Crynodeb cyflym

Cwestiynau:

1. Pa grwpiau poblogaeth sydd fwyaf tebygol o brofi'n bositif am COVID-19?
2. Unigolion o ba leoliadau sydd fwyaf tebygol o brofi'n bositif am COVID-19?
3. Pa grwpiau poblogaeth sydd â pherygl uwch o gael eu derbyn i'r ysbyty oherwydd haint COVID-19?
4. Pa grwpiau poblogaeth sydd â risg uwch o fod angen triniaeth mewn uned gofal dwys oherwydd haint COVID-19?
5. Pa grwpiau poblogaeth sydd â risg uwch o farw o haint COVID-19?

Crynodeb byr:

Nodwyd 80 o adolygiadau systematig (SRs) o chwiliad o'r llenyddiaeth a gynhaliwyd rhwng 12 a 15 Hydref, 2020. O'r rhain, ystyriwyd 28 yn ddefnyddiol yn dilyn arfarniad beirniadol, cymharu canfyddiadau ac ystyriaeth ynghylch pa mor ddiweddar oedd y dystiolaeth. Pennwyd ffactorau risg yn dilyn adolygiad o ddata a gyflwynwyd yn yr adolygiadau systematig hyn. Nid oedd data ar gael i ateb yr holl gwestiynau ar gyfer pob ffactor risg posibl.

Profi'n bositif	**Derbyn i'r ysbyty**	**Derbyn i uned gofal dwys**	**Marwolaeth**
Ffactor Risg Tebygol (*cynnydd mewn risg arwyddocaol yn ystadegol mewn amcangyfrifon risg wedi eu haddasu)*			
Ethnigrwydd Du ac Asiaidd	Oed	Gordewdra	Oed
	Gwryw		Gwryw
	Gordewdra		Gordewdra
	Clefyd Cronig yr Arennau		Clefyd Cronig yr Arennau
Ffactor risg posibl (*cynnydd mewn risg arwyddocaol yn ystadegol mewn amcangyfrifon risg heb eu haddasu)*			
	Ethnigrwydd Du	Ethnigrwydd Asiaidd	Ethnigrwydd Asiaidd
	Cyn-smygwyr	Oed	Cyn-smygwyr
	Digartrefedd	Cyn-smygwyr	Hanes o smygu
	Amddifadedd cymdeithasol uwch	Hanes o smygu	Amddifadedd Cymdeithasol uwch
	Diabetes	CVD	CVD
	Clefyd Alzheimer / dementia		Diabetes
			COPD
			Clefyd yr Iau

Crynodeb cyflym			
			Canser
			Clefyd Alzheimer / dementia
			Clefydau Niwrolegol

Efallai mai eglurhad o rôl risgiau sydd yn cynyddu trosglwyddiad COVID-19 mewn rhai grwpiau ethnig ac awgrym o rywfaint o'r ymchwil yn ymwneud â phenderfynyddion ehangach yw'r wybodaeth atodol mwyaf defnyddiol yn y gwaith hwn. Mae'r crynodeb yn cadarnhau ffactorau risg hysbys oed, gwrywod a gordewdra.

Mae'r crynodeb hwn yn ddefnyddiol i nodi'r amcangyfrifon o ffactorau risg presennol a geir mewn adolygiadau systematig. Ni wnaeth y gwaith hwn ystyried data sydd ar gael mewn llenyddiaeth lwyd ac mae'n bwysig nodi bod y maes hwn yn esblygu'n gyflym ac mae mwy o ddata'n ymddangos yn dyddiol. Gallai hyn arwain at newidiadau yn ein dealltwriaeth o ffactorau risg.

Efallai fod Cell Ataliaeth COVID-19 yn dymuno ystyried graddfa'r risgiau a nodwyd a mynychter ffactorau o'r fath yn y boblogaeth wrth benderfynu sut i ddefnyddio'r wybodaeth yma.

Cefndir

Nod cell ataliaeth COVID-19 yn PHW yw ategu gweithredoedd yn y Cynllun Rheoli Coronafeirws ar gyfer Cymru trwy nodi dulliau newid ymddygiad posibl i leihau trosglwyddiad y feirws a diogelu adrannau penodol o'r boblogaeth sydd â risg o ganlyniadau niweidiol. Nod y crynodeb cyflym hwn oedd canfod cyflwr presennol gwybodaeth ynghylch pa adrannau o'r boblogaeth ac ym mha leoliadau y mae risg cynyddol o heintio, derbyniadau i'r ysbyty, derbyniadau i unedau gofal dwys, a marwolaeth yn sgîl COVID-19.

Canfyddiadau

Nododd sgrinio a chwiliad llenyddiaeth cyflym 80 o adolygiadau systematig, gafodd eu harfarnu'n feirniadol (Protocol a Chwiliad ar gael ar gais). Mae diagram llif o'r broses sgrinio ar gael yn Atodiad 1. Cafodd adolygiadau eu hidlo yn dilyn arfarniad beirniadol i gadw'r ymchwil eilaidd â'r dulliau mwyaf cadarn a thryloyw, cynnwys data o gyd-destunau cyffredinoledig (gwledydd OECD) a cheisio amlygu papurau â'r canfyddiadau mwyaf diweddar tra'n lleihau ailadrodd yn sgîl astudiaethau'n gorgyffwrdd.

Yn dilyn y broses hon, echdynnwyd data o 28 o adolygiadau systematig. Mae cyfeiriadau at adolygiadau systematig na echdynnwyd data wrthynt, gyda'r rhesymau am beidio echdynnu, ar gael yn Atodiad 2. Dyrannwyd categori factor risg yn seiliedig ar arwyddocâd ystadegol y canfyddiadau ac wrth ystyried a oedd amcangyfrifon risg o'r astudiaethau arsylwi wedi cael eu haddasu ar gyfer dryswch yn codi o ffactorau ychwanegol. Gwiriodd ail adolygwr ddyraniad y categorïau risg. Mae canlyniad y broses hon wedi ei ddisgrifio yn Nhabl 1; mae allwedd fanwl i'r dyraniad uwchben y tabl. Efallai mai eglurhâd o rôl risgiau sydd yn cynyddu trosglwyddiad COVID-19 mewn rhai grwpiau ethnig ac arwydd o rywfaint o ymchwil yn ymwneud â phenderfynyddion ehangach yw'r wybodaeth atodol mwyaf defnyddiol o'r gwaith hwn.

Cyfyngiadau:

Mae'r defnydd o'r crynodeb hwn wedi ei gyfyngu gan y dull a ddefnyddir i'w gynhyrchu. Cynhaliwyd sgrinio, arfarnu beirniadol, echdynnu data a hidlo adolygiadau systematig gan adolygydd unigol gyda gwirio cysondeb yn gyfyngedig.

Mae'r crynodeb hwn yn ddefnyddiol yn nodi amcangyfrifon factor risg presennol a geir mewn adolygiadau systematig. Ni wnaeth y gwaith hwn ystyried data sydd ar gael mewn llenyddiaeth lwyd, fel adroddiadau'r llywodraeth, ac mae'n bwysig nodi bod y maes hwn yn esblygu'n gyflym a bod mwy o ddata'n ymddangos yn ddyddiol. Gallai hyn arwain at newidiadau yn ein dealltwriaeth o ffactorau risg, yn arbennig wrth i ddadansoddiadau sydd yn creu amcangyfrifon risg wedi eu haddasu weithiau gael eu cyhoeddi ar ôl amcangyfrifon heb eu haddasu, pan fydd clefydau newydd yn ymddangos.

Gall adolygiadau systematig sydd wedi eu cynnal yn dda gael eu cyfyngu gan argaeledd data. Yn ein tablau echdynnu data rydym wedi amlinellu:

- Cyfyngiadau'r ymchwil sydd wedi ei chynnwys yn y golofn *Pethau i'w hystyried*

- Cyfyngiadau'r dulliau adolygu systematig ar wahân.

Mae'r crynodeb cyflym hwn yn gwneud defnydd sylweddol o un adolygiad systematig da sydd yn aros i gael ei gyhoeddi[1]. Mae hyn am fod yr adolygiad hwn yn cynnwys, dim ond ymchwil a gynhaliwyd mewn gwledydd OECD ac yn darparu amcangyfrifon risg sydd, fel lleiafswm, wedi cael eu haddasu ar gyfer effeithiau drysu oed a rhyw. Cynhaliwyd yr adolygiad hwn gan ymchwilwyr o Canada er mwyn nodi'r rheiny ddylai gael blaenoriaeth o ran cael eu brechu. Dyma'r unig adolygiad a roddodd syniad o'r ymchwil sydd ar gael mewn perthynas â phenderfynyddion ehangach iechyd. Roedd yn rhoi eglurder mawr o ran ei ddata ategol ar y poblogaethau y mae'n eu defnyddio i greu amcangyfrifon risg. Seiliodd ei gasgliadau trosfwaol ar faint yr amcangyfrifiad o'r risg sydd wedi ei addasu ac asesiad o sicrwydd trwy ystyried cydrannau perthnasol GRADE.

Yn ein crynodeb (Tabl 1) nid ydym wedi ystyried maint y risg cynyddol, dim ond ei arwyddocâd ystadegol. Gall Cell Ataliaeth COVID-19 ddymuno ystyried maint y risgiau a nodir a mynychter ffactorau o'r fath wrth benderfynu sut i ddefnyddio'r wybodaeth yma. Mae'r data yma ar gael yn y tablau echdynnu data.

Fel arfer gydag astudiaethau arsylwi, gall amcangyfrifon risg gael eu drysu gan ffactorau hysbys ac anhysbys. Mae adolygwyr PHW wedi amlygu ac ystyried ble mae rhywfaint o addasiad wedi cael ei wneud i roi cyfrif am hyn. Mae addasiadau o'r fath yn debygol o fod yn anghyflawn ar yr adeg hon gan mai clefyd newydd yw hwn. Mae rhyngweithio rhwng risgiau lluosog â dryswyr gwahanol posibl hefyd yn arbennig o anodd ei asesu.

