1,059 61 (18) 58%	RT-PCR	Pre-existing condition (number of comorbidities); Age	ICU admission or mortality (composite)	Fair; Unclear if adjustment for sex, and did not report follow-up duration or censorship for outcomes
Hamer M, 2020 May 23 (published) UK Prospective cohort Mar 16-Apr 26	Adults in the community N=387,109 56 (8) 45%	RT-PCR	Pre-existing condition (overweight, obesity); Other factors (smoking status, level of alcohol consumption, level of physical activity)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Hur K, 2020 May 20 (accepted)	Patients hospitalized with laboratory-confirmed COVID-19 infection admitted to any of the 10	RT-PCR	Pre-existing condition (obesity, diabetes, hypertension);	MV	Good; No major concerns

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USA Retrospective cohort Mar 1-Apr 8; Follow-up to Apr 18	hospitals in the Northwestern Memorial HealthCare system spread across the Chicago metropolitan area N=486 Median 59 (IQR 19-101) 56%		Place of residence (suburban vs. urban hospital); Race/ethnicity; Sex; Age; Other factors (smoking status)		
Imam Z, 2020 June 4 (published) USA Retrospective cohort Mar 1-Apr 17; outcome analysis ended Apr 17	Individuals that were hospitalized at a hospital within Beaumont Health with SARS-CoV-2 infection demonstrated by a positive RT-PCR on nasopharyngeal swab per world health organization (WHO)guidance N=1,305 61 (16) 54%	RT-PCR	Pre-existing condition (Charlson Comorbidity Index >3); Age	Mortality (in-hospital)	Fair; Adjustment for Charlson Comorbidity Index score (>3) despite individual comorbidities being significant at univariate analysis, and some missing data for ethnicity (n=5) and smoking status (n=240)
Kalligeros M, 2020 June 12 (published) USA Retrospective cohort Feb 17-Apr 5	All consecutive adult (≥18 years old) patients who had a laboratory confirmed (using a reverse transcriptase–polymerase chain reaction assay) SARS-CoV-2 infection and who were hospitalized at the Rhode Island Hospital, The Miriam Hospital, or Newport Hospital in Rhode Island N=103 Median 60 (IQR 50-72) 61%	RT-PCR	Pre-existing condition (obesity, diabetes, hypertension, heart disease, lung disease);	ICU admission; MV	Good; No major concerns
Klang E, 2020 May 23 (accepted)	Adults hospitalized at five academic hospitals with COVID-19 with BMI information	PCR	Pre-existing condition (obesity, diabetes, heart disease, hypertension, lung disease); Race/ethnicity;	Mortality (in-hospital)	Fair; Did not report follow-up duration or censorship for outcomes, and a

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USA Retrospective cohort Mar 1-May 17	N=3,406 Range 34 to 84 y 58%		Sex; Age		large number of patients who were still hospitalized at time of analysis were excluded (n=1,047)
Lassale C, 2020 May 28 (accepted) UK Prospective cohort Mar 16-Apr 26	Adults in the community N=340,966 56 (8) 45%	RT-PCR	Pre-existing condition (obesity, cardiovascular disease, chronic bronchitis, ever seen a psychiatrist); Place of residence (number in household); Race/ethnicity; Sex; Education/literacy level (university degree vs. lower education); SES (Townsend index); Age; Other factors (smoking status, level of alcohol consumption, level of physical activity)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Okoh A, 2020 June 10 (published) USA Retrospective cohort Mar 10-Apr 10; Follow-up to Apr 20	Adults ≥18 years old of Black/African American or Latino/Hispanic ethnicity hospitalised at a quaternary care teaching hospital in New Jersey with COVID-19 N=251 Median 62 (IQR 49-74) 51%	RT-PCR	Pre-existing condition (coronary artery disease, chronic kidney disease, hypertension, HIV); Race/ethnicity; Sex; Age	Mortality (in-hospital)	Good; No major concerns
Palaiodimos L, 2020 May 14 (accepted) USA Retrospective cohort	Adults (first 200) admitted to the inpatient medicine service or the ICU of a tertiary academic institution with COVID-19 N=200	Lab-confirmed	Pre-existing condition (overweight, obesity, coronary artery disease, chronic kidney disease or end-stage renal disease, chronic obstructive pulmonary disease, diabetes,	MV; Mortality (in-hospital)	Good; No major concerns

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Mar 9-Mar 22; Follow-up 3 weeks to Apr 12	Median 64 (IQR 50-74) 49%		heart failure, hyperlipidemia, obstructive sleep apnea); Sex; Age; Other factors (smoking status)		
Patel AP, 2020 July 6 (published, letter) UK Prospective cohort Mar 16-Apr 14	Adults who were enrolled in a national health database N=418,794 66 (SD not reported) 45%	PCR	Pre-existing condition (obesity, chronic obstructive pulmonary disease, coronary artery disease, diabetes, chronic kidney disease, heart failure, hypertension, ischemic stroke, previous pneumonia, Alzheimer's or dementia); Race/ethnicity; Sex; SES (Townsend index, average income); Age; Other factors (smoking status)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Perez-Guzman PN, 2020 April 29 (published, report) UK retrospective cohort Feb 25-Apr 5; Follow-up to Apr 19	Adults hospitalized at three hospitals (with a multi-ethnic catchment) with COVID-19 N=520 Median 67 (IQR 26) 62%	RT-PCR	Pre-existing condition (Elixhauser score, obesity, diabetes, ischaemic heart, hypertension, hyperlipidemia, chronic heart failure, stroke, asthma, chronic obstructive pulmonary disease, dementia, chronic kidney disease, dementia, solid tumor, liver non-cirrhotic, liver cirrhotic, atrial fibrillation, deep vein thrombosis/pulmonary embolism); Race/ethnicity; Sex; Age	Mortality (in-hospital)	Good; No major concerns
Petrilli CM, 2020 May 14 (accepted) USA Prospective cohort	Adults tested for SARS-CoV-2 from 260 outpatient office sites and 4 acute care hospitals N=5,279 Median 54 (IQR 38-66)	RT-PCR	Pre-existing condition (obesity, asthma or chronic obstructive pulmonary disease, chronic lung disease, coronary artery disease, diabetes, heart failure, hyperlipidemia, hypertension, cancer); Race/ethnicity;	Rate of hospitalization; Severe disease; Mortality (in-hospital)	Good; No major concerns

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Mar 1-Apr 8; Follow-up to May 5	50%		Sex; Age; Other factors (smoking status)		
Piano S, 2020 June 11 (published) Italy Retrospective cohort Feb 22-Apr 8	Non-critically ill patients hospitalized with COVID-19 in five internal medicine COVID unit in two regions of Northern Italy N=565 66 (15) 63%	RT-PCR	Pre-existing condition (liver function, Charlson Comorbidity Index); Gender; Age	Transfer to ICU or mortality (composite)	Good; No major concerns
Price-Haywood EG, 2020 May 27 (published) USA Retrospective cohort Mar 1-Apr 11; Follow-up to May 7 for mortality	Adults attending integrated-delivery health system who tested positive for SARS-CoV-2 N=3,481 54 (17) 40%	PCR	Pre-existing condition (Charlson Comorbidity Index score, obesity); Place of residence (residence in low-income area); Race/ethnicity; Sex; Age	Rate of hospitalization; Mortality (in-hospital)	Good; No major concerns
Public Health England June (published) UK Retrospective cohort Mar 20-May 13	Patients admitted to hospital (ward or critical care) with COVID-19 N=130,091 No aggregate data for age (range 2% at <20 y to 29% at ≥80 y) 47%	Lab-confirmed	Race/ethnicity; SES (deprivation); Sex; Age	Mortality	Fair; No adjustment for pre-existing condition(s), and data for risk factors are derived from a 2011 census with some missing data for sex (n=10), age (n=38), and ethnicity (2,024)
Shah V, 2020 June 11 (accepted) UK	Haemato-oncology patients and patients without underlying haematological malignancies (first 80) admitted to the hospital with COVID-19	RT-PCR	Sex; Age	Mortality	Fair; Adjusted for age and sex only, and no explanation of discrepancy in cohort

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Retrospective cohort Until April 15; Follow-up of 30 days	N=1,183 Median 71 (IQR 57-82) 58%				sample size change during study (80 and 68)
Singh S, 2020 (#121) June 2 (accepted) USA Retrospective cohort Jan 20-May 26	Inflammatory bowel disease (IBD) patients diagnosed with COVID-19 and patients diagnosed with COVID-19 and who had no history of or documentation of a diagnosis of IBD ever were included in the non-IBD control group. N=464 No aggregate data for age (IBD vs. non-IBD: mean 51 y [18] vs. 50 y [19]) No aggregate data for sex (IBD vs. non-IBD: 37% vs. 45%)	Lab-confirmed or ICD code for COVID-19	Pre-existing condition (obesity, essential hypertension, chronic lower respiratory diseases [asthma and chronic obstructive pulmonary disease], diabetes, ischemic heart disease, chronic kidney disease, heart failure, cerebrovascular disease); Race/ethnicity; Sex; Age; Other factors (nicotine dependency)	Rate of hospitalization; Mortality	Good; No major concerns
Singh S, 2020 (#1201) Apr 28 (accepted) USA Retrospective cohort Apr 12 (search for patient records)	Patients ≥10 years old with COVID-19, with and without pre-existing liver disease, who presented to a health care organization N=2,780 No aggregate data for age (liver disease vs. non-liver disease: mean 55 y [15] vs. 52 y [18]) 38%	ICD codes per CDC guidelines	Pre-existing condition (obesity, diabetes, hypertension, liver disease with cirrhosis, liver disease without cirrhosis); Race/ethnicity; Age; Other factors (nicotine use)	Rate of hospitalisation; Mortality	Good; No major concerns
Violi F, 2020 June 22 (published) Italy	Consecutively hospitalized adult (≥18 years) patients with laboratory-confirmed COVID-19 and severe acute respiratory syndrome coronavirus-2 (SARS-CoV2)-related	RT-PCR	Pre-existing condition (heart failure); Age	Mortality (in-hospital)	Good; No major concerns

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Retrospective cohort Mar-Apr; Follow-up of 19 days (median, IQR: 12–27 days)	pneumonia, requiring or not mechanical ventilation. N=319 No aggregate data for age (survivors vs. non-survivors: mean 66 y vs. 77 y) No aggregate data for sex (survivors vs. non-survivors: 58% vs. 70%)				

[1] values for age are mean (SD), unless otherwise denoted

[2] risk factors adjusted for in multivariate analysis may differ for outcome(s) reported within a study

CDC: Centers for Disease Control and Prevention; COVID-19: novel coronavirus; ICD: International Classification of Diseases; IQR: interquartile range; MV: mechanical ventilation; RT-PCR/PCR: reverse transcriptase polymerase chain reaction/polymerase chain reaction; SD: standard deviation; SES: socio-economic status; UK: United Kingdom; USA: United States of America; vs.: versus; y: year(s)

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Supplement 5. All results data from the included studies

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Table 1. Body mass index (BMI) and weight

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
BMI unspecified							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.03**	**1.02**	**1.05**	**<0.001**	Fair
community sample	Patel AP (UK; pc)	418,794	**1.04**	**1.03**	**1.06**	**<0.001**	Fair
Underweight (BMI <18.5) vs. normal weight (BMI <25)							
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 0.68	0.21	2.17	0.519	Fair
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 0.48	0.11	2.12	0.333	Fair
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	0.76	0.26	2.22	0.613	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.64	0.84	3.19	0.145	Fair
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.37	0.52	3.64	0.527	Good
Overweight (BMI 25-29.9) vs. normal weight (BMI <25)**							
Hospitalization							
community sample positive for COVID-19	Hamer (UK; pc)	387,109	**aRR 1.32**	**1.09**	**1.6**	**NR**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.3**	**1.07**	**1.57**	**0.007**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.94	0.73	1.2	0.65	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	**11.65**	**3.88**	**34.96**	**<0.001**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.27	0.59	8.83	0.235	Good
Mechanical ventilation							
ventilation (non-invasive + mechanical) among hospitalized with COVID-19	Busetto L (Italy; rc)	92	**4.19**	**1.36**	**12.89**	**0.012**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	3.7	0.6	22.87	0.159	Good
Mortality							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.27	0.03	2.05	0.204	Fair
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.01	0.82	1.25	0.94	Good
Obese class I or greater (BMI ≥30) vs. normal weight (BMI <30)**							
Hospitalization							
community sample positive for COVID-19	Hamer (UK; pc)	387,109	**aRR 1.97**	**1.61**	**2.42**	**NR**	Fair
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.43**	**1.2**	**1.71**	**NR**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.8**	**1.47**	**2.2**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.11	0.85	1.5	0.44	Good

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.76**	**1.24**	**2.48**	**0.001**	Fair
hospitalized with COVID-19 (BMI 30-34.9)	Kalligeros M (USA; rc)	103	2.65	0.64	10.95	0.178	Good
hospitalized with COVID-19 (BMI ≥35)	Kalligeros M (USA; rc)	103	**5.39**	**1.13**	**25.64**	**0.034**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.72**	**1.22**	**2.44**	**0.002**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**6.85**	**1.05**	**44.82**	**0.045**	Good
hospitalized with COVID-19	Hur K (USA; rc)	486	1.46	0.87	2.46	0.151	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**9.99**	**1.39**	**71.69**	**0.022**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.87**	**1.47**	**10.18**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.15	0.62	2.14	0.663	Fair
hospitalized with COVID-19	Giacomelli A (Italy; pc)	233	**aHR 3.04**	**1.42**	**6.49**	**0.004**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.99	0.77	1.27	NR	Fair
hospitalized with COVID-19, ≤50 y	Klang E (USA; rc)	572	1.1	0.5	2.3	0.755	Fair
hospitalized with COVID-19, >50 y	Klang E (USA; rc)	2,834	1.1	0.9	1.3	0.421	Fair
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.08	0.87	1.36	0.48	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.78**	**1.45**	**9.83**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.45	0.99	2.13	0.05	Good
Obese class III (BMI ≥40) vs. normal weight (BMI <25)**							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.45**	**1.78**	**3.36**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.71**	**1.1**	**2.7**	**0.02**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	1.92	0.92	4	0.08	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.45**	**0.99**	**2.13**	**0.05**	Good
hospitalized with COVID-19, ≤50 y	Klang E (USA; rc)	572	**5.1**	**2.3**	**11.1**	**<0.001**	Fair
hospitalized with COVID-19, >50 y	Klang E (USA; rc)	2,834	**1.6**	**1.2**	**2.3**	**0.004**	Fair

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; BMI: body mass index; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; y: year(s)

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Table 2. Pre-existing disease, unspecified

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
CCI score							
Hospitalization							
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**aHR 1.05**	**1**	**1.1**	**NR**	Good
Severe disease							
ICU transfer or death (composite) among hospitalized for COVID-19	Piano S (Italy)	565	**1.21**	**1.03**	**1.42**	**0.021**	Good
Mortality							
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.99	0.95	1.04	NR	Good
hospitalized with COVID-19	Imam (USA; rc)	1,305	**2.71**	**1.85**	**3.97**	**<0.001**	Fair
Number of comorbidities							
Severe disease							
ICU or death (composite) among positive for COVID-19	Hajifathalian K (USA; rc) #1154	1,059	**1.19**	**NR**	**NR**	**0.021**	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CCI: Charlson Comorbidity Index; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; rc: retrospective cohort; USA: United States of America; y: year(s)

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Table 3. Respiratory disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Asthma							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.52	0.89	2.58	>0.05	Good
Asthma or COPD							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.08	0.88	1.33	0.47	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.99	0.76	1.3	0.93	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.03	0.83	1.29	0.76	Good
Chronic pulmonary disease or COPD							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.8	0.75	4.34	>0.05	Good
community sample	Patel AP (UK; pc)	418,794	**1.51**	**1**	**2.28**	**0.05**	Fair
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.17**	**1.09**	**1.27**	**<0.001**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	2.05	0.76	5.51	0.156	Good
Chronic bronchitis							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.34	0.81	2.21	0.259	Fair
Obstructive sleep apnea							
Mechanical ventilation							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.15	0.4	3.35	0.791	Good
Pneumonia, previous							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.31	0.83	2.05	0.25	Fair
Other respiratory disease (includes one or more of: asthma, COPD, lung disease, interstitial lung disease, and/or pulmonary hypertension)							
ICU admission							
hospitalized with COVID-19 (includes heart failure, coronary artery disease and cardiomyopathy)	Kalligeros M (USA; rc)	103	1.5	0.47	4.82	0.495	Good
Mechanical ventilation							
hospitalized with COVID-19 (includes heart failure, coronary artery disease and cardiomyopathy)	Kalligeros M (USA; rc)	103	0.76	0.2	2.86	0.687	Good
Mortality							
hospitalized with COVID-19 (chronic cardiac disease or congestive heart failure)	Cummings MJ (USA; pc)	257	**aHR 2.94**	**1.48**	**5.84**	**NR**	Good