Key

	SRs do not include data relevant to answer this question for this risk factor
No	Not currently identified as a risk factor, no statistically significant association found in adjusted risk estimates from observational studies identified by systematic reviews
Unlikely	No statistically significant association found in observational studies identified by systematic reviews, but risk estimates were unadjusted for confounders
Possible	Risk factor suggested from statistically significant associations found in unadjusted risk estimates from observational studies, or from adjusted risk estimates of low certainty from a single review, or where adjusted risk estimates change in significance depending on the source population
Probable	Risk factor suggested from statistically significant associations found in risk estimates, adjusted for confounders, from observational studies identified by systematic reviews
Uncertain	No or very low confidence in associations stated by SR authors or PHW reviewers
Limited data	Risk estimates have been sought by systematic reviewers but not identified or associations may be underpowered

Table 1. Potential risk factors

Note: references marked with are a preprint whereas those with ** are a corrected proof.*

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
Characteristics					
Age		Probable [1*]	Possible [1*, 2*] (composite measure- severe disease and/or mechanical ventilation)	Probable [1*, 2*]	Two SRs analysing age as a risk factor in COVID-19 were data extracted. Other SRs have considered the effects of age on specific risk factors (reported separately). Risk factor category was allocated from the most well conducted review[1*]. In this review, all studies controlled for sex, some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. This review was broad an examined the data for many risk factors and compared magnitude of effects for different risk factors. SR authors report that advancing age (≥45 years and especially ≥60 years) may be **the most important risk factor** for hospitalisation and mortality from COVID-19. See data extraction tables for detail on age bands.
Male gender/sex		Probable [1*]	Uncertain [1*, 2*] (for severe disease and mechanical ventilation)	Probable [1*, 2*]	Two SRs analysing gender as a risk factor in COVID-19 were data extracted. Other SRs have considered the effects of gender on specific risk factors (reported separately). Risk factor category was allocated from the most well conducted review and generalisable review[1*]. In this review, all studies controlled for age, some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. On severe disease, no statistically significant associations were found for male sex across 3 studies. One of these studies was large (n=2725). Data for mortality and gender were somewhat inconsistent with some studies showing a statistically significant difference and others not. One large fair quality study (n=130,091) from the UK that stratified its analysis by age showed that hospitalised males aged 20-64 may be at about two-fold increased risk of mortality compared to females dropping to aHR of 1.47 (95%CI 1.44, 1.51) in those >64.

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
Ethnicity **Black**	Probable [3**]	Possible [4]	Uncertain[3**, 4]	No [3**, 4]	Two SRs analysing ethnicity as a risk factor in COVID-19 were data extracted. Both reported risk estimates adjusted, where possible, for age, sex, and comorbidities. Multiple risk estimates in different source populations are provided in the data extraction tables. Authors conducted separate meta-analyses considering preprint and published research combined and published research separately. The allocation of possible increased risk of hospitalisation in people of Black ethnicity was based on the subgroup analysis of two UK studies, which showed a large magnitude of effect RR: 5.47 (95% CI 2.51-12.06). Confidence intervals were wide and this risk estimate is likely to be unadjusted. There are fewer published studies assessing the effects of Asian ethnicity than Black ethnicity and limited adjusted risk estimates. The data on mortality outcomes in Asian populations may change as a number of included studies were awaiting peer-review. Currently the pooled adjusted risk estimates for mortality from 2 peer-reviewed studies is not statistically significant[3**], however it is clear from data in Sze [3**] that there are many studies awaiting publication and that some of these are likely to show a significant effect. For the moment, we have classified this risk as possible, rather than not a risk factor, to acknowledge the uncertainty. Data on mixed ethnicities was limited. There was only one study, conducted in the UK, assessing admission to intensive care in those of mixed ethnicity aOR 1.48 (95% CI 0.98-2.24). Sze et al. [3**] noted that their findings indicate that the disproportionate impact of COVID-19 on Black and Asian communities is mainly attributable to the increased infection amongst these communities. The full paper proposes some potential factors that may lead to this including, lower socioeconomic status increasing the chances of crowded environments/ shared facilities, multigenerational households, and essential worker occupations that cannot be done from home. Raharja et al.[4] noted that whilst their review did not support ethnicity as an independent risk factor, the evidence is consistent on the disproportionate representation of ethnic minorities in COVID-19 mortality and morbidity. These authors suggest that disparities could be partially attributed to a greater burden of comorbidities in ethnic minority groups and socioeconomic factors. This review did not examine the question of increased risk of being infected with the virus for individuals from ethnic minorities, unlike Sze et al. [3**]
Asian	Probable[3**]	No[4]	Possible [3**, 4]	Possible [3**]	
Mixed			Uncertain[3**]	No[3**]	
Obesity BMI≥30Kg/m²		Probable [1,* 5]	Probable (ITU/ICU admission) [1,5,8] (Severity) [6**, 7*]	Probable [1*, 5, 6**, 7*]	Five systematic reviews analysing obesity as a risk factor in COVID-19 were data extracted. Research on the outcome of hospitalisation included community samples or samples in people testing positive for COVID-19. Research on outcomes of intensive care admission or mortality used samples of hospitalised patients. Where systematic reviews reported adjusted risk estimates, it was unclear which covariates were used for the adjusted analyses. Meta-analyses across studies commonly displayed high heterogeneity. For hospitalisation, ICU admission and death, one review[5] provided both adjusted and unadjusted risk estimates. Adjusted risk estimates had a tendency to be higher and in the vast majority of studies were statistically significant. A greater degree of obesity was significantly associated with increased risk of severity and mortality in two SRs[6**, 7*]. One systematic review[7*] found that those with severe obesity (BMI ≥35kg/m2) had higher risks of critical COVID-19 and mortality. Similarly, this review found that older patients with obesity (aged> 60 years) had higher risks of developing critical COVID-19 and mortality than obese individuals age ≤ 60. Confidence intervals widened for stratified analyses. Pranata et al. [6**] noted their meta-regression showed that the association between obesity and composite outcome for severe COVID-19 was not affected by the proportion of males, hypertension, diabetes or the continent on which the studies were conducted. Du[7*] found in their meta-regression that age may have a significant influence of the association between

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
					obesity and severe disease or mortality but that sex, diabetes, hypertension and cardiovascular diseases appeared not to exert a significant effect on the association between obesity and COVID-19 mortality. Male gender was also found not to affect the association between obesity and mortality in another SR[9].
Smoking **Current smokers** **Former smokers** **Smoking History**	Unlikely [10*] Unlikely [10*]	Unlikely [10*] Possible [10*]	Unlikely [10*] (severe disease) Possible [10*] (severe disease) Possible [2*] (severe disease)	No conclusion[10*,2*] Possible [10*] Possible [2*]	Two systematic reviews analysing smoking as a risk factor in COVID-19 were data extracted. Current and former smokers were compared with never smokers. It was not possible to reach a conclusion as to whether current smokers were at increased risk of death when compared to never smokers. One meta-analysis[2*] suggested increased risk (4 studies), the other [10] was not significant. The Simons study[10*], a living review, is more up-to-date. Note that data from a study in England (Williamson et al.[a]) of 10,296 COVID-19 related deaths reports a fully adjusted meta-analysis HR for death in current smokers 0.89 (95% CI 0.82 to 0.97) Risk estimates are unadjusted for confounders. Simons et al[10*] noted that smoking rates in most studies were lower than expected, in comparison with overall national prevalence estimates, and may be a result of reporting bias. No studies verified smoking status biochemically. They also noted the need to differentiate between recent vs long terms ex-smokers.
Alcohol		Uncertain [1*] (above vs within guidelines)			One SR analysing alcohol as a risk factor in COVID-19 was data extracted. In this review, all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. The review included two UK studies and mixed effects were observed. SR authors noted low certainty evidence of no important association (OR or RR ≤1.70) with an increased risk of hospitalisation in community samples.
Physical activity		Uncertain [1*]			One SR analysing physical activity as a risk factor in COVID-19 was data extracted. In this review, all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies managed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. The review included two UK studies and mixed effects were observed. SR authors noted low certainty evidence of no important association (OR or RR ≤1.70) with an increased risk of hospitalisation in community samples.
Education **Lower education vs. university degree**		Uncertain [1*]			One SR analysing education as a risk factor in COVID-19 was data extracted. In this review, all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies managed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. The increased risk observed in one study of fair quality from the UK was not statistically significant. SR authors noted low certainty evidence for no important (OR or RR ≤1.70) association with increased risk of hospitalisation in a community sample.
Residence **Homelessness**		Possible [1*]			One SR analysing place of residence as a risk factor in COVID-19 was data extracted. In this review, all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review.

[a] Williamson EJ et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. Nature. 2020. doi:10.1038/s41586-020-2521-4.

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
Live in low income area **No. of household members**		Uncertain [1*] Uncertain [1*]			This SR found only one study reporting data for each of the sub-categories of residence. The study reporting on homelessness is likely underpowered as though the effect size was large, the confidence interval was extremely wide and crossed the line of no effect. SR authors reported low certainty evidence for no important association (OR or RR ≤1.70) with increased risk of hospitalisation for living in a low income area and on household size (up to 4 residents). On household size, the only statistically significant effect was found when comparing 4 household members versus 2 household members with no difference shown for single households or those with three members. This review did not examine large (>4 members), or multigenerational living arrangements.
Socioeconomic status		Possible [1*]		Possible[1*]	One SR analysing socioeconomic status as a risk factor in COVID-19 was data extracted. In this review, all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. Increased risks for these outcomes were statistically significant in adjusted risk estimates. One fair quality, UK-based study was identified for each outcome. SR authors noted the evidence on hospitalisation was of low certainty and that the evidence for mortality was of moderate certainty. PHW reviewers are unable to reconcile this difference and have thus assigned a possible rather than probable allocation to socioeconomic status as a risk factor for mortality as it reflects review authors' conclusions on importance of association.
Co-morbidity					
CVD		No relevant data for CVD	Possible [11*]	Possible [12*]	Four systematic reviews analysing CVD as a risk factor in COVID-19 were data extracted. All were preprints and had not been subject to peer-review. Risk allocation was based on two of these reviews. Data extraction tables should be consulted for detailed risk estimates on various conditions. Clustering of a range of cardiovascular conditions makes estimation of risk difficult.
Diabetes		Possible [1*]	Uncertain [1* , 14]	Possible [1*, 13]	Three systematic reviews analysing diabetes as a risk factor in COVID-19 were data extracted. Two have been published and one was a preprint (not subject to peer-review). Risk estimates were unable to account for potential differences that may exist between those with uncontrolled and controlled diabetes. Only one small study was identified in SRs examining intensive care admission, significant findings from adjusted risk estimates for critical disease/ mechanical ventilation in two SRs were also limited. A possible lowered risk of mortality in diabetic patients taking metformin was identified in one SR[15].
COPD		Uncertain [1*]		Possible [1*. 12*, 2*]	Three SRs assessed COPD as a risk factor for poor outcomes in COVID-19 and none had been peer-reviewed. There were few studies contributing adjusted risk estimates giving rise to uncertainty in determination of COPD as a risk factor for hospitalisation. Unadjusted risk estimates for the outcome of mortality were larger in magnitude and statistically significant.
Asthma		Uncertain [1*, 16]	Uncertain [16, 17, 18] (severe disease/ICU admission)	No [16, 17, 18]	Five SRs assessed asthma as a risk factor for poor outcomes in COVID-19. One of these was an empty review (Castro-Rodriguez[19]); SR authors had sought to establish whether asthma was a risk factor for SARS-CoV-2 infection or COVID-19 severity in children but found no studies. Only one small study reporting on hospitalisation had adjusted for confounding.