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aHR: adjusted hazards ratio; CI: confidence interval; COPD=Chronic obstructive pulmonary disease; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 4. Cardiovascular disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Cardiovascular disease							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.06**	**0.79**	**1.42**	**0.001**	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	1.32	0.75	2.32	>0.05	Good
Heart failure							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**3.34**	**1.49**	**7.52**	**<0.001**	Good
community sample	Patel AP (UK; pc)	418,794	1.09	0.56	2.14	0.79	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**4.43**	**2.59**	**8.04**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.93**	**1.4**	**2.6**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.43	0.5	4.06	0.501	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.54**	**1.23**	**1.93**	**<0.001**	Good
Coronary artery disease (includes coronary heart disease)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	0.95	0.67	1.36	0.79	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.08	0.81	1.44	0.6	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.71	1.2	0.56	Good
ICU transfer or death (composite) among hospitalized with COVID-19	Cecconi M (Italy; rc)	239	**aHR 2.02**	**1.13**	**3.64**	**0.018**	Fair
Mortality							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.53	0.54	4.34	0.421	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.1	0.9	1.35	0.36	Good
Hyperlipidemia							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.62**	**0.52**	**0.74**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.93	0.75	1.2	0.51	Good
Mechanical ventilation							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.66	0.78	3.55	0.188	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.98	0.82	1.17	0.79	Good
Hypertension							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	0.98	0.82	1.17	0.84	Fair

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
community sample	Patel AP (UK; pc)	418,794	1.12	0.9	1.39	0.32	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	1.4	0.93	2.1	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.78**	**1.49**	**2.12**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.96	0.75	1.2	0.76	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.79	0.27	2.28	0.663	Good
Mechanical ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.47	0.13	1.66	0.242	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.58	0.89	2.81	NR	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.98	0.78	1.23	0.86	Good
Other cardiovascular disease (includes one or more of: chronic cardiac disease, heart disease, heart failure, coronary artery disease and cardiomyopathy)							
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.52	0.51	4.51	0.448	Good
Mechanical ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**3.41**	**1.05**	**11.06**	**0.041**	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	**aHR 1.76**	**1.08**	**2.86**	**NR**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.16**	**1.08**	**1.24**	**<0.001**	Good
Ischemic stroke							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	0.94	0.39	2.3	0.90	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 5. Endocrine disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Diabetes							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.52**	**1.14**	**2.03**	**0.01**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.24**	**1.84**	**2.73**	**<0.001**	Good
positive for COVID-19	Azar K (USA; rc)	1,052	**2.17**	**1.33**	**3.53**	**<0.01**	Fair
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.23	0.99	1.5	0.06	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.91	0.71	5.19	0.202	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	**1.64**	**1.02**	**2.66**	**0.046**	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.13	0.73	6.22	0.168	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.26	0.58	2.73	0.557	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.31	0.81	2.1	NR	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	aHR 1.06	0.99	1.14	0.087	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.16	0.55	2.44	0.698	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.01	0.85	1.21	0.87	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 6. Hepatic disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Liver disease							
Hospitalization							
positive for COVID-19	Singh S (USA; rc) #1201	464	**aRR 1.3**	**1.1**	**1.6**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.51**	**1.21**	**1.88**	**<0.001**	Good
positive for COVID-19	Singh S (USA; rc) #1201	464	**aRR 3.0**	**1.5**	**6.0**	**0.001**	Good
positive for COVID-19 (liver disease with cirrhosis)	Singh S (USA; rc) #1201	464	**aRR 4.6**	**2.6**	**8.3**	**<0.001**	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 7. Renal disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Chronic kidney disease							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**2.01**	**1.19**	**3.41**	**0.01**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.6**	**1.89**	**3.61**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.73**	**0.55**	**1**	**0.04**	Good
hospitalized with COVID-19	Bhargava A (USA; rc)	197	**7.4**	**2.5**	**22**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.28**	**1.18**	**1.39**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.73	1.16	0.49	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.15	0.49	2.68	0.746	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 8. Gastrointestinal disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Irritable bowel disease							
Hospitalization							
positive for COVID-19	Singh S (USA; rc) #121	464	aRR 1.10	0.74	1.4	0.91	Good
Severe disease							
positive for COVID-19	Singh S (USA; rc) #121	464	aRR 0.93	0.68	1.27	0.66	Good

* values are adjusted odds ratio, unless otherwise denoted
aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; rc: retrospective cohort; USA: United States of America

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Table 9. Neurological disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Alzheimer's disease or dementia							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	5.08	0.7	36.68	0.11	Fair
Dementia							
Mortality							
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	**1.84**	**1.08**	**3.13**	**0.024**	Fair
hospitalized with COVID-19 (dementia)	Docherty AB (UK; pc)	20,133	**aHR 1.40**	**1.28**	**1.52**	**<0.001**	Good
hospitalized with COVID-19	Covino M (Italy; rc)	69	**aHR 3.87**	**1.23**	**12.17**	**0.021**	Fair
hospitalized with COVID-19 (chronic neurological disorder)	Docherty AB (UK; pc)	20,133	**aHR 1.17**	**1.06**	**1.29**	**0.001**	Good

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom

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Table 10. Malignancy

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Cancer or tumor							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.96	0.45	2.03	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	0.88	0.65	1.19	0.41	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.3	0.95	1.8	0.1	Good
hospitalized with COVID-19	Colaneri M (Italy; rc)	44	22.199	0.826	596.152	0.0648	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.29**	**1.03**	**1.62**	**0.03**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.13**	**1.02**	**1.24**	**0.017**	Good
positive for COVID-19	Shah V (UK; rc)	1,183	**aHR 1.74**	**1.12**	**2.71**	**0.014**	Fair
Hematological cancer - lymphoid							
Mortality							
positive for COVID-19	Shah V (UK; rc)	1,183	**aHR 1.75**	**1.07**	**2.87**	**0.026**	Fair
Hematological cancer - myeloid							
Mortality							
positive for COVID-19	Shah V (UK; rc)	1,183	aHR 1.70	0.7	4.13	0.244	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 11. Immunocompromised

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Rheumatic disease							
Hospitalization							
positive for COVID-19	D'Silva K (USA; pc)	156	1.1	0.51	2.38	0.81	Fair
ICU admission							
ICU or mechanical ventilation among hospitalized with COVID-19	D'Silva K (USA; pc)	65	**2.92**	**1.002**	**8.49**	**0.049**	Fair
Mortality							
positive for COVID-19	D'Silva K (USA; pc)	156	1.58	0.31	8.03	0.58	Fair
HIV							
Mortality							
hospitalized with COVID-19	Okoh A (USA; rc)	251	**0.07**	**0.03**	**0.52**	**0.006**	Good

* values are adjusted odds ratio, unless otherwise denoted

CI: confidence interval; COVID-19: novel coronavirus disease 2019; HIV: human immunodeficiency virus; ICU: intensive care unit; pc: prospective cohort; rc: retrospective cohort; USA: United States of America

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Table 12. Mental health

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Depression							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.18	0.57	2.41	>0.05	Good
Ever seen a psychiatrist							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.24	0.99	1.55	0.057	Fair

* values are adjusted odds ratio, unless otherwise denoted
** the reference category differs slightly across studies
CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 13. Place/state of residence

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Low-income geographic area							
Hospitalization							
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.22**	**1.04**	**1.43**	**NR**	Good
Homeless							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	3.25	0.38	28.02	>0.05	Good
Number of people in household (1 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.15	0.93	1.43	0.195	Fair
Number of people in household (3 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.22	0.97	1.55	0.093	Fair
Number of people in household (4 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.59**	**1.26**	**2.01**	**<0.001**	Fair
Suburban vs. urban hospital							
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	1.35	0.82	2.23	0.241	Good

* values are adjusted odds ratio, unless otherwise denoted
CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 14. Race/ethnicity

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Black vs. non-Hispanic White							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**2.66**	**1.82**	**3.91**	**<0.001**	Fair
community sample	Patel AP (UK; pc)	418,794	**2.38**	**1.52**	**3.74**	**<0.001**	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	**2.67**	**1.3**	**5.47**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	0.81	0.65	1.01	0.06	Good
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.96**	**1.62**	**2.37**	**NR**	Good
Severe disease							
hospitalized with COVID-19	Gold JAW (USA; pc)	305	aHR 0.63	0.35	1.13	>0.05	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.57**	**0.41**	**0.8**	**0.001**	Good
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.16	0.7	1.94	0.558	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.8	0.26	2.45	0.701	Good
Mechanical Ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.83	0.55	6.11	0.327	Good
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.23	0.74	2.06	0.42	Fair
hospitalized with COVID-19	Hur K (USA; rc)	486	0.56	0.3	1.01	0.058	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.49	0.67	3.29	0.328	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	**1.86**	**1.03**	**3.35**	**NR**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.71**	**0.53**	**0.94**	**0.02**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.89	0.68	1.17	NR	Good
hospitalized with COVID-19 (Black-African)**	Public Health England (UK; rc)	130,091	aHR 1.06	0.96	1.18	0.24	Fair
hospitalized with COVID-19 (Black-Caribbean)**	Public Health England (UK; rc)	130,091	**aHR 1.10**	**1.02**	**1.19**	**0.01**	Fair
hospitalized with COVID-19 (Black-Other)**	Public Health England (UK; rc)	130,091	**aHR 1.35**	**1.18**	**1.55**	**<0.001**	Fair
Hispanic vs. Non-Hispanic White							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.24	0.78	1.98	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.63**	**1.35**	**1.97**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.89	0.69	1.2	0.38	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.56	0.19	1.58	0.271	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	0.83	0.44	1.55	0.565	Good

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.17	0.36	3.82	0.796	Good
Asian vs. non-Hispanic White							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.43	0.91	2.26	0.125	Fair
community sample	Patel AP (UK; pc)	418,794	**1.75**	**1.08**	**2.85**	**0.02**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.29	0.97	1.72	0.08	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.24	0.82	1.9	0.3	Good
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.65**	**1.05**	**2.6**	**0.031**	Fair
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.68**	**1.06**	**2.66**	**0.027**	Fair
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.47	0.85	2.55	0.168	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	1.74	0.9	3.36	NR	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.26	0.91	1.75	0.16	Good
hospitalized with COVID-19 (Asian-Bangladeshi)**	Public Health England (UK; rc)	130,091	**aHR 2.02**	**1.74**	**2.35**	**<0.001**	Fair
hospitalized with COVID-19 (Asian-Chinese)**	Public Health England (UK; rc)	130,091	**aHR 1.23**	**1.04**	**1.58**	**0.02**	Fair
hospitalized with COVID-19 (Asian-Indian)**	Public Health England (UK; rc)	130,091	**aHR 1.22**	**1.13**	**1.32**	**<0.001**	Fair
hospitalized with COVID-19 (Asian-Other)**	Public Health England (UK; rc)	130,091	**aHR 1.13**	**1.02**	**1.25**	**0.02**	Fair
hospitalized with COVID-19 (Asian-Pakistani)**	Public Health England (UK; rc)	130,091	**aHR 1.44**	**1.31**	**1.58**	**<0.001**	Fair

* values are adjusted odds ratio, unless otherwise denoted

**Findings were similar for ethnicity analyses stratified by age category, thus only results for the full sample are shown

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 15. Occupation

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Healthcare workers: laryngologist/intubator vs. assistant							
Hospitalization							
healthcare workers performing tracheal intubations on patients with COVID-19	El-Boghdadly (Multi-country; pc)	1,718	aHR 0.76	0.56	1.04	0.08	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; vs.: versus

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Table 16. Gender identity/sex

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Male vs. female							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.37**	**1.12**	**1.66**	**0.00**	Fair
community sample	Lassale C (UK; pc)	340,966	1.15	0.92	1.44	0.219	Fair
positive for COVID-19	Azar K (USA; rc)	1052	**1.94**	**1.33**	**2.81**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.67**	**2.39**	**3.2**	**<0.001**	Good
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.79**	**1.54**	**2.08**	NR	Good
healthcare workers performing tracheal intubations on patients with COVID-19	El-Boghdadly (Multi-country; pc)	1,718	**aHR 0.74**	**0.55**	**0.99**	**0.04**	Good
Severe disease							
hospitalized with COVID-19	Colaneri M (Italy; rc)	44	17.24	0.50	1000.00	0.1148	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.06	0.85	1.3	0.6	Good
death or transfer to the ICU (composite) among hospitalized for COVID-19	Piano S (Italy; rc)	565	1.42	0.8	2.52	0.236	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.54	0.19	1.52	0.24	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.4	0.87	6.64	0.09	Good
Mechanical ventilation							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	1.22	0.47	3.17	0.682	Fair
hospitalized with COVID-19	Hur K (USA; rc)	486	**1.69**	**1.04**	**2.77**	**0.034**	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.13	0.32	3.4	0.825	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.35**	**1.51**	**7.46**	**0.003**	Good
Mortality							
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	1.15	0.79	1.67	>0.05	Fair
hospitalized with COVID-19	Borobia A (Spain; rc)	2,226	**1.82**	**1.27**	**2.63**	**0.002**	Fair
hospitalized with COVID-19	Busetto L (Italy; rc)	92	2.51	0.37	16.94	0.346	Fair
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.13	0.71	1.81	NR	Good
hospitalized with COVID-19	Giacomelli A (Italy; pc)	233	aHR 1.42	0.62	3.28	0.409	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**2.74**	**1.25**	**5.98**	**0.011**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.77	1.11	0.39	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.23**	**1.16**	**1.33**	**<0.001**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 1.14	0.88	1.47	NR	Good
hospitalized with COVID-19 (20-64 years)	Public Health England (UK; rc)	64,961	aHR 1.99	1.85	2.14	<0.001	Fair
hospitalized with COVID-19 (>64 years)	Public Health England (UK; rc)	63,094	aHR 1.47	1.44	1.51	<0.001	Fair

* values are adjusted odds ratio, unless otherwise denoted

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** the reference category differs slightly across studies
aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 17. Education/literacy level

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Lower education vs. university degree							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.15	0.96	1.37	0.131	Fair

* values are adjusted odds ratio, unless otherwise denoted

CI: confidence interval; pc: prospective cohort; UK: United Kingdom

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Table 18. Socioeconomic status

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Material deprivation (Q2 vs. Q1 least deprived)							
Hospitalization (Townsend Index)**							
community sample	Lassale C (UK; pc)	340,966	1	0.76	1.33	0.989	Fair
Mortality (Index of Multiple Deprivation*)**							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.93**	**1.70**	**2.19**	**<0.001**	Fair
Town Material deprivation (Q3 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	0.99	0.75	1.31	0.937	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.65**	**1.46**	**1.88**	**<0.001**	Fair
Material deprivation (Q4 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	1.24	0.95	1.62	0.116	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.38**	**1.21**	**1.57**	**<0.001**	Fair
Material deprivation (Q5 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	**1.67**	**1.3**	**2.16**	**<0.001**	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.32**	**1.15**	**1.52**	**<0.001**	Fair
Townsend index (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.09**	**1.05**	**1.12**	**<0.001**	Fair
Average income (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.01	0.92	1.11	0.76	Fair
Income percentile (26th to 50th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.2	0.76	1.9	>0.05	Good
Income percentile (51st to 75th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**0.24**	**0.12**	**0.46**	**<0.001**	Good
Income percentile (>=75th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**0.55**	**0.33**	**0.91**	**<0.05**	Good

* values are adjusted odds ratio, unless otherwise denoted

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** Townsend index incorporates unemployment, car & home (non-)ownership & household crowding
*** Index of Multiple Deprivation is used within the UK and incorporates income, employment, education, health, crime, barriers to housing and services, and living environment
aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; Q1-5: quartile (first to fifth); rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 19. Age

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Age (continuous or incremental)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.02**	**1.01**	**1.03**	**0.003**	Fair
community sample	Patel AP (UK; pc)	418,794	**1.02**	**1**	**1.03**	**0.02**	Fair
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.29**	**1.25**	**1.33**	**NR**	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.97	0.93	1.01	0.18	Fair
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	aRR 1.01	1.01	1.02	0.123	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.03	1	1.07	0.059	Good
Mechanical ventilation							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.97	0.93	1	0.091	Fair
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	aRR 1.01	0.99	1.01	0.43	Fair
hospitalized with COVID -19	Kalligeros M (USA; rc)	103	1.02	0.98	1.06	0.271	Good
hospitalized with COVID-19 (quartiles of age)	Palaiodimos L (USA; rc)	200	**1.5**	**1.05**	**2.12**	**0.025**	Good
Severe disease							
positive for COVID-19	Hajifathalian K (USA; rc)	1,059	**1.03**	**NR**	**NR**	**<0.001**	Fair
death or transfer to the ICU (composite) among hospitalized with COVID-19	Piano S (Italy)	565	**1.03**	**1.01**	**1.05**	**0.012**	Good
Mortality							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	**1.21**	**1.05**	**1.39**	**0.007**	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	**2.16**	**1.5**	**3.12**	**<0.01**	Good
hospitalized with COVID-19	Violi F (Italy; rc)	319	**aHR 1.03**	**1.01**	**1.06**	**0.001**	Good
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	**aRR 1.06**	**1.04**	**1.08**	**<0.001**	Fair
hospitalized with COVID-19	Borobia A (Spain; rc)	2,226	**1.11**	**1.09**	**1.12**	**<0.001**	Fair
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	**1.09**	**1.07**	**1.12**	**<0.001**	Fair
hospitalized with COVID-19	Okoh A (USA; rc)	251	**1.04**	**1.01**	**1.06**	**0.003**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**1.73**	**1.13**	**5.98**	**0.011**	Good
hospitalized with COVID-19 (5-year increase)	Price-Haywood EG (USA; rc)	1,382	**aHR 1.18**	**1.13**	**1.24**	**NR**	Good
hospitalized with COVID-19 (10-year increase)	Cummings MJ (USA; pc)	257	**aHR 1.31**	**1.09**	**1.57**	**NR**	Good
hospitalized with COVID-19 (10-year increase)	Giacomelli A (Italy; pc)	233	**aHR 2.08**	**1.48**	**2.9**	**<0.0001**	Good
45-54 vs. ≤45 years old**							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**2.24**	**1.13**	**4.43**	**<0.05**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.14**	**1.76**	**2.59**	**<0.001**	Good
Severe Disease							