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
					Confidence intervals for severity outcomes were extremely wide in most instances. The adjusted pooled analysis of three studies showed as well that asthma was not associated with increased risk of mortality in patients with COVID-19. It should be noted that differing outcomes in those with COVID-19 with different severity of asthma and different medication management or control were not assessed by these SRs.
Chronic kidney Disease (CKD)		Probable [1*]	Uncertain [1*, 2*] (severe disease)	Probable [1*, 2*]	Two SRs assessed CKD as a risk factor for poor outcomes in COVID-19 and neither had been peer-reviewed. In one of these reviews[1*] all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. On hospitalisation, both prospective studies reporting adjusted risk factors showed OR>2 and were statistically significant. No included studies reported adjusted odds ratios for intensive care admission. Two studies reported on severe disease with one showing significant increased risk and the other not. Of three included cohort studies reporting on mortality only one, the largest, conducted in the UK showed statistical significance aHR 1.28 95%CI 1.18, 1.39. All three studies were conducted in hospitalised cohorts.
Liver disease		Uncertain [1*]		Possible [1*]	One SR assessed liver disease as a risk factor for poor outcomes in COVID-19. In this review all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review. On hospitalisation, one good quality, small, retrospective cohort study from the US assessing individuals positive for COVID-19 showed increased risk, aRR 1.3 95%CI 1.1, 1.6. On mortality, two good quality cohort studies showed a statistically significant increased risk. Adjusted risk estimates were larger in the study from individuals positive for COVID-19 as opposed to a cohort hospitalised with COVID-19 and higher still in individuals with liver disease with cirrhosis.
Alzheimer's disease or Dementia Neurological disorders		Possible [1*]		Possible [1*] Possible [1*]	One SR assessed dementia and neurological disease as a risk factor for poor outcomes with COVID-19 infection. In this review all studies controlled for age and sex; some also controlled for pre-existing disease. It is unlikely that the included studies addressed all confounding that could potentially affect associations. This review was a preprint and has not been subject to peer-review.
Pregnancy			Limited data[20]	Limited data[20]	One SR assessed pregnancy as a risk factor for poor outcomes with COVID-19 infection. Increased maternal age, high body mass index, chronic hypertension, and pre-existing diabetes showed a statistically significant association with the composite outcome of severe COVID-19 in pregnancy. Of these co-occurring factors, only chronic hypertension was associated with statistically significant increased risks for intensive care admission or mortality.
Cancer (non-specific)		No [1*]	Uncertain [1*, 21]	Possible [1*, 21]	Two SRs assessed cancer as a risk factor for poor outcomes with COVID-19 infection. Risk allocation was based on the SR with the most recent search and which provided adjusted risk estimates[1*]. This SR is a preprint.

Potential risk factor	Testing positive for COVID-19	Hospitalisation	Intensive care admission	Mortality	Comments/Caveats
					Two separate SRs[22, 25] reported that male gender was associated with a higher risk of death in cancer. One[22] also reported that age >65 patients was associated with a higher risk of death in cancer. Giannakoulis et al.[21], however, noted that subgroup analysis of patients >65 years of age found that all-cause mortality was comparable between those with versus without cancer. Both these reviews reported unadjusted analyses. Two SRs[1*, 22] suggested that mortality is higher for patients with haematological malignancies. One SR[22] noted that limited data suggested that tumour stage did not affect the prognosis of patients with COVID-19. One SR[22] specifically looked at characteristics/comorbidities in cancer patients and outcomes in COVID. This reported that the effects of hypertension and COPD on mortality in patients with cancer and COVID were significant but that no significant effect was seen for some other chronic diseases such as diabetes. This review[22] and two others[23, 24*] also discussed cancer therapies. Administration of most therapies was not associated with poorer COVID outcomes in unadjusted risk estimates. The data extraction forms provide further detail on the risks of chemotherapy and immunotherapy administered within shorter timescales of SARS-CoV-2 infection.
Treatment for comorbidities					
ACE1/ARB use	No [27, 28*]	No [28*]	No [26, 27, 28*]	Possible lowered risk of mortality [26, 27, 28*]	Three SRs[26, 27, 28*] assessed the use of angiotensin-converting enzyme inhibitors (ACE1)/ angiotensin receptor blockers (ARBs). Few adjusted risk estimates were statistically significant. Where they were significant for the outcomes of mortality the tendency was towards lower risk with ACE1 / ARB use.

Data extraction:

The tables below give the reference of the paper, access to the paper where freely available, key relevant findings, any considerations that arise and any caveats to bear in mind about the quality or limitations of the studies included in the SR in the column *Things to consider*. Limitations of the systematic review methods are outlined separately.

Characteristics

Reference	Relevant findings	Things to consider	Limitations of systematic review
Age			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv.* Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. The certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** 45-54 vs ≤45 years moderate certainty evidence of a large/important association (OR or RR ≥2.00) with hospitalisation in those testing positive for COVID-19	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study probably overlaps with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore their 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	There are some limitations of this systematic review; however, the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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

Reference	Relevant findings	Things to consider	Limitations of systematic review
	50-64 vs ≤45 years moderate certainty evidence of a large/important association (OR or RR ≥2.00) with hospitalisation in those testing positive for COVID-19 >60 vs ≤45 years moderate certainty evidence of a large/ important association (OR or RR ≥2.00) with hospitalisation and low certainty evidence of a very large important association (OR or RR ≥5.00) with hospitalisation in people testing positive for COVID-19 >70 or 75 vs ≤45 years moderate certainty evidence of a very large important association (OR or RR ≥5.00) with hospitalisation in people testing positive for COVID-19 >80 vs ≤45 years low certainty evidence of a very large important association (OR or RR ≥5.00) with hospitalisation in people testing positive for COVID-19 **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** 45-54 vs ≤45 years low certainty evidence of no association with severe disease in those testing positive for COVID-19 50-64 years vs ≤45 years low certainty evidence of no association with severe disease in those testing positive for COVID-19 >60 vs ≤45 low certainty evidence of a large/important association (OR or RR ≥2.00) with mechanical ventilation and low certainty evidence of a moderate association (OR or RR 1.71 to 1.99) with severe disease in those testing positive for COVID-19 >70 or 75 vs ≤45 low certainty evidence of a large/important association (OR or RR ≥2.00) with severe disease in those testing positive for COVID-19 **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** 45-54 vs ≤45 years low certainty evidence of a large/important association (OR or RR ≥2.00) with mortality in those testing positive for COVID-19 50-64 vs ≤45 years moderate certainty evidence of a large/important association (OR or RR ≥2.00) with mortality in those testing positive for COVID-19 >60 vs ≤45 years moderate certainty evidence of a large important association (OR or RR ≥2.00) with mortality and low certainty evidence of a very large important association (≥5.00) with mortality in people testing positive for COVID-19 >70 or 75 vs ≤45 years moderate certainty evidence of a very large important association (OR or RR ≥5.00) with mortality in people testing positive for COVID-19 >80 vs ≤45 years low certainty evidence of a very large important association (OR or RR ≥5.00) with mortality in people testing positive for COVID-19	Most studies of patients in the ICU setting that SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	some outcomes (e.g., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
2. Kunchok, D. and K. Hyunju (2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis." medRxiv. ***** Available here Supplementary material here	Forty-four studies comprising 20,594 hospitalised patients met inclusion criteria; 12,591 from the US-Europe and 7,885 from China. Looked at risk of severe disease or death in hospitalised COVID-19 patients. Defined outcome as severe disease for any of the following 1) the study classified COVID-19 disease as severe or critical 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. Severe disease was defined by studies as respiratory rate ≥30 per minute, oxygen saturation ≤93%, and PaO2/FiO2<300 and/or lung infiltrates >50% within 24-48 hours. Critical illness was defined as respiratory failure, shock and/or multiple organ dysfunction or failure. Studies were conducted in China (n=31), USA (n=8), Italy (n=2), UK (n=1), Iran (n=1) and Singapore (n=1). Two studies were prospective, one cross sectional and the remaining were retrospective in design (assume case series). Median age was 57 years; 65 years for the US and Europe and 54 years for China. Heart disease prevalence (16%) among COVID-19 patients in the US were substantially higher than the general US population. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** The outcome of severe disease was defined by a composite measure sRR for severe disease in patients ≥60 years 1.98 95% CI 1.60 to 2.44; I^2 82%; n=17 studies but it is not possible to tell which countries these studies came from. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Relative risk of death in patients ≥60 years RR 3.77; 95%; CI 2.94 to 4.82 I^2 73%; n=12 studies (10 studies from China and two from the USA)	Search conducted to 22nd May 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratios presented here are largely calculated from unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700. Included studies predominantly from China – may not be relevant to Wales/UK. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals. Also in the meta-analysis for death, 8 of the 10 Chinese studies were from Wuhan or included patients from Wuhan.	Search terms were not sufficiently sensitive. Three databases searched. No preprint or COVID specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was undertaken for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in the labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Male gender/sex			Back to Table 1
1. Wingert A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. * Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** There was moderate certainty of evidence for important/large associations (OR or RR ≥2.00) with increased risk of hospitalisation for males compared to females (all ages) in people positive for COVID 19 (3 studies, 3,812 patients) **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** The evidence that males of all ages who test positive for COVID-19 are at greater risk for ICU admission than females is uncertain. There was low certainty of evidence of a moderate association (OR or RR 1.71 to 1.99) with increased risk of mechanical ventilation in males compared to females (all ages) in people positive for COVID-19 (4 studies, 881 patients).	Searches were conducted up to 15th June 2020 This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors 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 SR authors 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.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment