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.78	0.54	1.1	0.21	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.95**	**1.16**	**3.31**	**0.01**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR 3.33**	**2.79**	**3.99**	**<0.001**	Fair
50-64 vs. ≤45 years old**							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**2.62**	**1.37**	**4.99**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**3.67**	**3.01**	**4.48**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.32	0.93	1.9	0.12	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 2.63**	**2.06**	**3.35**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**3.18**	**1.93**	**5.21**	**<0.001**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR 8.94**	**7.61**	**10.5**	**<0.001**	Fair
>60 vs. ≤45 years old							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**4.62**	**2.39**	**9.95**	**<0.001**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**8.7**	**6.77**	**11.22**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.73**	**1.19**	**2.5**	**0.004**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	**3.9**	**2.3**	**6.76**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Imam (USA; rc)	1,305	**1.93**	**1.26**	**2.94**	**0.002**	Fair
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 4.99**	**3.99**	**6.25**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**4.83**	**2.93**	**7.96**	**<0.001**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR**	**19.01**	**16.18**	**22.35**	<0.001
>70 vs. ≤45 years old							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**5.68**	**2.6**	**12.38**	**<0.001**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**37.87**	**26.1**	**56.03**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**2.32**	**1.57**	**3.4**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**7.69**	**4.6**	**12.84**	**<0.001**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 8.51**	**6.85**	**10.57**	**<0.001**	Good
>80 vs. ≤45 years old							

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**19.08**	**7.86**	**46.32**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 11.09**	**8.93**	**13.77**	**<0.001**	Good
70-79 vs. 65-69 years old							
Mortality							
hospitalized with COVID-19	Public Health England (UK; rc)	63,094	**aHR 1.55**	**1.47**	**1.64**	**<0.001**	Fair
80-89 vs. 65-69 years old							
Mortality							
hospitalized with COVID-19	Public Health England (UK; rc)	63,094	**aHR 2.15**	**2.05**	**2.26**	**<0.001**	Fair

* values are adjusted odds ratio, unless otherwise denoted
** the reference category differs slightly across studies
aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 20. Other factors

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Smoking (current vs. never)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.92	0.31	2.70	>0.05	Good
community sample	Hamer (UK; pc)	387,109	**aRR 1.36**	**1.08**	**1.71**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	1.25	0.96	1.62	0.095	Fair
community sample	Patel AP (UK; pc)	418,794	0.91	0.66	1.25	0.55	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.59**	**0.43**	**0.81**	**0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.82	0.53	1.3	0.39	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.62	1.38	0.69	Good
Smoking (former vs. never)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.36**	**1.15**	**1.59**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	**1.3**	**1.1**	**1.55**	**0.003**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.69**	**0.56**	**0.85**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.05	0.82	1.3	0.72	Good
Mechanical ventilation							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.05	0.82	1.3	0.72	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.07	0.88	1.31	0.49	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	0.83	0.37	1.87	0.647	Good
Smoking (former vs. current)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.77	0.25	2.35	>0.05	Good
Alcohol consumption (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.04	0.98	1.11	0.21	Fair
Alcohol consumption (never/rarely vs. within guideline)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.57**	**1.31**	**1.88**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	**1.3**	**1.07**	**1.59**	**0.01**	Fair
Alcohol consumption (above vs. within guideline)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.24**	**1.03**	**1.5**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	1.1	0.9	1.34	0.368	Fair
Rarely/never active vs. below guideline							

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Hospitalization							
community sample	Hamer (UK; pc)	387,109	aRR 0.99	0.84	1.18	NR	Fair
Rarely/never active vs. meeting guideline							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.22**	**1**	**1.48**	**0.049**	Fair
Some activity (>10 minutes but below guideline) vs. meeting guideline							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	0.93	0.77	1.13	0.466	Fair
Exceeding vs. meeting guideline							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.24**	**1.03**	**1.5**	**NR**	Fair

* values are adjusted odds ratio, unless otherwise denoted
** the reference category differs slightly across studies
aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Risk factors for severity of COVID-19: a rapid review to inform vaccine prioritization in Canada

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Title: Risk factors for severity of COVID-19: a rapid review to inform vaccine prioritization in Canada

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ABSTRACT: 292 words

Objectives: Rapid review to determine the magnitude of association between potential risk factors and severity of COVID-19, to inform vaccine prioritization in Canada.

Setting: Ovid MEDLINE(R) ALL, Epistemonikos COVID-19 in L·OVE Platform, McMaster COVID-19 Evidence Alerts, and websites were searched to 15 June 2020. Eligible studies were conducted in high-income countries and used multivariate analyses.

Participants: After piloting, screening, data extraction, and quality appraisal were performed by a single experienced reviewer. Of 3,740 unique records identified, 34 were included that reported on median 596 (range 44 to 418,794) participants, aged 42 to 84 years. 19/34 (56%) were good quality.

Outcomes: Hospitalization, intensive care unit admission, length of stay in hospital or intensive care unit, mechanical ventilation, severe disease, mortality.

Results: Authors synthesized findings narratively and appraised the certainty of the evidence for each risk factor-outcome association. There was low or moderate certainty evidence for a large (≥2-fold) magnitude of association between hospitalization in people with COVID-19, and: obesity class III, heart failure, diabetes, chronic kidney disease, dementia, age >45 years, male gender, Black race/ethnicity (vs. non-Hispanic white), homelessness, and low income. Age >60 and >70 years may be associated with large increases in mechanical ventilation and severe disease, respectively. For mortality, a large magnitude of association may exist with liver disease, Bangladeshi ethnicity (vs. British white), age >45 years, age >80 years (vs. 65-69 years), and male gender among 20-64 years (but not older). Associations with hospitalization and mortality may be very large (≥5-fold) for those aged ≥60 years.

Conclusions: Increasing age (especially >60 years) may be the most important risk factor for severe outcomes. High-quality primary research accounting for multiple confounders is needed to better understand the magnitude of associations for severity of COVID-19 with several other factors.

PROSPERO registration: CRD42020198001

Strengths and limitations of this study

- This rapid review captured a broad range of risk factors and outcomes associated with COVID-19 severity.
- Eligible studies reported independent associations through statistical adjustment and were applicable to high-income countries.
- The certainty of evidence was assessed for each risk factor-outcome-population association.
- The rapid approach involved pilot testing each review step with multiple reviewers until a high level of agreement was achieved; then a single experienced completed study selection, data extraction, and risk of bias assessments.
- The review includes studies published up to June 2020; guidance on vaccine prioritization should also consider emerging evidence.

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INTRODUCTION

Novel coronavirus disease 2019 (COVID-19) is an infectious respiratory disease caused by the newly identified Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2),[1] which reached worldwide pandemic status in early March 2020.[2] As of December 7, there were over 65.8 million confirmed cases worldwide and 1.5 million deaths attributed to the virus.[3] Most people who develop COVID-19 will experience mild-to-moderate illness primarily affecting the respiratory system and recover at home.[4] In more severe cases, patients may require specialized care (e.g., admission to hospital and/or intensive care unit [ICU], assisted ventilation)[5] as the disease can progress to respiratory failure and/or affect multiple organ systems.[4]

Given the rapid spread of COVID-19 since its first emergence in late 2019, and potential for severe illness (including death), the development of a preventive vaccine has become a global priority.[6] Vaccine development has been progressing at an unprecedented pace;[7-10] however, the initial vaccine supply is not expected to be sufficient to cover the entire population right away. Therefore, it is of high priority to policymakers to plan for the efficient, effective, and equitable allocation of vaccines when limited supply will necessitate recommendations for the vaccination of certain groups earlier than others. Due to the novel nature of COVID-19, these groups for early vaccination have not yet been established.[11]

The National Advisory Committee on Immunization (NACI) is an expert advisory body that provides advice on the use of vaccines in Canada.[12] At the time of writing, NACI is developing guidance on priority pandemic immunization strategies for COVID-19 vaccination when initial vaccine supply is limited.[11] To inform this guidance, NACI is using its recently published Ethics, Equity, Feasibility and Acceptability (EEFA) Framework[13] to ensure these factors are systematically and comprehensively considered. One of the evidence informed tools that make up this framework is the "Equity Matrix" which has adapted the PROGRESS-Plus model of health determinants and outcomes[14] to ensure important vaccine-specific equity factors are explicitly included. The resulting "P²ROGRESS And Other Factors" framework includes a range of biological and social factors that likely contribute to inequities in health outcomes across population groups (e.g., pre-existing disease/condition, place/state of residence, race/ethnicity/culture/language, occupation, gender identity/sex), but it is not yet clear how each factor might apply to COVID-19 outcomes. A discussion on the use of this Equity Matrix, with evidence from this rapid review, as a critical tool to guide the ethically just allocation of scarce resources is published elsewhere.[15]

With the aim of providing timely, evidence-informed guidance on pandemic vaccine prioritization, NACI required a rigorous and expedited synthesis of the available evidence on population groups that are at increased risk of severe illness and mortality as a result of COVID-19. Responding to this need, we conducted a rapid review to determine the magnitude of association between "P²ROGRESS And Other Factors" and risk of severe outcomes of COVID-19.

METHODS

Review Approach

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Rapid reviews are a form of knowledge synthesis that accelerate the process of conducting a traditional systematic review through streamlining or omitting some steps to produce evidence in a resource-efficient manner.[16] Methods for streamlining one or more stages of the review process are highly dependent on context such as the organizational capacity of the review producer (e.g., trained and experienced personnel), and needs of policy-makers for decision-making;[17, 18] one or more of the systematic review dimensions (i.e., scope, comprehensiveness, rigor/quality control, approach to synthesis, conclusions) may be modified for a rapid review.[17]

The need for empiric evidence to inform the prioritization of pandemic immunization strategies in Canada necessitated a rapid but rigorous approach to synthesizing the currently available data. Therefore, we performed a rapid review informed by traditional systematic review methodology,[19] with several modifications to allow for the evidence to be synthesized on an expedited timeline. We sought stakeholder input on the review question, eligibility criteria, and outcomes, to inform the protocol for applicability and feasibility. We used a single experienced reviewer to select studies, extract data, and assess risk of bias, whereas in traditional systematic reviews these steps typically involve two reviewers to some degree. To ensure methodological rigour, we conducted pilot testing with more than one reviewer at each step; once a high level of agreement was achieved, a single reviewer proceeded with completing the step. In addition, we focused the scope of the review to include only higher quality studies (i.e., using adjusted analysis), and those having high applicability to Canada (e.g., high-income countries with universal-like health care systems).

NACI's High Consequence Infectious Disease Vaccine Working Group was consulted to develop and refine the scope of the review (i.e., priority population(s), risk condition(s)/factor(s), and outcomes of interest), but was not involved in the conduct of the review. The working group was not involved in selection of studies nor the synthesis of findings.

The review was conducted following an *a-priori* protocol (PROSPERO #CRD42020198001). Because there is not yet formal guidance on the reporting of rapid reviews, reporting adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[20]

Literature Search

A health sciences librarian searched Ovid MEDLINE(R) ALL on 15 June 2020 using concepts related to COVID-19, P^{2}ROGRESS And Other Factors, and severe outcomes (Supplement File, Supplement 1). The search was limited to studies published in English or French in 2020. Additionally, the search was limited to populations in countries that are members of the Organisation for Economic Cooperation and Development (OECD),[21] in an effort to include studies of highest relevance to the Canadian context. Editorials and letters were excluded. We supplemented the Medline search by hand-searching Epistemonikos COVID-19 in L·OVE Platform (https://app.iloveevidence.com/topics) and McMaster COVID-19 Evidence Alerts (https://plus.mcmaster.ca/COVID-19/) for relevant prognosis or aetiology studies up to 12 June 2020. A hand-search of relevant websites recommended by the NACI working group was also undertaken, as well as continual surveillance for publication of relevant pre-prints

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located by the search. Searches were exported to an Endnote Library (X9, Clarivate Analytics, Philadelphia, PA) and duplicates removed.

Eligibility Criteria

We included studies published in English or French since 1 January 2020 that reported on the magnitude of association between potential P²ROGRESS And Other Factors and several outcomes of COVID-19 (Supplement File, Supplement 2). Eligible source populations, in order of priority, were people (a) from a general/community sample, (b) with COVID-19 confirmed (by laboratory testing or epidemiologic linkage), and (c) hospitalized with COVID-19. Although considered potentially of interest, studies only including people with a risk factor of interest were not included. We excluded studies where the entire study population had severe disease (e.g., ICU settings). To ensure relevance to the Canadian context, studies had to be conducted in OECD countries;[21] we included OECD studies from countries that do not provide universal (or near universal) coverage for core medical services (i.e., Chile, Greece, Mexico, Poland, the Slovak Republic, and the United States)[22] but considered these to be less applicable to the Canadian context when interpreting the findings. The infection must have been confirmed by laboratory testing or linked epidemiologically (e.g., household contact). Studies including populations with other pandemic-related infections (e.g., Severe Acute Respiratory Syndrome, Middle East Respiratory Syndrome) were excluded if data specific to COVID-19 cases could not be isolated.

The exposures of interest were any P²ROGRESS And Other Factors believed to be associated with differential outcomes across population groups (i.e., pre-existing conditions, place or state of residence, race/ethnicity/culture/language, immigration, refugee status, occupation, gender identity or sex, religion or belief system, education or literacy level, socioeconomic status, social capital, age, and other factors).[23, 24] We did not include as risk factors any signs or symptoms on presentation with COVID. Eligible comparators were those within the same source population (e.g., all hospitalized, as described above) that did not have the P²ROGRESS And Other Factor, or experienced a P²ROGRESS And Other Factor to a different degree (e.g., older vs. younger). We excluded studies of interventions.

Any length of follow-up for outcomes of interest was acceptable. Eligible studies reported on at least one primary outcome (i.e., rate of hospitalization, hospital length of stay, severe disease [as defined by study authors; for example, composite outcome of ICU transfer or death], ICU admission and length of stay, need for mechanical ventilation [MV], and mortality [case fatality or all-cause]). We refer to this range of outcomes as “severe COVID-19” or “severity of COVID-19” throughout the review, though distinct from the composite outcome of “severe disease”. Each of these outcomes are applicable to at least one of the abovementioned eligible populations. In order to prioritize the most rigorous and applicable evidence, we included only prospective and retrospective cohort studies that employed a multivariate analysis and provided results of the independent contribution of P²ROGRESS And Other Factors to severe outcomes, while accounting for potential confounders (minimally age and sex). Pre-prints were included only if they were accepted by a peer-reviewed journal; pre-prints that were later published (between the date of the search and manuscript submission) were included. Government reports from hand-searched websites were eligible.

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Study Selection

All records retrieved by the searches were exported to a Microsoft Office Excel (Microsoft Corporation, Redmond, WA) spreadsheet for screening. After piloting the eligibility criteria on a sample of 70 records, one reviewer independently screened records for inclusion by title/abstract, and those deemed to be potentially relevant were assessed by full text. Uncertainties about the inclusion of any full text study were resolved through consultation with a second reviewer.

Data Extraction

Following a pilot round, one reviewer independently extracted data from each included study into an Excel workbook. We extracted data on (a) population size and demographics, (b) setting, (c) dates of data collection, (d) COVID-19 ascertainment method, (e) co-infections, (f) outcomes reported with definitions for composite outcomes (e.g., severe disease), (f) number of participants analysed, (h) relevant outcome data related to P^2ROGRESS factors of interest (using the most adjusted model, if more than one was reported). For both continuous and dichotomous outcomes, we extracted adjusted relative effect sizes (i.e., odds ratio [OR], risk ratio [RR], hazard ratio [HR]) and measures of variability (95% confidence interval [CI]). A second reviewer was consulted in the event of uncertainty about any of the extracted data. Given the expedited approach, we extracted only data that were reported within the included studies and made no attempt to contact authors for missing or unclear data.