Reference	Relevant findings	Things to consider	Limitations of systematic review
	There was low certainty evidence of no large/important association (OR or RR ≤1.70) with increased risk of severe disease in males compared with females of all ages positive for COVID-19. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** There was moderate certainty evidence of no important association (OR or RR ≤1.70) of death in males of all ages positive for COVID-19 compared with females (all ages). There was low certainty evidence of a moderate association (OR or RR 1.71 to 1.99) of death in males hospitalised for COVID-19 compared with females when data looked at ages 20-64 years.	Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	of any individual study was difficult. A single reviewer assessed the certainty of the evidence.
2. Kunchok, D. and Hyunju, K. (2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis" medRxiv. ***** Available here. Supplementary material here	This SR explored the prevalence of adverse outcomes, risk factors, and association of risk factors with adverse outcomes in COVID-19 patients. Primary outcome was prevalence of death and association of risk factors with death. Secondary outcome was prevalence of severe disease and association with risk factors. The SR included 44 studies, comprising 20,594 hospitalised patients (58% were males). 12,591 patients from the US-Europe and 7,885 from China. Two studies were prospective, one cross-sectional, and the remaining retrospective in nature. Defined outcome as severe disease for any of the following 1) the study classified COVID-19 disease as severe or critical, 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Summary relative risk of severe disease in males 1.24 95% CI 1.11 to 1.36, 27 studies I^2 =17% (p=0.22) (from Forest plot in supplementary material). These 27 studies were all in China except USA n=3 **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Relative risk of death for males 1.34 (95% CI 1.2 to 1.50) I^2 19% 17 studies (fixed effects analysis) Relative risk of death for males 1.39 (95% CI 1.22 to 1.58) I^2 19% 17 studies (random effects analysis) China n=10, USA n=3, UK n=1, Iran n=1, Italy n=1, Poland n=1	Search conducted to 22nd May 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies simply reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratio they calculated from the frequencies were largely unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700 There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals.	Search terms were provided but the final search strategy was not available. No preprint or COVID specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was conducted for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Ethnicity			Back to Table 1
3. Sze, S., et al. (2020). "Ethnicity and clinical outcomes in COVID-19: A systematic review and meta-analysis." EClinicalMedicine** Available here	18,728,893 patients from 50 studies were included; 26 were peer-reviewed; 42 (84%) were from the USA and 8 (16%) from the UK. 14,506,023 (77%) were White; 1,267,802 (7%) were Asian; 527,944 (3%) were Black, 1,578,192 (8%) were Hispanic, 1,113 were Native American, 229,822 (2%) were Mixed, and 617,997(3%) were of other ethnic group. Patients with COVID-19 were defined as those testing positive for SARS-CoV-2 by nasopharyngeal swab or had clinical evidence of COVID-19 (indicated by clinical signs and symptoms) along with radiology and laboratory tests. They excluded studies that identified patients with COVID-19 through positive serology (as serological tests are not always initially positive during acute infection and were not widely available or validated when authors started their meta-analysis in April 2020). Patients were stratified into the following ethnic groups based on the categorisations used in the included papers: White (including White British, Caucasian, and White European); Asian (including South Asian, Asian/Pacific-Islander and Chinese); Black (including Black Caribbean and Black African); Hispanic (including Hispanic and Latino); Native American; Mixed and Other. One study described two separate cohorts from the USA and the UK. One study was a case series; one was a cohort and a case control; three were cross-sectional and the remaining were cohort studies. 28 (56%) reported on patients in hospital; nine (18%) reported on patients in the community; 13 (26%) reported on both. The overall quality of published articles was higher than those in preprint (median published quality score: 84%, interquartile range 73%−91%; median preprint article score: 73%, interquartile range 66%−82%); although both published articles and those presented on preprint servers maintained relatively high quality scores. White ethnicity is the reference in all analyses. All analyses were random effects. Statistically significant results are in bold. **Q1. Which population groups are most likely to test positive for COVID-19?** 14 (28%) studies investigated the risk of infection. **Pooled adjusted RR for Black ethnicity: 2.02 (95% CI 1.67–2.44, I^2 84.2%, 8 studies: UK n=4, USA n=4)** **Pooled adjusted RR for Asian ethnicity: 1.50 (95% CI 1.24–1.83, I^2 67.3%, 5 studies: UK n=3, USA n=2)** **Sensitivity analyses examining peer-reviewed studies only** **Pooled adjusted RR for Black ethnicity: 1.85 (95%CI: 1.46–2.35, I^2 84.2%, 5 studies)** **Pooled adjusted RR for Asian ethnicity: 1.51 (95% CI 1.22–1.88, I^2 74.8%, 4 studies)** Sensitivity analysis not undertaken for mixed ethnicities (small number of patients) **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?**	Search conducted 31st August 2020 Systematic review reported according to PRISMA guidelines. Protocol was registered on PROSPERO (180654) on 21st April 2020). PHW critical appraisal was on the preprint version of this paper. Data was extracted from the corrected proof that is currently in Press. This means the paper contains author's corrections, has been accepted by a journal and peer reviewed, but not yet assigned to volumes/issue. Heterogeneity was generally high, but this was explored through sensitivity analyses. Authors used broad categories of ethnicity. This was done in order to maximise inclusion within pooled analyses – however, this will have affected precise estimates of risk for any further subgroup categorisations of ethnicity. If studies assessed race and ethnicity separately, data were only extracted for mutually exclusive groups. For example, if two separate variables were presented: for 'race' and 'ethnicity', the variable which included 'Black, Asian and White' was chosen to represent ethnicity. Authors predicted this would most commonly occur in some American studies, where ethnicity may be used to refer to 'Hispanic' or 'Non-Hispanic', and race to refer to 'Black, Asian and White'. This was a pragmatic way of ensuring that they assessed ethnicity in a standardised way, across multiple studies which assessed ethnicity or race differently. Authors attempted to minimise the possibility of including patients from the same population twice when exploring one outcome. Where multiple studies of what is likely to be the same population were identified, the most recent version up to 31st August 2020 was used, with published peer-reviewed studies favoured over those in the preprint database (up to 31st August 2020). Papers which covered a larger number of patients over a longer period of time were favoured over smaller studies, should it be likely that they both investigated the	Quality assessment was carried out by six reviewers, but it is unknown if this was carried out in duplicate. Some differences between data presented in tables and the review narrative. Review authors noted that half of their pooled analysis included studies that had not been peer reviewed; the sensitivity analysis adjusted for this. They also noted that several studies they included may have overlapping populations.

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	15 (30%) studies investigated the risk of ITU admission (no definition of this outcome provided). Individuals of Asian ethnicity may be at higher risk of ITU admission. Hospitalised patients only: **Pooled adjusted RR for Asian ethnicity: 1.97 (95% CI 1.34–2.89, I^2 0.0%, 2 studies:** 1 USA, 1 UK) (but no studies had been peer-reviewed) Pooled adjusted RR for Black ethnicity: 1.10 (95% CI 0.83-1.44, I^2 54.4%, 4 studies: 3 USA, 1 UK) Pooled adjusted RR for mixed ethnicity: 1.48 (95% CI 0.98–2.24, 1 study, UK) Inpatient/outpatient populations: **Pooled adjusted RR for Black ethnicity: 1.90 (95% CI 1.38-2.61, I^2 52.7, 3 studies)** Pooled **unadjusted** (no studies reported adjusted data) OR for Asian ethnicity: 0.96 (95% CI 0.41-2.21, I^2 75.8%, 3 studies all unpublished as at 31st August) Sensitivity analyses examining peer-reviewed studies only Pooled adjusted RR for Black ethnicity: 1.00 (95% CI 0.88-1.13, 2 studies) ITU admissions included studies that reported suspected or confirmed COVID-19 patients in their analyses. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** 33 (66%) studies investigated the risk of death **Suspected or confirmed COVID-19 patients:** Pooled adjusted RR/HR for Asian ethnicity: 1.22 (95% CI 0.99–1.50, I^2 61.8%, 6 studies: UK 3, USA 3) (reported in table, forest plot and abstract) Pooled adjusted RR/HR for Asian ethnicity: 1.22 (95% CI 0.99–1.63, I^2 61.8%, 6 studies) (reported in narrative) Pooled adjusted HR/RR for Black ethnicity: 1.04 (95% CI 0.93-1.17, I^2 44.8%, 18 studies: USA 16, UK 2) Pooled adjusted HR/RR for mixed ethnicity: 1.13 (95% CI 0.46-2.77, I^2 76.2%, 2 studies, both UK) **Suspected or confirmed COVID-19 patients + general population**: **Pooled adjusted HR/RR for Asian ethnicity: 1.33 (95% CI 1.11–1.60, I^2 69.0%, 8 studies)** Pooled adjusted HR/RR for Black ethnicity: 1.09 (95% CI 0.95-1.26, I^2 68.8%, 20 studies) Pooled adjusted HR/RR for mixed ethnicity: 1.19 (95% CI 0.74-1.91, I^2 74.6%, 4 studies) **Hospitalised population only:** **Pooled adjusted HR/RR for Asian ethnicity: 1.27 (95% CI 1.01–1.58, I^2 64.7%, 5 studies)** Pooled adjusted HR/RR for Black ethnicity: 1.00 (95% CI 0.89-1.11, I^2 34.8%, 13 studies) Pooled adjusted HR/RR for Mixed ethnicity: 1.13 (95% CI 0.46-2.77, I^2 76.2%, 2 studies) **Documented outcome (discharge or death):** Pooled adjusted HR/RR for Asian ethnicity: 1.18 (95% CI 0.92–1.51, I^2 67.9%, 5 studies) Pooled adjusted HR/RR for Black ethnicity: 1.04 (95% CI 0.90-1.20, I^2 42.9%, 13 studies) Pooled adjusted HR/RR for Mixed ethnicity: 1.13 (95% CI 0.46-2.77, I^2 76.2%, 2 studies) **Peer reviewed only:** Pooled adjusted HR/RR for Asian ethnicity: 1.19 (95% CI 0.77–1.83, I^2 54.3%, 2 studies)	same patients. However, studies that assessed different cohorts of patients (for example, from different countries) in the same paper, or studies that were based on the same population but explored different outcomes were included in the analysis. Individuals with ethnicity data missing were excluded. When the proportion of patients of each ethnicity was not presented in the text SR authors calculated the proportion from data presented in tables, or supplementary material from the manuscript. Some studies presented multiple models with different sets of confounders. Authors included the model that most closely matched their *a priori* chosen confounders of age, sex, deprivation, obesity, and comorbidities. Authors recorded other confounders that a study had adjusted for, including the way comorbidities were considered. For both the adjusted and unadjusted comparisons, data were extracted for analyses that used White ethnicity as the reference group. Only one included paper investigating the risk of infection did not consider comorbidities. 15 (30%) studies did not adjust for any confounders when assessing outcomes related to ethnicity. Data for all ethnicities was limited by small numbers of studies for the outcome of intensive care admission. Studies with very low estimates of infection had very high precision, whereas studies with higher infection estimates had lower precision. Data on Hispanic populations was not extracted by PHW reviewers as it is not relevant to the UK/Wales population. Overlap in 14 studies between this SR and the other SR[4] data extracted (USA n=13, UK n=1).	