Quality Assessments

To expedite quality assessments, we did not use a formal tool; instead we focused on key variables that were considered to be most relevant to the topic, and that would allow for meaningful stratification of studies by quality. The key variables that we used to assess the quality of the included studies were (a) the extent of adjustment for relevant covariates (i.e., basic adjustment for age and sex, versus more extensive adjustment for numerous potential confounders including comorbidities), (b) follow-up duration and extent of censorship for some outcomes (e.g., $\geq$2 weeks for mortality), and (c) inappropriate or large exclusions from the study and/or analysis (e.g., missing data on risk factor status or analytical variables). Following assessment of these key variables by a single reviewer, studies without concerns for all three criteria were rated good while others were rated fair. A second reviewer was consulted in the case of uncertainty about the assessment of any individual study.

Synthesis

Given substantial clinical (e.g., risk factors and/or comparators examined, outcome definitions) and methodological (varying covariates included in the adjusted analyses, different measures of association) heterogeneity, it was not thought appropriate to pool the studies statistically. Instead, we present a narrative summary of the results across studies for each risk factor. When making conclusions about the association between a P^2ROGRESS And Other Factor and an outcome, we focused primarily on the magnitude of effect rather than statistical significance, which is heavily dependent on sample size. We categorized associations to be small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70), moderate (1.71 to 1.99), large (≥2.00), or very large (≥5.00).[25] When determining the magnitude, we compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies.

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Certainty of Evidence

The expedited approach to evidence synthesis did not allow for a formal appraisal of the certainty of evidence across studies for each P²ROGRESS And Other Factor-Outcome association. Instead, a single reviewer assessed the certainty of the evidence for each association considering relevant components of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach:[26, 27] (a) directness in terms of country (presence of universal healthcare) and source population (community sample vs. hospitalized patients), (b) sample size (n<500 considered small) and magnitude of association, (c) study quality, and (d) consistency of associations (in direction and magnitude) across studies. Bodies of evidence started at high certainty[28] and were rated down for weaknesses in any of the aforementioned characteristics. The level of certainty in associations are referred to using the terms 'uncertain' (no or very low certainty), 'may' (low or some certainty), and 'probably' (moderate certainty).[29] At least two other reviewers confirmed the certainty of evidence appraisals, with disagreements resolved by discussion.

RESULTS

Characteristics of Studies

Of 3,740 unique records identified by the searches, 949 were screened at full text, and 34 studies that reported on 32 unique populations were included in the review (Figure 1; Supplemental File [Supplement 3] shows studies excluded by full text, with reasons).[30-63] Three studies conducted in the United Kingdom (UK)[46, 51, 54] used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study[63] is likely to also be overlapping with these populations, but the degree of overlap is not known.

Table 1 shows the characteristics of the included studies (full details about individual studies in Supplemental File [Supplement 4]). The studies were published between 23 April and 6 July 2020, and half (17/34, 50%) reported on populations in the United States.[30, 31, 38, 39, 43-45, 47-50, 52, 53, 56, 58, 60, 61] The remaining countries represented (Italy,[32, 34-37, 42, 57, 62] Spain,[33] UK[40, 46, 51, 54, 55, 59, 63]) all have universal or universal-like healthcare (one study used data from 17 countries). All studies reported on adults, and the overall median was 596 participants (range 44 to 418,794). The mean or median age of the populations studied ranged from 42 to 84 years (in 32/34 [94%] mean age was 54 to 71 years). Most studies (16/34, 47%) examined the association between risk factors and outcomes in a hospitalized population. Studies reported variable definitions of "severe disease"; we considered them sufficiently similar to be grouped under this outcome. Studies most commonly reported on the independent association of pre-existing conditions (n=27 studies), gender identity or sex (n=18), and race or ethnicity (n=12) with severe outcomes (most commonly hospitalization, n=9). P²ROGRESS And Other Factors not examined in the included studies were immigration or refugee status, religion or belief system, social capital, and substance abuse disorders. There were also no data specific to pregnant women, indigenous populations, people with disabilities, nor different ages in children.

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Table 1. Included studies overview (n=34)

Study design & country (no. of studies)	**P²ROGRESS risk factors (no. of studies*)**	**COVID-19 (no. of studies)**	**Primary outcomes (no. of studies*)**	**Risk of bias (no. of studies)**
Study design: • Retrospective cohort (25) • Prospective cohort (9) Country: • USA (17) • Italy (8) • UK (7 studies in 5 populations) • Spain (1) • Multi-country§ (1)	❖ Pre-existing disease/disability: ○ Underweight, overweight or obesity (12 studies of 10 populations) ○ Cardiovascular (chronic cardiac disease/heart disease, congestive heart failure, coronary artery disease, hyperlipidemia, hypertension) (10 studies of 9 populations) ○ Endocrinologic (diabetes, hyperglycemia) (8) ○ Respiratory (asthma, COPD, chronic bronchitis, lung disease, previous pneumonia) (8 studies of 7 populations) ○ Renal (chronic kidney disease) (5) ○ Malignancy (cancer) (5) ○ Neurological (Alzheimer's, dementia, chronic neurological disorder) (4) ○ Hepatic (liver disease, with or without cirrhosis) (3) ○ Immunocompromised (rheumatic disease, HIV/AIDS) (2) ○ Mental health (2) ○ Gastrointestinal (irritable bowel disease) (1) ❖ Place of residence (4) ❖ Race or ethnicity (11 studies of 10 populations) ❖ Occupation (1) ❖ Gender identity or sex (18 studies of 17 populations) ❖ Education (1) ❖ Socioeconomic status (5 studies of 4 populations) ❖ Age (17 studies of 16 populations) ❖ Other factors: ○ Smoking status (7 studies of 5 populations) ○ Alcohol consumption (3 studies of 1 population) ○ Physical activity (2 studies of 1 population)	Diagnosis: • RT-PCR/PCR (25) • Lab-confirmed (5) • ICD codes (1) • Lab-confirmed or ICD codes (2) • Lab-confirmed or symptoms (1)	• Rate of hospitalization (9) • Hospitalization/self-isolation (composite) (1) • Hospital length of stay (0) • ICU admission (3) • ICU length of stay (0) • Severe disease† (14) • Mortality (19)	Good (19) Fair (15)

* a study may contribute to more than one risk group, or outcome

§ study of healthcare workers includes data from Australia, Canada, Chile, China, Germany, India, Ireland, Italy, Netherlands, New Zealand, Pakistan, Poland, Singapore, South Africa, Sweden, UK, and USA

† severe disease, defined by studies as (number of studies): requiring high-flow oxygen (1); ICU or MV (1); non-invasive ventilation or MV (1); MV (4); ICU or mortality (composite)(4); hospitalization and/or 30-day mortality (composite)(1); MV or mortality (composite)(1); ICU, MV, discharge to hospice, or death (composite)(1)

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BMI: body mass index; COVID-19: novel coronavirus; HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome; ICD: International Classification of Diseases; ICU: intensive care unit; MV: mechanical ventilation; No: number; NR: not reported; RT-PCR; reverse transcription polymerase chain reaction; UK: United Kingdom; USA: United States of America

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Study Quality

The majority of studies (19/34, 56%) were rated as good quality[30, 31, 36, 38, 40-43, 47, 49, 52, 53, 55-60, 62] because they adjusted for age, sex, and pre-existing disease in their analysis, had adequate follow-up of outcomes, and few or no missing data. The remaining studies had flaws in one or more of the three domains that we considered to be most important for this review.

Association Between Risk Factors and Outcomes

Table 2 shows a summary of findings for associations between each reported risk factor and outcomes of interest; detailed data are in the Supplemental File (Supplement 5).

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Table 2. Summary of evidence for associations between risk factors and severe outcomes of COVID-19

Risk factor (at-risk vs. reference population)[a]	**Population**[b]	**Magnitude of association (confidence in association)**[c]**, by outcome** *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Pre-existing conditions						
Body mass index(kg/m²)[d]						
Underweight (<18.5) vs. normal (18.5-24.9)	Hospitalized		- (low)	- (low)		- (low)
Overweight (25.0-29.9) vs. normal	Community sample or positive for COVID-19	- (low)	uncertain	uncertain	- (low)	- (low)
Obesity class I and II (≥30.0) vs. normal	Community sample or positive for COVID-19	+ (low)	+ (low)	+ (low)	- (low)	- (moderate)
Obesity class III (≥40.0) vs. normal	Positive for COVID-19	++ (low)		uncertain	+ (low)	- to + (low)
Respiratory conditions						
Chronic, varied (e.g., asthma, COPD)	Community sample or positive for COVID-19	- (moderate)	uncertain	uncertain	- (moderate)	- (moderate)
Prior pneumonia	Community sample	- (low)				
Cardiovascular disease						
Heart failure	Community sample	- (low)				
	Positive for COVID-19	++ (low)			+ (low)	- (low)
Coronary artery disease, hypertension, hyperlipidemia, composite outcomes	Community sample or positive for COVID-19	- (moderate)	uncertain	uncertain	- (low)	- (low)
Diabetes	Community sample	- (low)				
	Positive for COVID-19	++ (low)	uncertain	- (low)	- (low)	- (moderate)
Liver disease	Positive for COVID-19	- (low)				++ (low)
	Hospitalized					- (low)
Chronic kidney disease	Community sample or positive for COVID-19	++ (moderate)			- (moderate)	- (moderate)
Inflammatory bowel disease	Positive for COVID-19	- (low)			- (low)	
Dementia/chronic neurologic disorders						

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Alzheimer's disease or dementia	Community sample	++ (low)				- (low)
Chronic neurologic disorders	Hospitalized					- (low)
Cancer						
Any cancer	Positive for COVID-19	- (moderate)			- (moderate)	- (moderate)
Hematological malignancy	Positive for COVID-19					+ (low)
Immunocompromised						
Rheumatic disease	Positive for COVID-19	uncertain	uncertain			uncertain
Human immunodeficiency virus	Hospitalized					uncertain
Mental health						
Depression	Positive for COVID-19	- (low)				
Ever visited a psychiatrist	Community sample	- (low)				
Other factors						
Age[d]						
45-54 vs. ≤45 years old	Positive for COVID-19	++ (moderate)			- (low)	++ (low)
50-64 vs. ≤45 years old	Positive for COVID-19	++ (moderate)			- (low)	++ (moderate)
>60 vs. ≤45 years old	Positive for COVID-19	++/+++ (moderate/low)		++ (low)	+ (low)	++/+++ (moderate/low)
>70 or 75 vs. ≤45 years old	Positive for COVID-19	+++ (moderate)			++ (low)	+++ (moderate)
>80 vs. ≤45 years old	Positive for COVID-19	+++ (low)				+++ (low)
70-79 vs. 65-69 years old	Hospitalized					- (moderate)
>80 vs. 65-69 years old	Hospitalized					++ (low)
Increased age (continuous/incremental)[e]	Community sample or positive for COVID-19	Approximately 2-6% relative increase per year (moderate)	- (low)	- (low)	- (low)	Approximately 5-10% relative increase per year

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
						(moderate)
Gender or sex						
Male vs. female (all ages, mean 54 to 73)	Community sample	- (low)				
	Positive for COVID-19	++ (moderate)	uncertain	+ (low)	- (low)	- (moderate)
Male vs. female (20-64 years)[f]	Hospitalized					++ (low)
Race/ethnicity						
Black vs. non-Hispanic white	Community sample or positive for COVID-19	++ (low)	- (moderate)	- (moderate)	- (moderate)	- (moderate)
Hispanic vs. non-Hispanic white	Positive for COVID-19	- (low)	uncertain	- (low)	- (low)	
Asian vs. white	Community sample or positive for COVID-19	- (moderate)	- (low)	- (low)	- (low)	- (moderate)
Asian (Bangladeshi) vs. British white	Hospitalized					++ (low)
Culture/language/immigrant/refugee status						
Place of residence/household size						
Living in a low income area	Positive for COVID-19	- (low)				
Homeless vs. has a home	Positive for COVID-19	++ (low)				
Suburban vs. urban hospital	Hospitalized			uncertain		
1, 3, or 4 vs. 2 household members	Community sample	- (low)				
Occupation						
Laryngologist or intubator vs. assistant	Healthcare workers for COVID-19 patients	- (low)				
Education level						
Lower education vs. university degree	Community sample	- (low)				
Socioeconomic status						

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Risk factor (at-risk vs. reference population)[a]	Population[b]	Magnitude of association (confidence in association)[c], by outcome *Magnitude of associations are shown as: uncertain (no/very low confidence), no important association (-; OR or RR ≤1.70), moderate association (+; 1.71-1.99), large/important association (++; ≥2.00), or very large important association (+++; ≥5.00)*				
		Hospitalization	**ICU admission**	**Mechanical ventilation**	**Severe disease**	**Mortality**
Highest vs. lowest quintile of social deprivation	Community sample	+ (low)				- (moderate)
Income ≤25th vs. >50th or 75th percentile	Positive for COVID-19	++ (low)				
≥Average vs. below average income	Community sample	- (low)				
Smoking						
Current or former vs. never	Community sample or positive for COVID-19	- (moderate)		uncertain	- (low)	- (low)
Alcohol consumption						
Above vs. within guidelines	Community sample or positive for COVID-19	- (low)				
Physical activity level						
Below vs. within guidelines	Community sample or positive for COVID-19	- (low)				

COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; OR: odds ratio; RR: risk ratio

[a] When not listed, the reference group are those without the risk factor.

[b] Outcomes of severe disease (as defined by authors), ICU admission, mechanical ventilation, and mortality are all in a hospitalized population, except for Liver Disease, where findings differed depending on the population denominator used.

[c] A formal assessment of the quality/confidence of the evidence was not performed but was informed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. We determined our confidence in the magnitude of the associations by considering primarily study limitations (risk of bias), consistency in findings across studies, and precision (sample size). Very low confidence indicates that were have no/very low confidence about possible associations; low means that the evidence indicates that there ***may*** be an association; moderate means that the evidence indicates that there ***probably*** is an association. High certainty evidence was not found for any association.

[d] For categorical data for age, and BMI, the reference group differed slightly across studies.

[e] For continuous or incremental data for age, the rate of hospitalization and mortality outcomes, approximately half of the studies analyzed data on a continuum (with the remainder reporting in incremental categories, e.g., 5-year units)

[f] Subgroup data from one study that analyzed the younger population separately

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There was low or moderate certainty of evidence for important/large associations with increased hospitalization in people having confirmed COVID-19, for the following risk factors: obesity class III (body mass index ≥40 kg/m^2; 1 study, n=5,297),[56] heart failure (2 studies, n=6,331),[30, 56] diabetes (2 studies, n=6,331),[30, 56] chronic kidney disease (confirmed COVID-19 or community sample; 2 studies, n=424,073),[54, 56] dementia (1 study, n=418,794),[54] age over 45 years (vs. 45 or younger; 2 studies, n=6,331),[30, 56] male gender (3 studies, n=3,812),[30, 56, 58] black race/ethnicity (vs. non-Hispanic white; confirmed COVID-19 and community samples, 5 studies in 4 populations, n=428,606),[30, 51, 54, 56, 58] homelessness (1 study, n=1,052),[30] and low income (<25th vs. >50th percentile; 1 study, n=1,052).[30] Age over 60 and over 70 years may be associated with important increases in the rate of mechanical ventilation (1 study, n=486)[47] and severe disease (1 study, n=2,725),[56] respectively.

There may be important associations for increased mortality with liver disease (2 studies, n=20,597),[40, 60] Bangladeshi ethnicity (vs. British white; 1 study, n=130,091),[63] and age over 45 years (vs. <45 years; 3 studies, n=87,819).[40, 56, 63] The data were somewhat inconsistent for gender, with most studies showing moderate certainty of no important effect, but one large fair quality study (n=130,091)[63] from the UK that stratified its analysis by age showed that hospitalized males aged 20-64 years (but not older) may be at about two-fold increased risk of mortality compared to females.