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Pooled adjusted HR/RR for Black ethnicity: 1.05 (95% CI 0.90-1.22, I^2 41.7%, 8 studies) No data for mixed ethnicity Small numbers of studies limited data for Mixed and Other ethnicities. Mortality included studies that reported suspected or confirmed COVID-19 patients in their analyses. For mortality, further analysis included studies that looked at the risk of death from COVID-19 in the general population (i.e., those with and without COVID-19). Sensitivity analyses were also conducted excluding: For the outcome of death, studies which did not include data for those still hospitalised at the end of the follow-up, since these studies may underestimate death; Studies which were of mixed populations (hospitalised and non-hospitalised patients), since these studies may also underestimate ITU admission or death; Studies which were not peer reviewed.		
4. Raharja, A., Tamara, A. and Kok, L.T. (2020). "Association Between Ethnicity and Severe COVID-19 Disease: a Systematic Review and Meta-analysis." *J. Racial and Ethnic Health Disparities*. Available here Supplementary material here	Seventy-two articles (59 cohort studies with 17,950,989 participants, 13 ecological studies; 54 US-based, 15 UK-based; 41 peer-reviewed) were included for systematic review and 45 for meta-analyses. Primary outcome was all-cause mortality. Secondary outcomes were hospitalisation, critical care admission, advanced respiratory support requirement (such as invasive mechanical ventilation (IMV), extracorporeal membrane oxygenation (ECMO)) and acute kidney injury (any severity or the need for acute renal replacement therapy). Meta-analysis was carried out if two or more longitudinal cohort studies compared risk of outcomes in Black, Asian or Hispanic ethnic group with White participants (reference group) for each outcome. Twenty-one studies assessed **hospitalisation risk** in different ethnic groups. There were 20 cohort studies comprising 428,000 patients (90% White, 4.5% Black, 3.4% Asian, 1.6% Hispanic, 3.0% others and 0.19% missing ethnicity data); 14 articles were suitable for meta-analysis. Only one had a small sample size (n < 100). Eighteen studies assessed ethnicity as a **risk factor for ICU admission**, comprising 30,301 participants (45% White, 32% Black, 7.9% Asian, 7.9% Hispanic and 4.7% with missing ethnicity data). Eighteen cohort studies comprising 16,862 participants (41% White, 41% Black, 5.1% Asian, 3.9% Hispanic and 4.3% missing ethnicity data) reported ethnicity-aggregated data on the **need for advanced respiratory support**, i.e. invasive mechanical ventilation (IMV). Thirteen studies were suitable for meta-analysis. Fifty-one studies reported ethnicity-aggregated mortality data, including 38 cohort studies comprising 17,501,820 participants (63% White, 2.1% Black, 6.0% Asian, 0.069% Hispanic, 2.9% others and 26% missing ethnicity data). Total sample sizes were more than 100 participants (n > 100) in 26 of 28 (93%) cohort studies included in the meta-analysis. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Relative risk (RR) adjusted for age and sex: **Black v white, RR: 2.23 (95% CI: 1.54–3.19, I^2 92%, 5 studies)** Asian v white RR:1.16 (95% CI: 0.64–2.08, I^2 82%, 3 studies)	Search conducted 15th June 2020. Published 12 November 2020. PHW critical appraisal was on the preprint version of this paper; data was extracted from the printed article. Protocol was registered on PROSPERO. Authors used a CA tool and GRADE to assess quality and strength of evidence, however, the GRADE assessment is not really discussed but is presented in table 3. Where multiple articles studied the same patient cohort review authors used only those cohorts reporting the largest number of events in the analysis The level of evidence was high for Black ethnicity, but low for both Asian and Hispanic ethnicities. The certainty in the risk estimates for Asian and Hispanic was down-rated for risk of bias and indirectness due to relatively low number of studies providing age, sex and comorbidity-adjusted association, and potential differences between study participants and target population. The meta-analysis demonstrates significantly elevated age and sex adjusted-risks across several outcome measures. The consistent attenuation of estimates by further adjustment for comorbidities indicates that disparities could be partially attributed to a greater burden of comorbidities in ethnic minority groups. Socioeconomic factors have also	Difference between data reported in paper and supplementary material. Study characteristics are aggregated and it is not possible to determine which studies contributed to the outcomes, nor the individual characteristics of those studies.

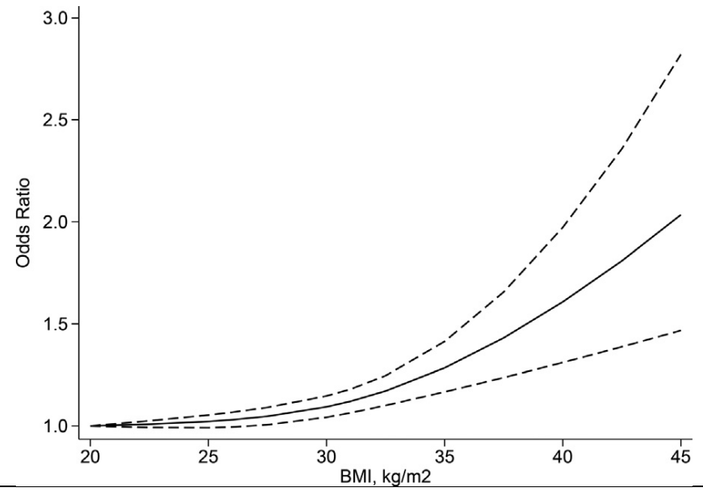
Reference	Relevant findings	Things to consider	Limitations of systematic review
	Relative risk adjusted for age, sex and comorbidities: Black v white RR: 1.40 (95% CI 0.93–2.12, I^2 95%, 4 studies) Asian v white RR: 1.04 (95% CI: 0.99–1.11, I^2 0%, 3 studies) Five studies considered further socioeconomic factors in their analysis and showed that adjusting for socioeconomic factors could reduce the disparity in hospitalisation risk. Subgroup analysis showed strongly significant interaction p value between UK and US subgroups. The hospitalisation risk of Black and Asian were markedly higher in UK. For Black ethnicity, RR: 5.47 (95% CI 2.51-12.06) in 2 UK studies v. RR 1.36 (95% CI 1.08-1.72) in 11 US studies (p 0.0008) note wide confidence interval for the UK estimate For Asian ethnicity, RR: 2.94 (95% CI 1.55-5.53) in 2 UK studies v. RR: 0.90 (95% CI 0.82-1.66) in 6 US studies (p 0.0003) note wide confidence interval for the UK estimate It is unclear whether these risk estimates specific to UK studies are adjusted for age, sex and comorbidities but given the magnitude of effect and number of studies PHW reviewers consider that they are unadjusted. Subgrouping by Newcastle Ottawa Scale (NOS) did not show significant interaction, although there was a trend towards greater risk in studies with lower NOS. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Risk of ICU admission Black ethnicity adjusted for age and sex RR:1.39 [95% CI: 0.85–2.27], I^2 69%, 3 studies in paper Black ethnicity vs white adjusted for age and sex RR: 1.60 (CI 0.03 to 2.72, 2 studies in Forest plot in supplementary material Black ethnicity adjusted for age, sex and comorbidities RR: 1.31 [95% CI: 0.84–2.03], I^2 95, 4 studies in paper Black vs white ethnicity adjusted for age, sex and comorbidities RR: 1.42 (95% CI 0.86 to 2.43), 3 studies in Forest plot in supplementary material There was inadequate data for meta-analysis for Asian ethnicity; one study reported significantly increased age- and sex-adjusted risk of ICU admission for Asian ethnicity. Seven studies were not suitable for meta-analysis. Five UK-based studies reported over-representation of the BAME communities in ICU cohorts, with two reporting higher age-adjusted risk for BAME. On the other hand, two US studies did not find a significant difference in risk of ICU admission between Black and non-Black study participants. Outcome of invasive mechanical ventilation (IMV) due to respiratory failure. Adjusted relative risks for age and sex**:** **Black v white ethnicity RR: 1.40 (95% CI 1.13-1.75, I^2 0%, 3 studies)** **Asian v white ethnicity RR: 1.54 (95% CI 1.17-2.02, I^2 0%, 2 studies)** (no Forest plot for this) Adjusted relative risks for age, sex and comorbidities:	been suggested to contribute to this disparity, this review underlined paucity of evidence. Substantial heterogeneity is attributed to difference in magnitude rather than the direction of effect. Methodological differences such as dissimilar combinations of comorbidities adjusted for also contributed to overall heterogeneity, but has not necessarily rendered the findings less useful. Clinical heterogeneity is also expected in risk estimates for Asians since Asian ethnicity is not a homogenous group, consisting of individuals from widely diverse origins such as Indian, Pakistani, Bangladeshi, Chinese and others. Subgrouping by location aims to provide context-specific and clinically useful risk estimates, whilst sacrificing precision for general applicability in public health policy decision-making. For this reason, authors down-rate certainty of risk estimates for Asian and Hispanic ethnicity. Data on Hispanic populations was not extracted by PHW reviewers as it is not relevant to the UK/Wales population.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Black v white ethnicity RR: 1.23 (95% CI 0.61-2.51, I^2 91%, 3 studies) Subgrouping by location was not possible as all but one study was US-based **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Age- and sex-adjusted mortality risks **Black HR: 1.38 [95% CI: 1.09–1.75], I^2 94%, 5 studies** **Asian HR: 1.42 [95% CI: 1.15–1.75], I^2 87%, 3 studies** Adjusted for age, sex and comorbidities HR (Black): 0.95 [95% CI: 0.72–1.25], I^2 79%, 4 studies HR (Asian): 1.17 [95% CI: 0.84–1.63], I^2 73%, 3 studies Subgroup analysis by location showed a consistent trend towards greater mortality risk estimates in UK ethnic minorities, but difference was not significant. Subgrouping by risk of bias did not demonstrate different effects.		