Associations with hospitalization and mortality may be very large for those aged over 60 years (2 studies, n=6,331 for hospitalization;[30, 56] 3 studies, n=24,163 for mortality[40, 48, 56]) and are probably very large for those over 70 years (2 studies, n=6,331 for hospitalization;[30, 56] 2 studies, n=22,858 for mortality[40, 56]). One study (n=63,094)[63] directly compared subgroups of older hospitalized adults, showing that compared to those aged 65-69 years, there may be no important association with mortality among adults aged 70-79 years, but the strength of associations may increase about a magnitude of 2-fold for those 80 years and older. Studies treating age on a continuum or across small increments consistently found that the magnitude of association for hospitalization and mortality increased with increasing age (e.g., approximately 2-6% and 5-10% relative increase per year) (3 studies in 2 populations, n=422,275 for hospitalization;[51, 54, 58] 11 studies, n=6,877 for mortality).[32-34, 38, 42, 45, 52, 53, 55, 58, 62]

A moderate magnitude of association may exist between mechanical ventilation (4 studies, n=1,559)[45, 47, 49, 53], ICU admission (2 studies, n=873),[45, 49] and severe disease (1 study, n=2,725)[56] and obesity (body mass index ≥30 or 40 kg/m^2); severe disease and heart failure (1 study, n=2,725);[56] mortality and haematological malignancy (1 study, n=1,183);[59] mechanical ventilation and male gender (4 studies, n=881);[34, 47, 49, 53] and hospitalization and social deprivation (highest vs. lowest quintile; 1 study, n=340,996).[51]

There was moderate certainty evidence for no important increase in hospitalization with chronic respiratory conditions (4 studies in 3 populations, n=425,125),[30, 51, 54, 56] cardiovascular disease apart from heart failure (i.e., coronary artery disease, hypertension, hyperlipidaemia; 4 studies in 3 populations, n=425,125),[30, 51, 54, 56] non-specific cancer (2 studies, n=6,331),[30, 56] Asian race/ethnicity other than Bangladeshi (vs. non-Hispanic white; 3 studies in 2 populations,

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n=424,073),[51, 54, 56] and current or former smoking (5 studies in 3 populations, n=425,125).[30, 46, 51, 54, 56] Additionally, there was moderate certainty evidence for no important increase in severe disease with chronic respiratory conditions (1 study, n=2,725),[56] chronic kidney disease (2 studies, n=2,922),[31, 56] nonspecific cancer (2 studies, n=2,769),[36, 56] and Black race/ethnicity (vs. non-Hispanic white; 2 studies, n=3,030);[43, 56] and no important increase in mortality with obesity (body mass index ≥30 kg/m^2; 6 studies, n=8,716),[42, 45, 50, 53, 56, 58] chronic respiratory conditions (4 studies, n=23,315),[38, 40, 53, 56] diabetes (4 studies, n=23,315), [38, 40, 53, 56] chronic kidney disease (3 studies, n=23,058), nonspecific cancer (3 studies, n=24,041),[40, 56, 59] male gender (9 studies, n=27,875),[32-34, 38, 40, 42, 53, 56, 58] Black (5 studies, n=135,418)[45, 55, 56, 58, 63] or Asian race/ethnicity (vs. non-Hispanic white; 3 studies, n=4,015),[45, 55, 56] and social deprivation (lowest vs. highest quintile; 1 study, n=130,091).[63] Overall, there were few data for the ICU and mechanical ventilation outcomes.

DISCUSSION

Responding to a need for empiric evidence to inform decision-making on Canada's immunization strategies,[11] in this rapid review we synthesized studies employing multivariate analysis to ascertain potential independent associations between "P^{2}ROGRESS And Other Factors" and severe outcomes of COVID-19. Among 22 potential risk factors examined across the included studies, the most important risk factors (i.e., those associated with large/important increased risk or odds; RR or OR ≥2.0) for hospitalization among those with confirmed COVID-19 were several pre-existing chronic health conditions (obesity class III, heart failure, diabetes, chronic kidney disease [community sample or with COVID-19], dementia [community sample]), older age (>45 years vs. younger), male gender, Black race/ethnicity (community sample or with COVID-19), homelessness, and low income (≤25th vs. >50th percentile). Liver disease may be have a large magnitude of association with increased mortality among people with COVID-19; advancing age (>45 years vs. younger) and Bangladeshi ethnicity (vs. British white) are likely to have large magnitude of associations with increased mortality among hospitalized patients. There is evidence to suggest that male gender may be associated with increased mortality among younger (20-64 years), but not older men.

Among the factors that increase the chance of severe outcomes, age seemed to be the most influential; adults older than 60 years may have at least 5 times the magnitude of association with hospitalization and mortality from COVID-19 compared to those aged less than 45 years. This association with increased hospitalization and mortality appears to magnify at least to some degree even for those older than 60 years, with those aged over 80 years possibly having double the magnitude of association for mortality of those aged 65-69 years.

The findings of this rapid review will be used to populate the Equity Matrix of NACI's Ethics, Equity, Feasibility, and Acceptability Framework,[13] which will be a part of a suite of considerations for informing the development of NACI recommendations on priority pandemic immunization strategies when initial COVID-19 vaccine supply is limited. NACI will be using the results of this rapid review and their current understanding of the epidemiology of COVID-19 in Canada to identify distinct inequities associated with COVID-19, potential reasons for these inequities, and suggested interventions to reduce

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inequities and improve access to vaccine when it becomes available. The Equity Matrix applied to COVID-19 with evidence to-date can be found elsewhere.[15]

Limitations of the Evidence

There are several limitations to the evidence base. Though we focused the review on better quality studies that minimally controlled for age and sex, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for. For example, studies reporting on associations between outcomes and age did not adjust for nursing home residency and studies examining race did not account for occupation which may be an important confounder influencing susceptibility to the infection.[63] In addition, it is important to be aware that criteria for COVID-19 testing and hospitalization may differ by place and time, but it is difficult to predict how this may have impacted the findings. In general, many studies conducted testing based on symptoms and the evidence is likely most applicable to these populations. The evidence for mechanical ventilation, ICU admission, and severe disease outcomes was relatively sparse. As we located no evidence meeting our publication date and inclusion criteria to inform the impact of immigration or refugee status, religion or belief system, social capital, substance abuse disorders, pregnancy, Indigenous identity, living with a disability, nor differing levels of risk among children in various age groups, there is a need for high quality primary research (accounting for multiple confounders) to better understand the magnitude of association with these risk factors. Given the rapid emergence of new evidence on the topic, potential associations (or lack of association) for which only low or very low certainty of evidence is available should continue to be reviewed as new primary research is published.

Strengths and Limitations of the Review

Our analysis across a large range of risk factors by detailed outcomes along the continuum of the natural history of COVID-19 disease highlights the methodological rigour and comprehensiveness of the present work. Whereas many rapid reviews omit all assessment of study quality and certainty of the evidence, we felt this was critical for rigour of interpretation and undertook these steps. Given our rapid approach, it is possible that studies were missed and that undetected errors in data exist. We mitigated this by piloting the screening and data extraction process and using experienced reviewers, and it is unlikely that any important studies were missed that would have altered the findings of the review.[64] We conducted risk of bias assessments at the study level, rather than at the outcome level, and incorporated these into our GRADE assessments at the risk factor-outcome-population level. Given that our eligibility criteria narrowed inclusion to higher quality studies that were most applicable to the review objective, it is unlikely that our appraisals of the certainty of evidence would be substantially impacted. Nevertheless, an in-depth evaluation of the study quality at the outcome level may be worth undertaking if feasible in future work.

The evidence presented in this review should be interpreted as most applicable to people with COVID-19 symptoms or in general populations, but not necessarily to those with severe infections because studies focused solely on patients with severe COVID-19 (i.e., in ICU settings) were excluded. Most studies of patients in the ICU setting that we located were relatively small and descriptive in nature,

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such that many would have been otherwise excluded, due to lack of adjustment, or only have been able to provide low or very low certainty evidence due to their lack of precision. Additionally, generalizations to other countries should be made with caution, as high-risk groups in these populations may differ.

FIGURE

Figure 1. PRISMA flow of study selection

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ABBREVIATIONS

COVID-19	Novel coronavirus disease 2019
ICU	Intensive care unit
NACI	National Advisory Committee on Immunization
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
P^2ROGRESS	Pre-existing disease or disability, place of residence, race, ethnicity, culture, language, immigrant/refugee status, occupation, gender, religion/belief system, education, socioeconomic status, social capital, age, and other factors
RR	Risk ratio

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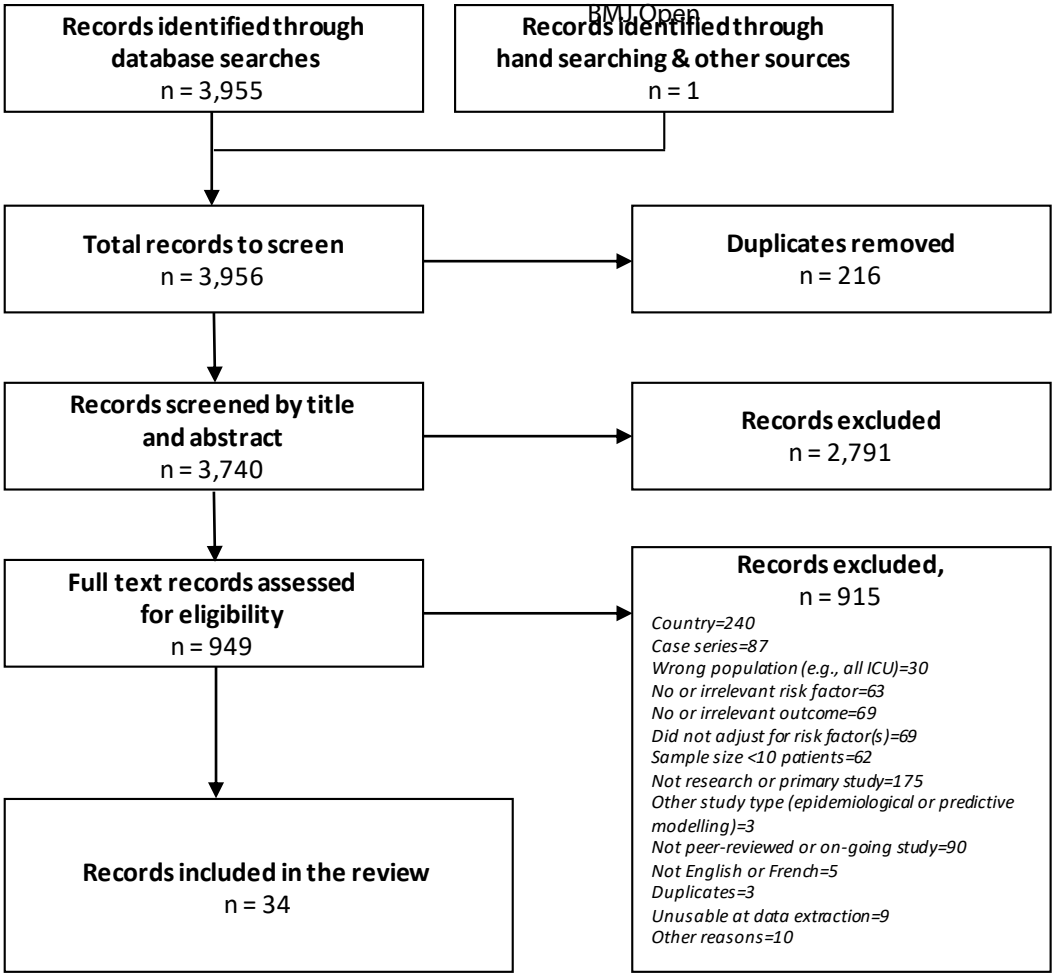

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Figure 1. PRISMA flow of study selection

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Supplement 1. Search strategy

Ovid MEDLINE(R) All 1946 to June 15, 2020

1	(Risk factor* or relative risk or odds ratio or between group* or Regression or multi-variate or multivaria* or covariate or univariate or co-variate or matching or ANOVA or Analysis of variance or ANCOVA or Correlation or Covariance or Principal Component Analysis or cohort* or follow-up or prognos* or predict*).mp.
2	exp cohort studies/ or cohort*.mp.
3	("Associated with" or "Association of" or "impact of" or "Correlated with" or "Impact* on" or characteristics or characterise or features or clinical findings or clinical outcomes or clinical manifestations or clinical course).ti.
4	(clinical data or (clinical adj5 (characteristics or features or manifestations))).tw,kf.
5	1 or 2 or 3 or 4
6	(Mortal* or fatal* or death* or died or discharged alive or poor prognos* or good prognos* or clinical outcome* or adverse outcome* or disease course or clinical course or ((severe* or serious* or critical*) adj4 (ill* or outcome* or course or case or cases or patient* or condition)) or Severity or ((ICU or hospital or intensive care) adj7 (admission* or admit*)) or Ventilator* or ventilation or Hospitaliz* or hospitalis* or (Length adj3 stay)).mp.
7	((pregnan* or maternal or perinatal or birth or neonat* or infant*) adj7 outcome*).mp.
8	6 or 7
9	5 and 8
10	(Coronavirus* or corona-virus* or betacoronavirus* or nCOV* or 2019nCoV or 2019-ncov or covid or covid19 or SARS-CoV*or SARSCov*).mp.
11	limit 10 to yr="2020 -Current"
12	limit 11 to abstracts
13	(11 not 12) and (1 or 2 or 3 or 4 or 6 or 7)
14	9 and 11
15	13 or 14
16	(exp China/ or Iran/ or exp Russia/) not (canada/ or exp united states/ or europe/ or austria/ or belgium/ or exp france/ or exp germany/ or exp united kingdom/ or exp italy/ or spain/ or netherlands/ or exp "scandinavian and nordic countries"/ or australia/ or new zealand/ or mexico/ or chile/ or colombia/ or exp japan/ or korea/ or exp "republic of korea"/ or baltimore/ or berlin/ or boston/ or chicago/ or "district of columbia"/ or london/ or los angeles/ or new orleans/ or new york city/ or paris/ or philadelphia/ or rome/ or san francisco/ or estonia/ or latvia/ or lithuania/ or czech republic/ or hungary/ or poland/ or slovakia/ or slovenia/ or greece/ or luxembourg/ or portugal/ or switzerland/ or israel/ or turkey/)
17	((China or wuhan or hubei or beijing).tw,kf. and china.in.) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle).tw,kf.

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18	((russia* or iran* or tehran or brazil*) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle)).tw,kf.
19	((china or russia or iran or tehran or Brazil) not (canada or italy or italian or spain or spanish or france or french or united kingdom or UK or england or english or NHS or ireland or irish or wales or welsh or scotland or scottish or german* or austria* or sweden or swedish or netherlands or norwegian or norway or finland or finnish or denmark or danish or european or belgium or belgian or Czech or Estonia* or Greece or Greek or Hungar* or Latvia* or Lithuania* or Luxembourg or Iceland* or Poland or Portugal or Slovak Republic or Slovenia* or Switzerland or Japan* or Tokyo or Korea* or Seoul or Chile* or Colombia* or Mexico or Mexican or Israel* or Turkey or Turkish or australia* or new zealand* or united states or USA or american or "U.S." or new york or california* or washington or seattle)).in.
20	15 not (16 or 17 or 18 or 19)
21	limit 20 to (english or french)
22	limit 21 to editorial
23	21 not 22
24	Remove duplicates from 23

Online databases, hand-searched up to June 12, 2020:

Epistimonikos COVID-19 in L*VE Platform (epidemiology, etiology and prognosis questions) at:
https://app.iloveevidence.com/loves/5e6fdb9669c00e4ac072701d?utm=epdb_en

McMaster COVID-19 Evidence Alerts (prognosis or etiology studies) at:
https://plus.mcmaster.ca/COVID-19/

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Supplement 2. Eligibility criteria

Criterion	Include	Exclude
Population/ Exposure	P[2]ROGRESS risk factors[1], with or without infection with COVID-19[2] [1]Risk factors include: – Pre-existing disease/condition, disability (e.g., chronic disease, immunocompromised, pregnancy) – Place/state of residence (e.g., remote, overcrowding, homeless, institutionalization) – Race/ethnicity/culture/language/immigrant/refugee status – Occupation – Gender identity/sex – Religion/belief system – Education/literacy level – Socio-economic status – Social capital (e.g., social support/networks/trust) – Age – Other (risk behaviours e.g., drug and alcohol use disorders, smoking) [2]COVID-19 infection may include lab-confirmed, or epidemiologically-linked cases (e.g., transmission/cases within households). Cases with co-infections (e.g., influenza such as H1N1) will be accepted, but may be analyzed separately from COVID-19-only infections.	Studies including populations with pandemic-related infections (e.g., SARS, MERS) without data isolated for COVID-19
Comparator	Staged, in the following order: i) The same P[2]ROGRESS factor experienced differently or to a different degree (e.g., higher or lower socioeconomic status, higher or lower literacy level) or the absence of a P[2]ROGRESS factor (e.g., non-refugee; no pre-existing disease). ii) None (in some circumstances such as pregnancy and immunocompromised)	Not applicable
Outcomes	Primary outcomes[3] – Hospitalization rate (including readmissions) – Hospital length of stay (binary or continuous) – Admission to ICU – ICU length of stay (binary or continuous) – Need for mechanical ventilation – Case fatality – All-cause fatality – Severe or critical infection (composite; as defined by authors) [3]Data may be extracted for outcomes listed above for the following population denominators, in order of priority: i) General population ii) Population positive for COVID-19 iii) Population hospitalized for COVID-19 iv) Population with a risk factor	COVID-19 infection requiring outpatient treatment (e.g., treatment at primary care office, attendance at ED) Hospitalization for an illness other than COVID-19 infection Outcomes post-hospital discharge (e.g., readmissions unrelated to index COVID-19 infection)
Timing	Any follow-up duration	Not applicable

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Criterion	Include	Exclude
Setting	OECD countries (https://www.oecd.org/about/document/list-oecd-member-countries.htm)	Non-OECD countries
Study design	Prospective and retrospective cohort studies	Studies of interventions/treatments
Language	Full text in English or French; pre-prints if accepted for publication in a peer-reviewer journal.	Language other than English or French

COVID-19: novel coronavirus 2019; ED: emergency department; ICU: intensive care unit; MERS: Middle East Respiratory Syndrome; MV: mechanical ventilation; OECD: Organisation for Economic Co-operation and Development; SARS: severe acute respiratory syndrome

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Supplement 3. Excluded studies

Excluded – case series (n=87)

1. Akdur A, Karakaya E, Ayvazoglu Soy EH, Alshalabi O, Kirnap M, Arslan H, et al. Coronavirus Disease (COVID-19) in Kidney and Liver Transplant Patients: A Single-Center Experience. Exp Clin Transplant. 2020;18(3):270-4.