Reference	Relevant findings	Things to consider	Limitations of systematic review
Obesity BMI≥30Kg/m2			Back to Table 1
5. Huang, Y., et al. (2020). "Obesity in patients with COVID-19: a systematic review and meta-analysis." Metabolism 113: 154378-154378. Available here.	This SR explored the effects of obesity on the risk of hospitalisation, ICU admission, IMV and death in patients with COVID-19. The SR used BMI and visceral adipose tissue (VAT) accumulation identified on CT scan as obesity indicators. The SR included 33 cohorts involving 45, 650 patients (11,509 with obesity) with COVID-19 from the USA, Italy, China, Spain, The state of Kuwait, Mexico, France, Switzerland and Greece. The SR included one study conducted in children but this does not appear to have been included in the meta-analyses. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Univariate analysis The univariate analysis showed that COVID-19 patients with obesity had a statistically significant higher risk of hospitalisation but the heterogeneity among the studies was high and significant (OR:1.76, 95% CI: 1.21, 2.56, P = 0.003, I^2 95.8%, P-heterogeneity = 0.000, 7 studies with 22,817 patients (5,284 with obesity)) Multivariate analysis The multivariate analysis detected that COVID-19 patients with obesity showed a statistically significant higher risk of hospitalisation. The heterogeneity among the studies was even higher than in the univariate analysis and significant (OR 2.36, 95% CI: 1.37, 4.07, P = 0.002, I^2 96.0%, P-heterogeneity = 0.000, 4 studies with 19,531 patients (5,089 with obesity)) **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Univariate analysis The univariate analysis showed that COVID-19 patients with obesity had a statistically significant higher risk of ICU admissions but the heterogeneity among the studies was high and significant (OR: 1.67, 95% CI: 1.26, 2.21, P<0.001, I^2 = 70.0%, P-heterogeneity = 0.000, 11 studies with 9,511 patients (2,723 with obesity)) NB: One study from the meta-analysis did not appear in the list of included studies (Jerry Y 2020) The univariate analysis found that COVID-19 patients with obesity had a statistically significant higher risk of IMV. The heterogeneity among the studies was moderate-high but not significant (OR:2.19, 95%CI: 1.56, 3.07, P<0.001, I^2= 59.2%, P-heterogeneity = 0.017, 8 studies with 2,258 patients (918 with obesity)) Multivariate analysis The multivariate analysis indicated that COVID-19 patients with obesity had a statistically significant higher risk of ICU admissions. The heterogeneity among the studies was higher than the univariate analysis and significant (OR: 2.32, 95%CI: 1.38, 3.90, P = 0.001, I^2= 82.5%, P-heterogeneity = 0.000, 6 studies with 4,608 patients (1,658 with obesity)) The multivariate analysis revealed that COVID-19 patients with obesity had a statistically significant higher risk of IMV. The heterogeneity among the studies was higher than the univariate analysis but not	Searches were conducted to 10 August. The SR excluded studies where BMI data was provided as a continuous rather than categorical variable. As VAT requires identification by CT scanning, we have not extracted these outcomes here for PHW prevention cell purposes, as BMI is a more useful population measure. The terms severe COVID-19 and severity are used sometimes to refer to the composite outcome and other times to patients who needed to be hospitalised. SR authors highlighted that most of the included studies were retrospective limiting ascertainment of a causal relationship. Authors stated that the patients included in the meta-analyses might overlap, because there are several single centre and multicentre studies from the same areas. The SR included studies with different BMI cut-off points for obesity. The authors did not perform a sensitivity analysis to exclude the studies with a cut-off different to BMI≥30g/m^2.	There was a lack of information about whether the selection of studies, data extraction and quality assessment was consistency checked. SR authors did not consider the implications that the quality of the included studies may have on their findings. The meta-analyses included several studies that were not reported in the list of included studies and quality assessment is not reported for these studies. The meta-analyses included preprint studies. The authors could have conducted a sensitivity analysis to exclude the preprints. In general, preprint studies are rated with lower quality than published peer-reviewed papers. These authors reported pooling of multivariate analyses. PHW reviewers consider that this is likely to be inappropriate. The SR did not give information about which variables were used for adjustment in each study and authors themselves noted that these variables were different across the different studies. However to note, PHW reviewers examined the Forest plots for each outcome and the vast majority of adjusted estimates for each individual study showed statistical significance.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	significant IMV (OR: 2.63, 95%CI: 1.32, 5.25, P=0.006, I^2 = 64.4%, P-heterogeneity = 0.038, 4 studies with 1,155 patients (438 with obesity)) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Univariate analysis The univariate analysis showed that COVID-19 patients with obesity had a statistically significant higher risk of death but the heterogeneity among the studies was high and significant (OR: 1.37, 95%CI: 1.06, 1.75, P = 0.014, I^2= 87.8%, P-heterogeneity = 0.000, 14 studies with 28,318 patients (6,445 with obesity)) Multivariate analysis The multivariate analysis showed that COVID-19 patients with obesity had a statistically significant higher risk of death but the heterogeneity among the studies was high and significant (OR: 1.49, 95%CI: 1.20, 1.85, P<0.001, I^2 = 69.2%, P-heterogeneity = 0.003, 7 studies with 16,876 patients (4,617 with obesity)) NB: One study from the meta-analysis did not appear in the list of included studies (Antwi-Amoabeng 2020 Preprint)		
6. Pranata, R., et al. (2020). "Body mass index and outcome in patients with COVID-19: A dose–response meta-analysis." Diabetes & metabolism.** Available here.	The aim of this SR was to evaluate the dose-response relationship between body mass index (BMI) and poor outcome in patients with COVID-19. The primary outcome was a composite poor outcome composed of mortality and severity. The secondary outcomes were severity and mortality. The severity outcome included the need for intubation and referrals to ICU. The SR included 12 cohort studies involving 34,390 patients with COVID-19 conducted in US (n=7), China (n=2), UK, Italy, France. Three studies were prospective cohorts (PC). Authors reported that included studies scored highly on critical appraisal indicating a low risk of bias. SR authors conducted analyses for outcomes using comparisons of obesity versus normal reference weight and highest BMI versus normal reference weight. The cut off for obesity was BMI≥30 and for Asian studies was >28kg/m^2. **4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** This SR did not report on intensive care admissions, instead using a composite severity outcome. The severity outcome measured by this SR included the need for intubation and the referrals to ICU, according to the definition of severe COVID-19 by the WHO-China Joint Mission COVID-19. The SR identified seven retrospective cohorts for the outcome severity. Four studies were from the USA, two from China and one from France. Obesity and severity The subgroup analysis for obesity and severity showed that obesity produced a statistically significant increase of severity (OR 1.90 95% CI 1.45, 2.48, P < 0.001; I^2 5.2%, P-heterogeneity = 0.394) The authors performed a sensitive analysis that removed the study with an obesity cut-off of BMI>28kg/m^2 (Cai Q 2020, China) and showed that obesity was associated with a statistically significant increase of severity (OR of 1.77 95% CI 1.35, 2.31, P < 0.001; I^2 0%, P-heterogeneity = 0.472) in COVID-19 patients.	Searches conducted to 28 May 2020. This systematic review is a corrected proof that is currently in Press. This means the paper contains authors' corrections, has been accepted by a journal and peer reviewed, but not yet assigned to volumes/issues. The authors commented that the asymmetrical shape of the funnel plot and the Egger's test suggested the possibility of publication bias, small-studies effect and a possible overestimation of the effect. The authors noted that meta-regression has a limited power to detect legitimate relations and the power is further reduced with a low number of studies.	The search for this systematic review may have missed some relevant papers because it used only free text terms. The results for the severity and mortality were obtained by subgroup analyses. The SR did not specify which studies were included in this dose-response meta-analysis as pooled aORs and associated confidence intervals for the composite outcome are represented graphically. Adjusted odds ratios (ORs) were used for effect estimates for pooled results on BMI but not for obesity analyses. There is no discussion of whether individual studies adjusted for different confounding factors therefore PHW reviewers are unable to ascertain whether this was reasonable.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Highest BMI and severity The subgroup analysis for BMI and severity included four retrospective cohorts. Two studies were from the USA, two from China and one from France. The authors used adjusted odds ratios (aOR) to reduce the effect of possible confounders. The subgroup analysis showed that a higher BMI was associated with a statistically significant increase of severity (aOR 3.08 95% CI 1.78, 5.33, P < 0.001; I^2 11.7%, P-heterogeneity = 0.334, 4 studies) in patients with COVID-19. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** The SR identified five cohort studies for the outcome mortality; three were prospective cohorts (PC). Three studies were from the USA, one from the UK and one from Italy. Obesity and mortality The subgroup analysis for obesity and mortality showed that obesity produced a statistically significant increase of mortality (OR 1.55 95% CI 1.16, 2.06, P = 0.003; I^2 74.4%, P heterogeneity = 0.002, 4 studies) in COVID-19 patients. The authors conducted a leave-one-out sensitive analysis due to the high heterogeneity among the included studies. This analysis excluded the study that produced the greatest reduction of heterogeneity (Klang E). The effect estimate of obesity on mortality was still statistically significant with a moderate heterogeneity among the studies (OR of 1.35 95% CI 1.08, 1.68, P < 0.001; I^2:62.1%, P-heterogeneity = 0.048). Highest BMI and mortality The subgroup analysis for BMI and mortality included three cohorts from the USA. The authors used adjusted odd ratios (aOR) to reduce the effect of possible confounders. The subgroup analysis showed that a higher BMI was associated with mortality (aOR 2.85 95% CI 1.17, 6.92, P = 0.002; I^2 79.7%, P-heterogeneity = 0.021, 3 studies). The authors conducted a leave-one out sensitive analysis due to the high heterogeneity between the included studies. This analysis excluded the study that produced the greatest reduction of heterogeneity (Petrilli). The effect estimate of BMI on mortality was still statistically significant with a low heterogeneity among the studies (OR 4.52 95% CI 2.46, 8.30, P < 0.001; I^2 0%, P-heterogeneity = 0.636). **Composite poor outcome (mortality and severity)** The SR identified twelve cohort studies for the composite outcome. Three studies were prospective cohorts (PC). Seven studies were from the USA, two from China, one from France, one from the UK and one from Italy. Obesity and composite poor outcome The SR included eleven cohort studies in the meta-analysis for obesity and composite poor outcome. Three studies were prospective cohorts (PC). Six studies were from the USA, one from France, one from the UK and one from Italy. The meta-analysis showed that obesity produced a statistically significant increase of the composite poor outcome in COVID-19 patients. Heterogeneity among the studies was moderate but significant (OR 1.73 95% CI 1.40, 2.14, P < 0.001; I^2 55.6%, P-heterogeneity = 0.003)		

Reference	Relevant findings	Things to consider	Limitations of systematic review
	The authors conducted a leave-one out sensitive analysis to reduce the heterogeneity between the included studies. This analysis excluded the study that produced the greatest reduction of heterogeneity (Klang E). The effect estimate of obesity on composite poor outcome was still statistically significant with a moderate heterogeneity among the studies (OR of 1.60 95% CI 1.31, 1.94, P < 0.001; I^2 44.1%, P-heterogeneity = 0.034). The meta-regression showed that the association between obesity and composite poor outcome was not affected by the proportion of males, hypertension, diabetes or continent where the studies were conducted. <u>Highest BMI and composite poor outcome</u> The SR included seven cohorts for the meta-analysis for BMI and composite poor outcome. Five studies were from the USA, one from China and, one from France. The pooled analysis showed that a higher BMI was statistically significant associated to composite poor outcome (aOR 3.02 95% CI 1.82, 5.00, P < 0.001; I^2 59.8%, P-heterogeneity = 0.021) The authors conducted a leave-one out sensitive analysis to reduce the heterogeneity between the included studies. This analysis excluded the study that produced the greatest reduction of heterogeneity (Petrilli). The effect estimate of BMI on composite poor outcome was still statistically significant with a low heterogeneity among the studies (OR 3.53 95% CI 2.39, 5.19, P < 0.001; I^2 0%, P-heterogeneity = 0.453) <u>BMI dose-response and composite outcome</u> The SR included seven studies for the dose-response meta-analysis but did not specify which studies these were; BMI of 20Kg/m^2 was used as the reference. Linear association analysis demonstrated an increased risk of composite poor outcome by aOR of 1.052 (95% CI 1.028, 1.077), P < 0.001 for every 5 kg/m2 increase in BMI. Linearity occurred at BMI of 30–35 kg/m2 and the curves became steeper. Using BMI of 20 kg/m2 as the reference, the ORs for patients with BMI of 25, 30, 35, and 40 kg/m2 were 1.02 ((5% CI 0.99, 1.05), 1.09 (95% CI 1.04, 1.15), 1.28 (95% CI 1.17, 1.41), and 1.61 (95% CI 1.31, 1.97), respectively.  		

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Fig. 1 Dose-response meta-analysis between body mass index and composite poor outcome in patients with COVID-19 with restricted cubic splines in a multivariate random-effects dose-response model. Adjusted odds ratio (solid line) with 95% confidence interval (long dashed lines) for the association of the body mass index level with the risk of composite poor outcome.		
7. Du, Y., et al. (2020). "Association of Body mass index (BMI) with Critical COVID-19 and in-hospital Mortality: a dose-response meta-analysis." Metabolism: clinical and experimental: 154373. * Available here	The aim of this SR was to explore the association between BMI and COVID-19 severity and mortality. Obesity was defined as BMI ≥30kg/m^2 and critical illness referred to patients with acute respiratory distress syndrome requiring life support, mechanical ventilation, or intensive care unit (ICU) support. The SR included 16 observational studies (14 cohorts and two cross-sectional studies) including a total of 109,881 patients with COVID-19 from the US, Italy, China, Mexico, Kuwait and France. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** This SR did not report on intensive care admissions, instead using a composite critical illness outcome. The subgroup analysis of cohort studies comparing BMI≥30Kgm^2 vs, BMI<30Kgm^2 revealed that obesity significantly increased the risk of critical illness in COVID-19 (OR 2.14, 95% CI 1.47 − 3.12, p<0.001, I^2 85%, 10 studies). The subgroup analysis of non-Asian studies showed that obesity significantly increased the risk of critical illness in COVID-19 (OR 2.25, 95% CI 1.48-3.43, I^2 79%, p (het) < 0.001, 9 studies.) Severe obesity (BMI ≥35kg/m2) significantly increased the risk of critical COVID-19 (OR 3.64, 95% CI 1.97 − 7.45, I^2 88%, p(het)<0.001, 7 studies) Older patients (aged> 60 years) had a significantly higher risk of developing into the critical COVID-19 (OR 3.11, 95% CI 1.73 − 5.61, I^2 87%, p (het) < 0.001, 6 studies) than age ≤ 60 years (OR 1.77, 95% CI 1.17 − 2.69, I^2 76.8%, p (het) =0.001, 6 studies). Pooled results based on the adjusted OR showed significant difference in effect of obesity on critical COVID-19 (multivariate analysis: OR 1.69, 95% CI 1.27 − 2.27, I^2 75.7%, p(het)<0.001, 8 studies; univariate analysis: OR 5.15, 95% CI 3.06 − 8.69, I^2 37.4%, p(het)=0.188, 4 studies) Meta-regression analysis results showed that age (Coef =0.038, P=0.054) may have a significant influence on the association between obesity and critical COVID-19. However, sex (P=0.89) and some comorbidities (diabetes: P=0.145, hypertension: P=0.169, cardiovascular diseases: P=0.36) did not appear to exert a significant effect on the association between obesity and critical COVID-19. Random-effects dose-response meta-analysis showed a linear association between BMI and critical COVID-19 (Pnon-linearity = 0.242). The risk of critical COVID-19 increased by 9% (OR 1.09, 95% CI 1.04 -1.14, P< 0.001, 6 studies) for each 1 kg/m2 increase in BMI. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Patients with a BMI≥30kg/m^2 had a significantly higher risk of COVID-19 mortality with a moderate but significant heterogeneity among the studies (OR 2.68, 95% CI 1.65−4.37, I^2 79.3%, p (het) < 0.001, 7 studies).	Searches were conducted to 27 August 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Most of the included patients were from the US which may reduce the generalisability of these results.	BMI range classifications are different. The SR did not report the quality of the included studies. Quality of included studies and its implications on the conclusions have not been discussed.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Subgroup analysis results showed that patients with obesity and age > 60 years was associated with a significantly increased risk of COVID-19 mortality (OR 3.93, 95% CI 2.18 − 7.09, I^2 48.6%, p (het) < 0.001, 4 studies). Subgroup analysis results showed that severe obesity (BMI >35kg/m^2) was associated with a significantly increased risk of COVID-19 mortality (OR 3.54, 95% CI 1.48 – 8.48, I^2 72%, p (het) < 0.001, 3 studies). Pooled results based on the adjusted OR showed significant difference in effect of obesity on mortality (multivariate analysis: OR 3.34, 95% CI 1.89 – 5.90, I^2 78.4%, p(het)=0.003, 4 studies; univariate analysis: OR 1.83, 95% CI 1.23 – 2.71, I^2 0%, p(het)=0.957, 3 studies) Meta-regression analysis results showed that age had a significant influence on the association between BMI and COVID-19 mortality (Coef.=0.036, p=0.048). However, sex (P=0.737), diabetes (P=0.354), hypertension (P=0.412) and cardiovascular diseases (P=0.165) did not exert a significant effect on the association between obesity and COVID-19 mortality. Random-effects dose-response meta-analysis showed a linear association between BMI and mortality (Pnon-linearity = 0.116). The risk of mortality increased by 6% (OR 1.06, 95% CI 1.02 −1.10, P 0.002, 4 studies) for each 1 kg/m2 increase in BMI.		
1. Wingert, A., et al. (2020). “Risk factors for severe outcomes of COVID-19: a rapid review.” medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00)	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but considered less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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),