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14. Caron B, Arondel Y, Reimund J-M. Covid-19 and inflammatory bowel disease: questions on incidence, severity, and impact of treatment? Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2020.

15. Chao JY, Derespina KR, Herold BC, Goldman DL, Aldrich M, Weingarten J, et al. Clinical Characteristics and Outcomes of Hospitalized and Critically Ill Children and Adolescents with Coronavirus Disease 2019 (COVID-19) at a Tertiary Care Medical Center in New York City. The Journal of pediatrics. 2020.

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Supplement 4. Characteristics of included studies

Author, year; Publication date; Country; Study design; Study period & follow-up	Enrolled cohort; Study sample; Mean age (SD), years[1] Male, proportion	COVID-19 diagnosis	P[2]ROGRESS risk factors, adjusted for in multivariate regression analysis[2]	Outcomes	Quality rating & concerns (if any)
Azar K, 2020 May 21 (published) USA Retrospective cohort Jan 1-Apr 8	Patients ≥18 years old who had at least one encounter at a Sutter facility (integrated health system) during the study period for suspected or confirmed COVID-19 infection N=1,052 53 (95% CI 52-54) 49%	ICD codes or evidence in lab records (reports suspected cases but confirmed cases analyzed separately)	Pre-existing condition (asthma, cardiovascular disease, cancer, chronic pulmonary disease, congestive heart failure, type II diabetes, hypertension, depression); Place of residence (homeless); Race/ethnicity; Sex; SES (household income); Age; Other factors (smoking status)	Rate of hospitalization	Good; No major concerns
Bhargava A, 2020 May 30 (published) USA Retrospective cohort Mar 8-Apr 8	Adults admitted to a tertiary care urban academic medical center with COVID-19 N=197 61 (16) 52%	RT-PCR	Pre-existing condition (renal disease); Sex; Age	Severe disease	Good; No major concerns
Bianchetti A, 2020 May 11 (accepted) Italy Retrospective cohort Study period not reported	Adults admitted to acute medical wards with COVID-19 pneumonia in Brescia N=627 71 (13) 47%	RT-PCR	Pre-existing condition (dementia); Sex; Age	Mortality	Fair; Did not report follow-up duration or censorship for outcomes

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Borobia A, 2020 June 4 (published) Spain Retrospective cohort Feb 25-Apr 19; Follow-up to Apr 19	Adults >=18 years old hospitalized in wards or the ED at a university hospital with COVID-19 N=2,226 Median 61 (IQR 46-78) 48%	Lab-confirmed	Pre-existing condition (not clearly specified for multivariate analysis); Sex; Age	Mortality	Fair; No follow-up and censored to patients who died or were discharged by April 19
Busetto L, 2020 May 28 (accepted) Italy Retrospective cohort Mar 14-Apr 11	Adults hospitalized in a medical COVID-19 ward with SARS-CoV-2 related pneumonia N=92 71 (13) 62%	RT-PCR	Pre-existing condition (BMI/obesity, chronic respiratory disease, dementia, type II diabetes); Sex; Age	ICU admission; Noninvasive ventilation or MV (composite); Mortality (in-hospital)	Fair; Did not report follow-up duration or censorship for outcomes
Cecconi M, 2020 May 20 (published) Italy Retrospective cohort Feb 22-Mar 22	Adults ≥18 years old admitted to a hospital with COVID-19 N=239 64 (14) 71%	Positive assay	Pre-existing condition (coronary heart disease); Age	ICU admission or mortality (composite)	Fair; No adjustment for sex and patients were censored as of March 25 (inadequate for patients enrolled on March 22)
Colaneri M, 2020 Apr 23 (published) Italy Retrospective cohort Feb 21-28; Follow-up to Mar 4	Patients admitted to a hospital with COVID-19 N=44 Median 68 (IQR 29) 64%	RT-PCR	Pre-existing condition (tumor); Sex	Severe disease	Good; No major concerns

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Covino M, 2020 May 18 (accepted) Italy retrospective cohort Mar 1-31; Follow-up at 30 days from ED admission	Adults ≥80 years old admitted to ED of urban teaching hospital for suspected COVID-19 N=69 Median 84 (IQR 82-89) 54%	RT-PCR	Pre-existing condition (severe dementia)	Mortality	Fair; No adjustment for age or sex, or other pre-existing conditions
Cummings MJ, 2020 May 19 (published) USA Prospective cohort Mar 2-Apr 1; Follow-up to Apr 28	Adults admitted to high-dependency unit (O2) or ICU (MV) of two hospitals in New York with COVID-19 and were critically ill with acute hypoxaemic respiratory failure N=257 Median 62 (IQR 51-72) 67%	Lab-confirmed	Pre-existing condition (chronic cardiac disease [coronary artery disease or congestive heart failure], chronic pulmonary disease [chronic obstructive pulmonary disease/interstitial lung disease], diabetes, hypertension); Sex; Age	Mortality (in-hospital)	Good; No major concerns
Docherty AB, 2020 May 15 (accepted) UK Prospective cohort Feb 6-Apr 19; Follow-up at least 2 weeks to May 3	Children and adults admitted to 208 acute care hospitals with COVID-19 in England, Wales, and Scotland N=20,133 Median 73 (IQR 58-82) 60%	RT-PCR	Pre-existing condition (chronic cardiac disease, chronic pulmonary disease, asthma, CKD, DM, obesity, chronic neurological disorder, dementia, malignancy, moderate/severe liver disease, mild liver disease, chronic hematologic disease, rheumatologic disorder, HIV/AIDS, malnutrition); Sex; Age; Other factors (smoking status)	Mortality (in-hospital)	Good; No major concerns
D'Silva K, 2020 May 18 (accepted) USA Retrospective cohort	Patients seen at PHS who were ≥18 years of age and had a positive test result for SARS-CoV-2 by PCR clinical assay. *PHS is a large healthcare system that includes tertiary care hospitals (Massachusetts General Hospital	PCR	Pre-existing condition (rheumatic disease)	Rate of hospitalization; ICU admission/ or MV (all with MV); Mortality	Fair; No adjustment for sex, and mortality only adjusted for age and BMI

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Mar 1-Apr 8; Follow-up averaged 29 days	and Brigham and Women's Hospital), community hospitals and primary and specialty outpatient centres in the greater Boston N=156 63 (15) 31%				
El-Boghdadly K, 2020 June 9 (accepted) Multi-country Prospective cohort Mar 23-Jun 2	Healthcare workers from 503 hospitals in 17 countries who performed tracheal intubations, with data for new COVID-19 infection or new COVID-19 symptoms requiring self-isolation or hospitalization. N=1,718 42 (9) 60%	Lab-confirmed or symptoms	Occupation (intubator/laryngologist vs. assistant); Sex	Self-isolation/ hospitalization (composite)	Good; No major concerns
Giacomelli A, 2020 May 22 (published) Italy Prospective cohort Feb 21-Mar 19; Follow-up to Apr 20	Adults hospitalized at one hospital with COVID-19 N=233 Median 61 (IQR 50-72) 62%	RT-PCR	Pre-existing condition (age unadjusted Charlson Comorbidity Index, obesity, anemia); Sex; Age	Mortality	Good; No major concerns
Gold J, 2020 May 8 (published, MMWR weekly report) USA Prospective cohort Mar 1-30; Follow-up to Apr 28	Adults ≥18 years old hospitalized at eight hospitals with COVID-19 N=305 Median 60 (IQR 46-69) 49%	Lab-confirmed	Pre-existing condition (obesity, diabetes, cardiovascular disease, coronary artery disease, congenital heart disease, arrhythmia, chronic lung disease, asthma, chronic obstructive pulmonary disease, immunocompromising conditions/therapies, end-stage renal disease on dialysis, liver disease, hypertension,	MV or mortality (composite)	Good; No major concerns

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			neurologic disorder, chronic liver disease without dialysis, cancer, rheumatologic or autoimmune condition); Race/ethnicity; Sex; Age		
Hajifathalian K, 2020 (#163) May 29 (accepted) USA Retrospective cohort Mar 4-Apr 9; Follow-up to Apr 16	Adults ≥18 years old with and without obesity hospitalized in ED or inpatient wards with COVID-19 N=770 64 (17) 61%	RT-PCR	Pre-existing condition (obesity)	ICU admission; MV; Mortality (in-hospital)	Fair; No adjustment for sex, and 7-day follow-up inadequate for mortality
Hajifathalian K, 2020 (#1154) May 1 (accepted) USA Retrospective cohort Mar 4-Apr 9	Adults with SARS-CoV-2 N=1,059 61 (18) 58%	RT-PCR	Pre-existing condition (number of comorbidities); Age	ICU admission or mortality (composite)	Fair; Unclear if adjustment for sex, and did not report follow-up duration or censorship for outcomes
Hamer M, 2020 May 23 (published) UK Prospective cohort Mar 16-Apr 26	Adults in the community N=387,109 56 (8) 45%	RT-PCR	Pre-existing condition (overweight, obesity); Other factors (smoking status, level of alcohol consumption, level of physical activity)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Hur K, 2020 May 20 (accepted)	Patients hospitalized with laboratory-confirmed COVID-19 infection admitted to any of the 10	RT-PCR	Pre-existing condition (obesity, diabetes, hypertension);	MV	Good; No major concerns

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USA Retrospective cohort Mar 1-Apr 8; Follow-up to Apr 18	hospitals in the Northwestern Memorial HealthCare system spread across the Chicago metropolitan area N=486 Median 59 (IQR 19-101) 56%		Place of residence (suburban vs. urban hospital); Race/ethnicity; Sex; Age; Other factors (smoking status)		
Imam Z, 2020 June 4 (published) USA Retrospective cohort Mar 1-Apr 17; outcome analysis ended Apr 17	Individuals that were hospitalized at a hospital within Beaumont Health with SARS-CoV-2 infection demonstrated by a positive RT-PCR on nasopharyngeal swab per world health organization (WHO)guidance N=1,305 61 (16) 54%	RT-PCR	Pre-existing condition (Charlson Comorbidity Index >3); Age	Mortality (in-hospital)	Fair; Adjustment for Charlson Comorbidity Index score (>3) despite individual comorbidities being significant at univariate analysis, and some missing data for ethnicity (n=5) and smoking status (n=240)
Kalligeros M, 2020 June 12 (published) USA Retrospective cohort Feb 17-Apr 5	All consecutive adult (≥18 years old) patients who had a laboratory confirmed (using a reverse transcriptase–polymerase chain reaction assay) SARS-CoV-2 infection and who were hospitalized at the Rhode Island Hospital, The Miriam Hospital, or Newport Hospital in Rhode Island N=103 Median 60 (IQR 50-72) 61%	RT-PCR	Pre-existing condition (obesity, diabetes, hypertension, heart disease, lung disease);	ICU admission; MV	Good; No major concerns
Klang E, 2020 May 23 (accepted)	Adults hospitalized at five academic hospitals with COVID-19 with BMI information	PCR	Pre-existing condition (obesity, diabetes, heart disease, hypertension, lung disease); Race/ethnicity;	Mortality (in-hospital)	Fair; Did not report follow-up duration or censorship for outcomes, and a

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USA Retrospective cohort Mar 1-May 17	N=3,406 Range 34 to 84 y 58%		Sex; Age		large number of patients who were still hospitalized at time of analysis were excluded (n=1,047)
Lassale C, 2020 May 28 (accepted) UK Prospective cohort Mar 16-Apr 26	Adults in the community N=340,966 56 (8) 45%	RT-PCR	Pre-existing condition (obesity, cardiovascular disease, chronic bronchitis, ever seen a psychiatrist); Place of residence (number in household); Race/ethnicity; Sex; Education/literacy level (university degree vs. lower education); SES (Townsend index); Age; Other factors (smoking status, level of alcohol consumption, level of physical activity)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Okoh A, 2020 June 10 (published) USA Retrospective cohort Mar 10-Apr 10; Follow-up to Apr 20	Adults ≥18 years old of Black/African American or Latino/Hispanic ethnicity hospitalised at a quaternary care teaching hospital in New Jersey with COVID-19 N=251 Median 62 (IQR 49-74) 51%	RT-PCR	Pre-existing condition (coronary artery disease, chronic kidney disease, hypertension, HIV); Race/ethnicity; Sex; Age	Mortality (in-hospital)	Good; No major concerns
Palaiodimos L, 2020 May 14 (accepted) USA Retrospective cohort	Adults (first 200) admitted to the inpatient medicine service or the ICU of a tertiary academic institution with COVID-19 N=200	Lab-confirmed	Pre-existing condition (overweight, obesity, coronary artery disease, chronic kidney disease or end-stage renal disease, chronic obstructive pulmonary disease, diabetes,	MV; Mortality (in-hospital)	Good; No major concerns

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Mar 9-Mar 22; Follow-up 3 weeks to Apr 12	Median 64 (IQR 50-74) 49%		heart failure, hyperlipidemia, obstructive sleep apnea); Sex; Age; Other factors (smoking status)		
Patel AP, 2020 July 6 (published, letter) UK Prospective cohort Mar 16-Apr 14	Adults who were enrolled in a national health database N=418,794 66 (SD not reported) 45%	PCR	Pre-existing condition (obesity, chronic obstructive pulmonary disease, coronary artery disease, diabetes, chronic kidney disease, heart failure, hypertension, ischemic stroke, previous pneumonia, Alzheimer's or dementia); Race/ethnicity; Sex; SES (Townsend index, average income); Age; Other factors (smoking status)	Rate of hospitalization	Fair; One of three publications reporting on same or similar population, significant amount of missing data and data on risk factors are from 2006-2010
Perez-Guzman PN, 2020 April 29 (published, report) UK retrospective cohort Feb 25-Apr 5; Follow-up to Apr 19	Adults hospitalized at three hospitals (with a multi-ethnic catchment) with COVID-19 N=520 Median 67 (IQR 26) 62%	RT-PCR	Pre-existing condition (Elixhauser score, obesity, diabetes, ischaemic heart, hypertension, hyperlipidemia, chronic heart failure, stroke, asthma, chronic obstructive pulmonary disease, dementia, chronic kidney disease, dementia, solid tumor, liver non-cirrhotic, liver cirrhotic, atrial fibrillation, deep vein thrombosis/pulmonary embolism); Race/ethnicity; Sex; Age	Mortality (in-hospital)	Good; No major concerns
Petrilli CM, 2020 May 14 (accepted) USA Prospective cohort	Adults tested for SARS-CoV-2 from 260 outpatient office sites and 4 acute care hospitals N=5,279 Median 54 (IQR 38-66)	RT-PCR	Pre-existing condition (obesity, asthma or chronic obstructive pulmonary disease, chronic lung disease, coronary artery disease, diabetes, heart failure, hyperlipidemia, hypertension, cancer); Race/ethnicity;	Rate of hospitalization; Severe disease; Mortality (in-hospital)	Good; No major concerns

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Mar 1-Apr 8; Follow-up to May 5	50%		Sex; Age; Other factors (smoking status)		
Piano S, 2020 June 11 (published) Italy Retrospective cohort Feb 22-Apr 8	Non-critically ill patients hospitalized with COVID-19 in five internal medicine COVID unit in two regions of Northern Italy N=565 66 (15) 63%	RT-PCR	Pre-existing condition (liver function, Charlson Comorbidity Index); Gender; Age	Transfer to ICU or mortality (composite)	Good; No major concerns
Price-Haywood EG, 2020 May 27 (published) USA Retrospective cohort Mar 1-Apr 11; Follow-up to May 7 for mortality	Adults attending integrated-delivery health system who tested positive for SARS-CoV-2 N=3,481 54 (17) 40%	PCR	Pre-existing condition (Charlson Comorbidity Index score, obesity); Place of residence (residence in low-income area); Race/ethnicity; Sex; Age	Rate of hospitalization; Mortality (in-hospital)	Good; No major concerns
Public Health England June (published) UK Retrospective cohort Mar 20-May 13	Patients admitted to hospital (ward or critical care) with COVID-19 N=130,091 No aggregate data for age (range 2% at <20 y to 29% at ≥80 y) 47%	Lab-confirmed	Race/ethnicity; SES (deprivation); Sex; Age	Mortality	Fair; No adjustment for pre-existing condition(s), and data for risk factors are derived from a 2011 census with some missing data for sex (n=10), age (n=38), and ethnicity (2,024)
Shah V, 2020 June 11 (accepted) UK	Haemato-oncology patients and patients without underlying haematological malignancies (first 80) admitted to the hospital with COVID-19	RT-PCR	Sex; Age	Mortality	Fair; Adjusted for age and sex only, and no explanation of discrepancy in cohort

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Retrospective cohort Until April 15; Follow-up of 30 days	N=1,183 Median 71 (IQR 57-82) 58%				sample size change during study (80 and 68)
Singh S, 2020 (#121) June 2 (accepted) USA Retrospective cohort Jan 20-May 26	Inflammatory bowel disease (IBD) patients diagnosed with COVID-19 and patients diagnosed with COVID-19 and who had no history of or documentation of a diagnosis of IBD ever were included in the non-IBD control group. N=464 No aggregate data for age (IBD vs. non-IBD: mean 51 y [18] vs. 50 y [19]) No aggregate data for sex (IBD vs. non-IBD: 37% vs. 45%)	Lab-confirmed or ICD code for COVID-19	Pre-existing condition (obesity, essential hypertension, chronic lower respiratory diseases [asthma and chronic obstructive pulmonary disease], diabetes, ischemic heart disease, chronic kidney disease, heart failure, cerebrovascular disease); Race/ethnicity; Sex; Age; Other factors (nicotine dependency)	Rate of hospitalization; Mortality	Good; No major concerns
Singh S, 2020 (#1201) Apr 28 (accepted) USA Retrospective cohort Apr 12 (search for patient records)	Patients ≥10 years old with COVID-19, with and without pre-existing liver disease, who presented to a health care organization N=2,780 No aggregate data for age (liver disease vs. non-liver disease: mean 55 y [15] vs. 52 y [18]) 38%	ICD codes per CDC guidelines	Pre-existing condition (obesity, diabetes, hypertension, liver disease with cirrhosis, liver disease without cirrhosis); Race/ethnicity; Age; Other factors (nicotine use)	Rate of hospitalisation; Mortality	Good; No major concerns
Violi F, 2020 June 22 (published) Italy	Consecutively hospitalized adult (≥18 years) patients with laboratory-confirmed COVID-19 and severe acute respiratory syndrome coronavirus-2 (SARS-CoV2)-related	RT-PCR	Pre-existing condition (heart failure); Age	Mortality (in-hospital)	Good; No major concerns

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Retrospective cohort Mar-Apr; Follow-up of 19 days (median, IQR: 12–27 days)	pneumonia, requiring or not mechanical ventilation. N=319 No aggregate data for age (survivors vs. non-survivors: mean 66 y vs. 77 y) No aggregate data for sex (survivors vs. non-survivors: 58% vs. 70%)				

[1] values for age are mean (SD), unless otherwise denoted

[2] risk factors adjusted for in multivariate analysis may differ for outcome(s) reported within a study

CDC: Centers for Disease Control and Prevention; COVID-19: novel coronavirus; ICD: International Classification of Diseases; IQR: interquartile range; MV: mechanical ventilation; RT-PCR/PCR: reverse transcriptase polymerase chain reaction/polymerase chain reaction; SD: standard deviation; SES: socio-economic status; UK: United Kingdom; USA: United States of America; vs.: versus; y: year(s)

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Supplement 5. All results data from the included studies

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Table 1. Body mass index (BMI) and weight

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
BMI unspecified							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.03**	**1.02**	**1.05**	**<0.001**	Fair
community sample	Patel AP (UK; pc)	418,794	**1.04**	**1.03**	**1.06**	**<0.001**	Fair
Underweight (BMI <18.5) vs. normal weight (BMI <25)							
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 0.68	0.21	2.17	0.519	Fair
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 0.48	0.11	2.12	0.333	Fair
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	0.76	0.26	2.22	0.613	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.64	0.84	3.19	0.145	Fair
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.37	0.52	3.64	0.527	Good
Overweight (BMI 25-29.9) vs. normal weight (BMI <25)**							
Hospitalization							
community sample positive for COVID-19	Hamer (UK; pc)	387,109	**aRR 1.32**	**1.09**	**1.6**	**NR**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.3**	**1.07**	**1.57**	**0.007**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.94	0.73	1.2	0.65	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	**11.65**	**3.88**	**34.96**	**<0.001**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.27	0.59	8.83	0.235	Good
Mechanical ventilation							
ventilation (non-invasive + mechanical) among hospitalized with COVID-19	Busetto L (Italy; rc)	92	**4.19**	**1.36**	**12.89**	**0.012**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	3.7	0.6	22.87	0.159	Good
Mortality							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.27	0.03	2.05	0.204	Fair
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.01	0.82	1.25	0.94	Good
Obese class I or greater (BMI ≥30) vs. normal weight (BMI <30)**							
Hospitalization							
community sample positive for COVID-19	Hamer (UK; pc)	387,109	**aRR 1.97**	**1.61**	**2.42**	**NR**	Fair
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.43**	**1.2**	**1.71**	**NR**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.8**	**1.47**	**2.2**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.11	0.85	1.5	0.44	Good

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.76**	**1.24**	**2.48**	**0.001**	Fair
hospitalized with COVID-19 (BMI 30-34.9)	Kalligeros M (USA; rc)	103	2.65	0.64	10.95	0.178	Good
hospitalized with COVID-19 (BMI ≥35)	Kalligeros M (USA; rc)	103	**5.39**	**1.13**	**25.64**	**0.034**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.72**	**1.22**	**2.44**	**0.002**	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**6.85**	**1.05**	**44.82**	**0.045**	Good
hospitalized with COVID-19	Hur K (USA; rc)	486	1.46	0.87	2.46	0.151	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**9.99**	**1.39**	**71.69**	**0.022**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.87**	**1.47**	**10.18**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.15	0.62	2.14	0.663	Fair
hospitalized with COVID-19	Giacomelli A (Italy; pc)	233	**aHR 3.04**	**1.42**	**6.49**	**0.004**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.99	0.77	1.27	NR	Fair
hospitalized with COVID-19, ≤50 y	Klang E (USA; rc)	572	1.1	0.5	2.3	0.755	Fair
hospitalized with COVID-19, >50 y	Klang E (USA; rc)	2,834	1.1	0.9	1.3	0.421	Fair
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.08	0.87	1.36	0.48	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.78**	**1.45**	**9.83**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.45	0.99	2.13	0.05	Good
Obese class III (BMI ≥40) vs. normal weight (BMI <25)**							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.45**	**1.78**	**3.36**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.71**	**1.1**	**2.7**	**0.02**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	1.92	0.92	4	0.08	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.45**	**0.99**	**2.13**	**0.05**	Good
hospitalized with COVID-19, ≤50 y	Klang E (USA; rc)	572	**5.1**	**2.3**	**11.1**	**<0.001**	Fair
hospitalized with COVID-19, >50 y	Klang E (USA; rc)	2,834	**1.6**	**1.2**	**2.3**	**0.004**	Fair

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; BMI: body mass index; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; y: year(s)

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Table 2. Pre-existing disease, unspecified

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
CCI score							
Hospitalization							
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**aHR 1.05**	**1**	**1.1**	**NR**	Good
Severe disease							
ICU transfer or death (composite) among hospitalized for COVID-19	Piano S (Italy)	565	**1.21**	**1.03**	**1.42**	**0.021**	Good
Mortality							
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.99	0.95	1.04	NR	Good
hospitalized with COVID-19	Imam (USA; rc)	1,305	**2.71**	**1.85**	**3.97**	**<0.001**	Fair
Number of comorbidities							
Severe disease							
ICU or death (composite) among positive for COVID-19	Hajifathalian K (USA; rc) #1154	1,059	**1.19**	**NR**	**NR**	**0.021**	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CCI: Charlson Comorbidity Index; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; rc: retrospective cohort; USA: United States of America; y: year(s)

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Table 3. Respiratory disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Asthma							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.52	0.89	2.58	>0.05	Good
Asthma or COPD							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.08	0.88	1.33	0.47	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.99	0.76	1.3	0.93	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.03	0.83	1.29	0.76	Good
Chronic pulmonary disease or COPD							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.8	0.75	4.34	>0.05	Good
community sample	Patel AP (UK; pc)	418,794	**1.51**	**1**	**2.28**	**0.05**	Fair
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.17**	**1.09**	**1.27**	**<0.001**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	2.05	0.76	5.51	0.156	Good
Chronic bronchitis							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.34	0.81	2.21	0.259	Fair
Obstructive sleep apnea							
Mechanical ventilation							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.15	0.4	3.35	0.791	Good
Pneumonia, previous							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.31	0.83	2.05	0.25	Fair
Other respiratory disease (includes one or more of: asthma, COPD, lung disease, interstitial lung disease, and/or pulmonary hypertension)							
ICU admission							
hospitalized with COVID-19 (includes heart failure, coronary artery disease and cardiomyopathy)	Kalligeros M (USA; rc)	103	1.5	0.47	4.82	0.495	Good
Mechanical ventilation							
hospitalized with COVID-19 (includes heart failure, coronary artery disease and cardiomyopathy)	Kalligeros M (USA; rc)	103	0.76	0.2	2.86	0.687	Good
Mortality							
hospitalized with COVID-19 (chronic cardiac disease or congestive heart failure)	Cummings MJ (USA; pc)	257	**aHR 2.94**	**1.48**	**5.84**	**NR**	Good

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* values are adjusted odds ratio, unless otherwise denoted
aHR: adjusted hazards ratio; CI: confidence interval; COPD=Chronic obstructive pulmonary disease; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 4. Cardiovascular disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Cardiovascular disease							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.06**	**0.79**	**1.42**	**0.001**	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	1.32	0.75	2.32	>0.05	Good
Heart failure							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**3.34**	**1.49**	**7.52**	**<0.001**	Good
community sample	Patel AP (UK; pc)	418,794	1.09	0.56	2.14	0.79	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**4.43**	**2.59**	**8.04**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.93**	**1.4**	**2.6**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.43	0.5	4.06	0.501	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.54**	**1.23**	**1.93**	**<0.001**	Good
Coronary artery disease (includes coronary heart disease)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	0.95	0.67	1.36	0.79	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.08	0.81	1.44	0.6	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.71	1.2	0.56	Good
ICU transfer or death (composite) among hospitalized with COVID-19	Cecconi M (Italy; rc)	239	**aHR 2.02**	**1.13**	**3.64**	**0.018**	Fair
Mortality							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.53	0.54	4.34	0.421	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.1	0.9	1.35	0.36	Good
Hyperlipidemia							
Hospitalization							
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.62**	**0.52**	**0.74**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.93	0.75	1.2	0.51	Good
Mechanical ventilation							
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.66	0.78	3.55	0.188	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.98	0.82	1.17	0.79	Good
Hypertension							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	0.98	0.82	1.17	0.84	Fair

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
community sample	Patel AP (UK; pc)	418,794	1.12	0.9	1.39	0.32	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	1.4	0.93	2.1	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.78**	**1.49**	**2.12**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.96	0.75	1.2	0.76	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.79	0.27	2.28	0.663	Good
Mechanical ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.47	0.13	1.66	0.242	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.58	0.89	2.81	NR	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.98	0.78	1.23	0.86	Good
Other cardiovascular disease (includes one or more of: chronic cardiac disease, heart disease, heart failure, coronary artery disease and cardiomyopathy)							
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.52	0.51	4.51	0.448	Good
Mechanical ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	**3.41**	**1.05**	**11.06**	**0.041**	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	**aHR 1.76**	**1.08**	**2.86**	**NR**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.16**	**1.08**	**1.24**	**<0.001**	Good
Ischemic stroke							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	0.94	0.39	2.3	0.90	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 5. Endocrine disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Diabetes							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.52**	**1.14**	**2.03**	**0.01**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.24**	**1.84**	**2.73**	**<0.001**	Good
positive for COVID-19	Azar K (USA; rc)	1,052	**2.17**	**1.33**	**3.53**	**<0.01**	Fair
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.23	0.99	1.5	0.06	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.91	0.71	5.19	0.202	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	**1.64**	**1.02**	**2.66**	**0.046**	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.13	0.73	6.22	0.168	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.26	0.58	2.73	0.557	Good
Mortality							
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.31	0.81	2.1	NR	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	aHR 1.06	0.99	1.14	0.087	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.16	0.55	2.44	0.698	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.01	0.85	1.21	0.87	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 6. Hepatic disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Liver disease							
Hospitalization							
positive for COVID-19	Singh S (USA; rc) #1201	464	**aRR 1.3**	**1.1**	**1.6**	**0.006**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.51**	**1.21**	**1.88**	**<0.001**	Good
positive for COVID-19	Singh S (USA; rc) #1201	464	**aRR 3.0**	**1.5**	**6.0**	**0.001**	Good
positive for COVID-19 (liver disease with cirrhosis)	Singh S (USA; rc) #1201	464	**aRR 4.6**	**2.6**	**8.3**	**<0.001**	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 7. Renal disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Chronic kidney disease							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**2.01**	**1.19**	**3.41**	**0.01**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.6**	**1.89**	**3.61**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.73**	**0.55**	**1**	**0.04**	Good
hospitalized with COVID-19	Bhargava A (USA; rc)	197	**7.4**	**2.5**	**22**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.28**	**1.18**	**1.39**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.73	1.16	0.49	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	1.15	0.49	2.68	0.746	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 8. Gastrointestinal disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Irritable bowel disease							
Hospitalization							
positive for COVID-19	Singh S (USA; rc) #121	464	aRR 1.10	0.74	1.4	0.91	Good
Severe disease							
positive for COVID-19	Singh S (USA; rc) #121	464	aRR 0.93	0.68	1.27	0.66	Good

* values are adjusted odds ratio, unless otherwise denoted

aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; rc: retrospective cohort; USA: United States of America

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Table 9. Neurological disease

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Alzheimer's disease or dementia							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	5.08	0.7	36.68	0.11	Fair
Dementia							
Mortality							
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	**1.84**	**1.08**	**3.13**	**0.024**	Fair
hospitalized with COVID-19 (dementia)	Docherty AB (UK; pc)	20,133	**aHR 1.40**	**1.28**	**1.52**	**<0.001**	Good
hospitalized with COVID-19	Covino M (Italy; rc)	69	**aHR 3.87**	**1.23**	**12.17**	**0.021**	Fair
hospitalized with COVID-19 (chronic neurological disorder)	Docherty AB (UK; pc)	20,133	**aHR 1.17**	**1.06**	**1.29**	**0.001**	Good

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom

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Table 10. Malignancy

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Cancer or tumor							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.96	0.45	2.03	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	0.88	0.65	1.19	0.41	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.3	0.95	1.8	0.1	Good
hospitalized with COVID-19	Colaneri M (Italy; rc)	44	22.199	0.826	596.152	0.0648	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.29**	**1.03**	**1.62**	**0.03**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.13**	**1.02**	**1.24**	**0.017**	Good
positive for COVID-19	Shah V (UK; rc)	1,183	**aHR 1.74**	**1.12**	**2.71**	**0.014**	Fair
Hematological cancer - lymphoid							
Mortality							
positive for COVID-19	Shah V (UK; rc)	1,183	**aHR 1.75**	**1.07**	**2.87**	**0.026**	Fair
Hematological cancer - myeloid							
Mortality							
positive for COVID-19	Shah V (UK; rc)	1,183	aHR 1.70	0.7	4.13	0.244	Fair

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 11. Immunocompromised

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Rheumatic disease							
Hospitalization							
positive for COVID-19	D'Silva K (USA; pc)	156	1.1	0.51	2.38	0.81	Fair
ICU admission							
ICU or mechanical ventilation among hospitalized with COVID-19	D'Silva K (USA; pc)	65	**2.92**	**1.002**	**8.49**	**0.049**	Fair
Mortality							
positive for COVID-19	D'Silva K (USA; pc)	156	1.58	0.31	8.03	0.58	Fair
HIV							
Mortality							
hospitalized with COVID-19	Okoh A (USA; rc)	251	**0.07**	**0.03**	**0.52**	**0.006**	Good

* values are adjusted odds ratio, unless otherwise denoted

CI: confidence interval; COVID-19: novel coronavirus disease 2019; HIV: human immunodeficiency virus; ICU: intensive care unit; pc: prospective cohort; rc: retrospective cohort; USA: United States of America

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Table 12. Mental health

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Depression							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.18	0.57	2.41	>0.05	Good
Ever seen a psychiatrist							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.24	0.99	1.55	0.057	Fair

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America

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Table 13. Place/state of residence

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Low-income geographic area							
Hospitalization							
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.22**	**1.04**	**1.43**	**NR**	Good
Homeless							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	3.25	0.38	28.02	>0.05	Good
Number of people in household (1 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.15	0.93	1.43	0.195	Fair
Number of people in household (3 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.22	0.97	1.55	0.093	Fair
Number of people in household (4 vs. 2)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.59**	**1.26**	**2.01**	**<0.001**	Fair
Suburban vs. urban hospital							
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	1.35	0.82	2.23	0.241	Good

* values are adjusted odds ratio, unless otherwise denoted

CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 14. Race/ethnicity

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Black vs. non-Hispanic White							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**2.66**	**1.82**	**3.91**	**<0.001**	Fair
community sample	Patel AP (UK; pc)	418,794	**2.38**	**1.52**	**3.74**	**<0.001**	Fair
positive for COVID-19	Azar K (USA; rc)	1,052	**2.67**	**1.3**	**5.47**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	0.81	0.65	1.01	0.06	Good
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.96**	**1.62**	**2.37**	**NR**	Good
Severe disease							
hospitalized with COVID-19	Gold JAW (USA; pc)	305	aHR 0.63	0.35	1.13	>0.05	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.57**	**0.41**	**0.8**	**0.001**	Good
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.16	0.7	1.94	0.558	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.8	0.26	2.45	0.701	Good
Mechanical Ventilation							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.83	0.55	6.11	0.327	Good
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.23	0.74	2.06	0.42	Fair
hospitalized with COVID-19	Hur K (USA; rc)	486	0.56	0.3	1.01	0.058	Good
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.49	0.67	3.29	0.328	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	**1.86**	**1.03**	**3.35**	**NR**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**0.71**	**0.53**	**0.94**	**0.02**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 0.89	0.68	1.17	NR	Good
hospitalized with COVID-19 (Black-African)**	Public Health England (UK; rc)	130,091	aHR 1.06	0.96	1.18	0.24	Fair
hospitalized with COVID-19 (Black-Caribbean)**	Public Health England (UK; rc)	130,091	**aHR 1.10**	**1.02**	**1.19**	**0.01**	Fair
hospitalized with COVID-19 (Black-Other)**	Public Health England (UK; rc)	130,091	**aHR 1.35**	**1.18**	**1.55**	**<0.001**	Fair
Hispanic vs. Non-Hispanic White							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.24	0.78	1.98	>0.05	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**1.63**	**1.35**	**1.97**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.89	0.69	1.2	0.38	Good
ICU admission							
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	0.56	0.19	1.58	0.271	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	0.83	0.44	1.55	0.565	Good

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.17	0.36	3.82	0.796	Good
Asian vs. non-Hispanic White							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.43	0.91	2.26	0.125	Fair
community sample	Patel AP (UK; pc)	418,794	**1.75**	**1.08**	**2.85**	**0.02**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	1.29	0.97	1.72	0.08	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.24	0.82	1.9	0.3	Good
ICU admission							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.65**	**1.05**	**2.6**	**0.031**	Fair
Mechanical ventilation							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	**aRR 1.68**	**1.06**	**2.66**	**0.027**	Fair
Mortality							
hospitalized with COVID-19	Hajifathalian (USA; rc) #163	770	aRR 1.47	0.85	2.55	0.168	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	1.74	0.9	3.36	NR	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.26	0.91	1.75	0.16	Good
hospitalized with COVID-19 (Asian-Bangladeshi)**	Public Health England (UK; rc)	130,091	**aHR 2.02**	**1.74**	**2.35**	**<0.001**	Fair
hospitalized with COVID-19 (Asian-Chinese)**	Public Health England (UK; rc)	130,091	**aHR 1.23**	**1.04**	**1.58**	**0.02**	Fair
hospitalized with COVID-19 (Asian-Indian)**	Public Health England (UK; rc)	130,091	**aHR 1.22**	**1.13**	**1.32**	**<0.001**	Fair
hospitalized with COVID-19 (Asian-Other)**	Public Health England (UK; rc)	130,091	**aHR 1.13**	**1.02**	**1.25**	**0.02**	Fair
hospitalized with COVID-19 (Asian-Pakistani)**	Public Health England (UK; rc)	130,091	**aHR 1.44**	**1.31**	**1.58**	**<0.001**	Fair

* values are adjusted odds ratio, unless otherwise denoted

**Findings were similar for ethnicity analyses stratified by age category, thus only results for the full sample are shown

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 15. Occupation

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Healthcare workers: laryngologist/intubator vs. assistant							
Hospitalization							
healthcare workers performing tracheal intubations on patients with COVID-19	El-Boghdadly (Multi-country; pc)	1,718	aHR 0.76	0.56	1.04	0.08	Good

* values are adjusted odds ratio, unless otherwise denoted

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; vs.: versus

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Table 16. Gender identity/sex

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Male vs. female							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.37**	**1.12**	**1.66**	**0.00**	Fair
community sample	Lassale C (UK; pc)	340,966	1.15	0.92	1.44	0.219	Fair
positive for COVID-19	Azar K (USA; rc)	1052	**1.94**	**1.33**	**2.81**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.67**	**2.39**	**3.2**	**<0.001**	Good
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.79**	**1.54**	**2.08**	NR	Good
healthcare workers performing tracheal intubations on patients with COVID-19	El-Boghdadly (Multi-country; pc)	1,718	**aHR 0.74**	**0.55**	**0.99**	**0.04**	Good
Severe disease							
hospitalized with COVID-19	Colaneri M (Italy; rc)	44	17.24	0.50	1000.00	0.1148	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.06	0.85	1.3	0.6	Good
death or transfer to the ICU (composite) among hospitalized for COVID-19	Piano S (Italy; rc)	565	1.42	0.8	2.52	0.236	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.54	0.19	1.52	0.24	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	2.4	0.87	6.64	0.09	Good
Mechanical ventilation							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	1.22	0.47	3.17	0.682	Fair
hospitalized with COVID-19	Hur K (USA; rc)	486	**1.69**	**1.04**	**2.77**	**0.034**	Good
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.13	0.32	3.4	0.825	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**3.35**	**1.51**	**7.46**	**0.003**	Good
Mortality							
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	1.15	0.79	1.67	>0.05	Fair
hospitalized with COVID-19	Borobia A (Spain; rc)	2,226	**1.82**	**1.27**	**2.63**	**0.002**	Fair
hospitalized with COVID-19	Busetto L (Italy; rc)	92	2.51	0.37	16.94	0.346	Fair
hospitalized with COVID-19	Cummings MJ (USA; pc)	257	aHR 1.13	0.71	1.81	NR	Good
hospitalized with COVID-19	Giacomelli A (Italy; pc)	233	aHR 1.42	0.62	3.28	0.409	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**2.74**	**1.25**	**5.98**	**0.011**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.77	1.11	0.39	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 1.23**	**1.16**	**1.33**	**<0.001**	Good
hospitalized with COVID-19	Price-Haywood EG (USA; rc)	1,382	aHR 1.14	0.88	1.47	NR	Good
hospitalized with COVID-19 (20-64 years)	Public Health England (UK; rc)	64,961	aHR 1.99	1.85	2.14	<0.001	Fair
hospitalized with COVID-19 (>64 years)	Public Health England (UK; rc)	63,094	aHR 1.47	1.44	1.51	<0.001	Fair

* values are adjusted odds ratio, unless otherwise denoted

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** the reference category differs slightly across studies
aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 17. Education/literacy level

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Lower education vs. university degree							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	1.15	0.96	1.37	0.131	Fair

* values are adjusted odds ratio, unless otherwise denoted
CI: confidence interval; pc: prospective cohort; UK: United Kingdom

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Table 18. Socioeconomic status

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Material deprivation (Q2 vs. Q1 least deprived)							
Hospitalization (Townsend Index)**							
community sample	Lassale C (UK; pc)	340,966	1	0.76	1.33	0.989	Fair
Mortality (Index of Multiple Deprivation*)**							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.93**	**1.70**	**2.19**	**<0.001**	Fair
Town Material deprivation (Q3 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	0.99	0.75	1.31	0.937	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.65**	**1.46**	**1.88**	**<0.001**	Fair
Material deprivation (Q4 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	1.24	0.95	1.62	0.116	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.38**	**1.21**	**1.57**	**<0.001**	Fair
Material deprivation (Q5 vs. Q1)							
Hospitalization (Townsend Index)							
community sample	Lassale C (UK; pc)	340,966	**1.67**	**1.3**	**2.16**	**<0.001**	Fair
Mortality (Index of Multiple Deprivation)							
Hospitalized	Public Health England (UK; rc)	130,091	**aHR 1.32**	**1.15**	**1.52**	**<0.001**	Fair
Townsend index (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	**1.09**	**1.05**	**1.12**	**<0.001**	Fair
Average income (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.01	0.92	1.11	0.76	Fair
Income percentile (26th to 50th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	1.2	0.76	1.9	>0.05	Good
Income percentile (51st to 75th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**0.24**	**0.12**	**0.46**	**<0.001**	Good
Income percentile (>=75th vs. 25th and below)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**0.55**	**0.33**	**0.91**	**<0.05**	Good

* values are adjusted odds ratio, unless otherwise denoted

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** Townsend index incorporates unemployment, car & home (non-)ownership & household crowding
*** Index of Multiple Deprivation is used within the UK and incorporates income, employment, education, health, crime, barriers to housing and services, and living environment
aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; pc: prospective cohort; Q1-5: quartile (first to fifth); rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 19. Age

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Age (continuous or incremental)							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.02**	**1.01**	**1.03**	**0.003**	Fair
community sample	Patel AP (UK; pc)	418,794	**1.02**	**1**	**1.03**	**0.02**	Fair
positive for COVID-19	Price-Haywood EG (USA; rc)	3,481	**1.29**	**1.25**	**1.33**	**NR**	Good
ICU admission							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.97	0.93	1.01	0.18	Fair
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	aRR 1.01	1.01	1.02	0.123	Fair
hospitalized with COVID-19	Kalligeros M (USA; rc)	103	1.03	1	1.07	0.059	Good
Mechanical ventilation							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	0.97	0.93	1	0.091	Fair
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	aRR 1.01	0.99	1.01	0.43	Fair
hospitalized with COVID -19	Kalligeros M (USA; rc)	103	1.02	0.98	1.06	0.271	Good
hospitalized with COVID-19 (quartiles of age)	Palaiodimos L (USA; rc)	200	**1.5**	**1.05**	**2.12**	**0.025**	Good
Severe disease							
positive for COVID-19	Hajifathalian K (USA; rc)	1,059	**1.03**	**NR**	**NR**	**<0.001**	Fair
death or transfer to the ICU (composite) among hospitalized with COVID-19	Piano S (Italy)	565	**1.03**	**1.01**	**1.05**	**0.012**	Good
Mortality							
hospitalized with COVID-19	Busetto L (Italy; rc)	92	**1.21**	**1.05**	**1.39**	**0.007**	Fair
hospitalized with COVID-19	Perez-Guzman PN (UK; rc)	520	**2.16**	**1.5**	**3.12**	**<0.01**	Good
hospitalized with COVID-19	Violi F (Italy; rc)	319	**aHR 1.03**	**1.01**	**1.06**	**0.001**	Good
hospitalized with COVID-19	Hajifathalian K (USA; rc)	770	**aRR 1.06**	**1.04**	**1.08**	**<0.001**	Fair
hospitalized with COVID-19	Borobia A (Spain; rc)	2,226	**1.11**	**1.09**	**1.12**	**<0.001**	Fair
hospitalized with COVID-19	Bianchetti A (Italy; rc)	627	**1.09**	**1.07**	**1.12**	**<0.001**	Fair
hospitalized with COVID-19	Okoh A (USA; rc)	251	**1.04**	**1.01**	**1.06**	**0.003**	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	**1.73**	**1.13**	**5.98**	**0.011**	Good
hospitalized with COVID-19 (5-year increase)	Price-Haywood EG (USA; rc)	1,382	**aHR 1.18**	**1.13**	**1.24**	**NR**	Good
hospitalized with COVID-19 (10-year increase)	Cummings MJ (USA; pc)	257	**aHR 1.31**	**1.09**	**1.57**	**NR**	Good
hospitalized with COVID-19 (10-year increase)	Giacomelli A (Italy; pc)	233	**aHR 2.08**	**1.48**	**2.9**	**<0.0001**	Good
45-54 vs. ≤45 years old**							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**2.24**	**1.13**	**4.43**	**<0.05**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**2.14**	**1.76**	**2.59**	**<0.001**	Good
Severe Disease							

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.78	0.54	1.1	0.21	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.95**	**1.16**	**3.31**	**0.01**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR 3.33**	**2.79**	**3.99**	**<0.001**	Fair
50-64 vs. ≤45 years old**							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**2.62**	**1.37**	**4.99**	**<0.01**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**3.67**	**3.01**	**4.48**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.32	0.93	1.9	0.12	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 2.63**	**2.06**	**3.35**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**3.18**	**1.93**	**5.21**	**<0.001**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR 8.94**	**7.61**	**10.5**	**<0.001**	Fair
>60 vs. ≤45 years old							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**4.62**	**2.39**	**9.95**	**<0.001**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**8.7**	**6.77**	**11.22**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**1.73**	**1.19**	**2.5**	**0.004**	Good
Mechanical ventilation							
hospitalized with COVID-19	Hur K (USA; rc)	486	**3.9**	**2.3**	**6.76**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Imam (USA; rc)	1,305	**1.93**	**1.26**	**2.94**	**0.002**	Fair
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 4.99**	**3.99**	**6.25**	**<0.001**	Good
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**4.83**	**2.93**	**7.96**	**<0.001**	Good
hospitalized with COVID-19	Public Health England (UK; rc)	64,961	**aHR**	**19.01**	**16.18**	**22.35**	<0.001
>70 vs. ≤45 years old							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**5.68**	**2.6**	**12.38**	**<0.001**	Good
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**37.87**	**26.1**	**56.03**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**2.32**	**1.57**	**3.4**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	**7.69**	**4.6**	**12.84**	**<0.001**	Good
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 8.51**	**6.85**	**10.57**	**<0.001**	Good
>80 vs. ≤45 years old							

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Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	**19.08**	**7.86**	**46.32**	**<0.001**	Good
Mortality							
hospitalized with COVID-19	Docherty AB (UK; pc)	20,133	**aHR 11.09**	**8.93**	**13.77**	**<0.001**	Good
70-79 vs. 65-69 years old							
Mortality							
hospitalized with COVID-19	Public Health England (UK; rc)	63,094	**aHR 1.55**	**1.47**	**1.64**	**<0.001**	Fair
80-89 vs. 65-69 years old							
Mortality							
hospitalized with COVID-19	Public Health England (UK; rc)	63,094	**aHR 2.15**	**2.05**	**2.26**	**<0.001**	Fair

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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Table 20. Other factors

Risk factor; Outcome among population	Study	Total number of patients	Adjusted odds ratio*	95% CI lower bound	95% CI upper bound	p-value	Quality rating
Smoking (current vs. never)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.92	0.31	2.70	>0.05	Good
community sample	Hamer (UK; pc)	387,109	**aRR 1.36**	**1.08**	**1.71**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	1.25	0.96	1.62	0.095	Fair
community sample	Patel AP (UK; pc)	418,794	0.91	0.66	1.25	0.55	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.59**	**0.43**	**0.81**	**0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.82	0.53	1.3	0.39	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	0.92	0.62	1.38	0.69	Good
Smoking (former vs. never)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.36**	**1.15**	**1.59**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	**1.3**	**1.1**	**1.55**	**0.003**	Fair
positive for COVID-19	Petrilli CM (USA; pc)	5,279	**0.69**	**0.56**	**0.85**	**<0.001**	Good
Severe disease							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.05	0.82	1.3	0.72	Good
Mechanical ventilation							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.05	0.82	1.3	0.72	Good
Mortality							
hospitalized with COVID-19	Petrilli CM (USA; pc)	2,725	1.07	0.88	1.31	0.49	Good
hospitalized with COVID-19	Palaiodimos L (USA; rc)	200	0.83	0.37	1.87	0.647	Good
Smoking (former vs. current)							
Hospitalization							
positive for COVID-19	Azar K (USA; rc)	1,052	0.77	0.25	2.35	>0.05	Good
Alcohol consumption (continuous)							
Hospitalization							
community sample	Patel AP (UK; pc)	418,794	1.04	0.98	1.11	0.21	Fair
Alcohol consumption (never/rarely vs. within guideline)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.57**	**1.31**	**1.88**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	**1.3**	**1.07**	**1.59**	**0.01**	Fair
Alcohol consumption (above vs. within guideline)							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.24**	**1.03**	**1.5**	**NR**	Fair
community sample	Lassale C (UK; pc)	340,966	1.1	0.9	1.34	0.368	Fair
Rarely/never active vs. below guideline							

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Hospitalization							
community sample	Hamer (UK; pc)	387,109	aRR 0.99	0.84	1.18	NR	Fair
Rarely/never active vs. meeting guideline							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	**1.22**	**1**	**1.48**	**0.049**	Fair
Some activity (>10 minutes but below guideline) vs. meeting guideline							
Hospitalization							
community sample	Lassale C (UK; pc)	340,966	0.93	0.77	1.13	0.466	Fair
Exceeding vs. meeting guideline							
Hospitalization							
community sample	Hamer (UK; pc)	387,109	**aRR 1.24**	**1.03**	**1.5**	**NR**	Fair

* values are adjusted odds ratio, unless otherwise denoted

** the reference category differs slightly across studies

aHR: adjusted hazards ratio; aRR: adjusted risk ratio; CI: confidence interval; COVID-19: novel coronavirus disease 2019; ICU: intensive care unit; NR: not reported; pc: prospective cohort; rc: retrospective cohort; UK: United Kingdom; USA: United States of America; vs.: versus

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1, rapid review
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3 (Abstract); 5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7

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PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8; Supplement 3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8; Supplement 4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplement 4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Supplement 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	16-17; Table 2; Supplement 5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19

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FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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