Reference	Relevant findings	Things to consider	Limitations of systematic review
	In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. In analysis of BMI, all categories were compared to normal BMI defined as 18.5-24.9. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** 2 studies involving 392,388 participants from UK and US provided low certainty evidence no important/large associations with increased risk of hospitalisation (OR or RR ≤1.7) in overweight (BMI 25.0-29.9) people having confirmed COVID-19. 3 studies involving 396,869 participants from UK and US provided low certainty evidence of a moderate association with increased risk of hospitalisation (OR or RR 1.71-1.99) in people with obesity class I and II ((BMI $\geq$ 30) having confirmed COVID-19. 1 study involving 5279 participants from the US provided low certainty evidence of important/large associations with increased risk of hospitalisation (OR or RR ≥2.00) in people with obesity class III (BMI ≥40) having confirmed COVID-19. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** 1 study involving 770 participants from the US provided low certainty evidence of no important/large associations with increased risk of ICU admission (OR or RR ≤1.7) in underweight (BMI<18.5) people having confirmed COVID-19. 2 studies involving 873 participants from the USA provided low certainty evidence of moderate association with increased risk ICU admission (OR or RR 1.71-1.99) in people with obesity class I and II (BMI ≥30) having confirmed COVID-19. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** 2 studies involving 970 participants from the US provided low certainty evidence of no important/large associations with increased risk of mortality (OR or RR ≤1.7) in underweight (BMI<18.5) people having confirmed COVID-19 2 studies involving 2817 participants from Italy and the US provided low certainty evidence of no important/large associations with increased risk of mortality (OR or RR ≤1.7) in overweight (BMI 25.0-29.9) people having confirmed COVID-19. 6 studies involving 8716 participants from Italy and the USA provided moderate certainty evidence of no important/large associations with increased risk of mortality (OR or RR ≤1.7) in people with obesity class I and II (BMI ≥30) having confirmed COVID-19.	Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	(b) follow-up duration and extent of censorship for some outcomes (e.g., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	2 studies involving 6131 participants from the US provided low certainty evidence of borderline moderate association with increased risk of mortality (OR or RR 1.71-1.99) in people with obesity class III (BMI ≥40) having confirmed COVID-19.		
8. Földi, M., et al. (2020). "Obesity is a risk factor for developing critical condition in COVID-19 patients: A systematic review and meta-analysis." Obesity reviews: an official journal of the International Association for the Study of Obesity 21(10): e13095. Available here.	This systematic review (SR) explored the role of obesity and overweight as risk factors for ICU admission and invasive mechanical ventilation (IMV) in COVID-19 patients. The SR included 24 retrospective cohort studies. The SR included 24 retrospective cohorts involving with COVID-19. 9 studies were included in the meta-analyses (conducted in China, US (n=3), Italy, France (n=2), Singapore, Israel. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** A meta-analysis that included six studies (including 2,770 individuals) showed that COVID-19 patients with obesity had a statistically significant higher risk of ICU admission (OR 1.21, 95% CI 1.002-1.46; p 0.048; I^2 0.0%, 6 studies). There was insufficient data to compare ICU admission ratios between different BMI ranges using subgroup analyses. COVID-19 patients with obesity had a statistically significant higher risk of IMV according to a meta-analysis of five studies (OR 2.05, 95% CI 1.16-3.64; p 0.014; I^2 34.86%, 5 studies). BMI subgroup analyses (BMI ranges <25, 25-30, 30-35 and ≥35) found that higher BMI ranges always showed a statistically significant increased risk for IMV. The SR found in a meta-analysis of three studies that COVID-19 patients with BMI≥25kg/m^2 (overweight and obesity) compared with COVID-19 patients with BMI≤25kg/m^2 had a statistically significant higher risk of IMV (OR 2.63, 95% CI: 1.64-4.22; p 0.000; I^2 0.0%, 3 studies).	Searches conducted to 11 May 2020. All the studies included in this SR had a lower proportion of females. The authors used different cut-off values for obesity in Asian-Pacific (obesity >25 kg/m2) and Caucasian (obesity >30 kg/m2) population Two studies from the USA contributed over 80% of the weight to the meta-analysis on ICU admission. These had a higher prevalence of obese patients. SR authors noted that the lower range of the confidence interval for ICU admission was close to zero. SR authors noted the results could be limited due to the different strategies for ICU admissions and IMV requirement applied by different hospitals. Results presented here are unadjusted for confounding variables. SR authors conducted a meta-regression for BMI and IMV that showed no correlation. This was not extracted here as the majority of the studies were non-OECD countries.	The SR searched five databases but provided insufficient information to evaluate the search strategy. Although the quality assessment of the included studies was conducted, overall quality scores were not reported and SR authors did not discuss the implications of the quality of included studies on their findings.
9. Hussain, A., et al. “Obesity and mortality of COVID-19. Meta-analysis.” Obesity Research and Clinical Practice. 2020; 14: 295 to 300. Available here.	This SR explored the effect of overweight, obesity in COVID-19 patients in terms of mortality, needs for advanced and basic respiratory support and critical illness. Second analyses observed the effect of comorbidities, gender and age on mortality of COVID-19 patients. The SR compared patients with BMI>25Kg/m^2 (including overweight and obesity) and patients with BMI<25Kg/m^2. The SR included 14 studies involving 403,535 patients with COVID-19 from OECD and non-OECD countries. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Male gender was not a statistically significant factor for increased mortality in COVID-19 in a subset of studies in this review primarily looking at obesity. The odds ratio for death from COVID-19 in men was 0.89 (95% CI 0.70 to 1.12, I^2 93%. P=0.32; n=4, two from China, one Italy and one UK (except Scotland)).	Searches conducted to 1 May 2020. This review is of poorer quality than others on obesity are, therefore PHW reviewers have only extracted data on gender in obese patients and risks of dying (this was only tangentially reported elsewhere). The UK study (excluded Scotland) reported a finding that was in a different direction to the meta-analysis in this review (OR 1.56 95% CI 1.11 to 2.18.) 1,034 participants were included in this meta-analysis, 659 from the UK study. Review authors do not mention confounding or adjustment. However, they used NOS for quality and	The focus of the review was on obesity. The search was conducted across nine databases but there are no search terms in the paper, therefore PHW reviewers are unable to assess whether authors are likely to have missed research. PHW reviewers were unable to access supplementary data giving study characteristics. Therefore, we do not know the study designs, or the countries where the research took place.

Reference	Relevant findings	Things to consider	Limitations of systematic review
		only 5/14 have a star for comparability. However, all the studies included in the meta-analysis included here did have a star for this suggesting that they did consider confounding	Review authors noted as a limitation the inclusion of retrospective clinical reports. There is a lack of information about the consistency checking for the data extraction and quality assessment. Despite high heterogeneity, reviewers have not used a random-effects model (REM) for meta-analysis for most risk factors. Even though quality scores for individual studies have been provided, their impact on results and conclusions has not been discussed. Little detail on how the analysis was done. There are some issues with the referencing between the text and the graphics.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Smoking			Back to Table 1
10. Simons, D., et al. (2020). "The association of smoking status with SARS-CoV-2 infection, hospitalisation and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 9)." Qeios. ***** Available here (Link does not work with Internet Explorer) Version 7 published in Addiction – available here Supplementary data v 7 available here	This systematic review investigates the association of smoking status with SARS-CoV-2 infection, hospitalisation and mortality from COVID-19. Most were observational and only those of 'good' or 'fair' quality were included in the meta-analysis. Studies were conducted across 34 countries (78 in USA, 57 in China, 31 in the UK, 16 in Spain, 14 in France and Mexico, 9 in Italy, 8 across multiple international sites, 5 in Brazil and Iran, 4 in Israel, 3 in Turkey, 2 in Australia, Bangladesh, Chile, Colombia, Denmark, Finland, Germany, India, Japan, the Netherlands and Qatar and 1 each from 13 further countries). Version 9 (searches up to 27 October 2020) included 279 studies with 42 studies rated 'good' or 'fair' included in unadjusted meta-analysis. The majority of included studies are described (in the supplementary material) as retrospective cohorts. Studies were judged as 'good' quality if they: i) had <20% missing data on smoking status and used a reliable self-report measure that distinguished between current, former and never smoking status; AND ii) used biochemical verification of smoking status and reported results from adjusted analyses; OR reported data from a representative/random sample. Studies were rated as 'fair' if they fulfilled only criterion i) and were otherwise rated as 'poor'. Participants were adults 16+ years, self-reported or biochemically verified smoking status (e.g. current smoker, former smoker or never smoker) or vaping and nicotine replacement therapy (NRT) use. 64% of all included studies were conducted in hospital settings, 28% included a community component in addition to hospital patients, 8% were exclusively in the community and one study was conducted in a quarantine centre and one study failed to report setting. Most studies (89%) used reverse transcriptase polymerase chain reaction (RT-PCR) for confirmation of SARS-CoV-2 infection, 5.7% used an antibody test to confirm prior infection and 5.3% of studies relied on a combination of RT-PCR and clinical diagnosis Most studies (180) collected data on smoking status through routine electronic health records, 80 used a bespoke case report form, and 29 did not state the source of information for smoking status. **Q1. Which population groups are most likely to test positive for COVID-19?** Twenty-one studies (two 'good' and 19 'fair' quality) included in meta-analysis (note seem to be 22 studies in Forest plots): Risk of current smokers testing positive for SARS-CoV-2 compared with never smokers: RR 0.69, 95% CI 0.57-0.83 (heterogeneity τ 0.38, 95% CI 0.25-0.56)) Probability of current smokers being at reduced risk of infection compared with never smokers (RR ≤0.9) was 99.6%. Risk of former smokers compared with never smokers testing positive for SARS-CoV-2 was inconclusive and favoured there being no important association: RR 1.02, 95% CI 0.93-1.12 (heterogeneity τ 0.18, 95% CI 0.12-0.26)	Searches were conducted up to 27 October 2020 Living review, which is being continually updated with new studies, currently on version 9. This version of the systematic review (9) has not been peer reviewed. A previous version (7) has been peer reviewed and published as of 19th November 2020. A further ten studies have now been included in the meta-analyses since version 7. No protocol was pre-registered but evolved from a report written for the UK medical society. Systematic review was conducted in accordance with PRISMA guidelines. None of the studies verified smoking status biochemically. At least three large population surveys were not included due to their reliance on self-reported suspected or confirmed SARS-CoV-2 infection. Reporting and categorisation of smoking status (never, current, former, ever) across studies was varied. For example, some studies did not report whether participants who were not current or former smokers were never smokers. Recorded smoking rates in most studies were lower than expected (compared to overall national prevalence estimates). This may highlight an issue with reporting bias within included studies. Sensitivity analyses for groups most likely to test positive for SARS-CoV-2 infection and groups most at risk of hospitalisation, disease severity and mortality left results materially unchanged. Authors reported several issues complicating interpretation of their results including heterogeneous subgroups at heightened risk of infection because of potential confounders associated with smoking status. The majority of included studies relied on electronic health records (EHRs) as the source of information	The current version of this systematic review (version 9) has not been peer reviewed. The SR provides search terms and not a search strategy so PHW reviewers were unable to assess it. However, a large number of studies were identified. The quality appraisal of included studies is not well reported and does not use a recognised tool. No exclusion criteria were outlined in the SR. One reviewer screened and selected the studies, leading to a lack of consistency checking and possibly increasing bias. Study design of included studies is available for version 7, as this has been published. The supplementary data files for version 9 are not publicly available.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Probability of former smokers being at increased risk of infection (RR ≥1.1) compared with never smokers was 5%. Results were materially unchanged in two sensitivity analyses. Data not reported. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Ten 'fair' quality studies were included in the meta-analysis: Current smokers risk of hospitalisation with COVID-19 compared with never smokers: RR 1.06, 95% CI 0.89-1.27 (heterogeneity τ 0.23, 95% CI 0.09-0.43) The probability of current smokers being at increased risk of hospitalisation (RR ≥1.1) compared with never smokers was 32% Former smokers risk of hospitalisation with COVID-19 compared with never smokers: RR 1.17, 95% CI 1.04-1.36 (heterogeneity τ = 0.17, 95% CI 0.08-0.32) The probability of former smokers being at increased risk of hospitalisation (RR ≥1.1) compared with never smokers was 87%. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** The outcome of disease severity was defined by a composite measure (defined as intensive treatment unit (ITU) admission, requiring oxygen as a hospital inpatient or in-hospital death). Meta-analysis was performed for 8 'fair' quality studies. Risk of severe disease among current smokers compared with never smokers: RR 1.26, 95% CI 0.86-1.94 (heterogeneity τ 0.34, 95% CI 0.01-0.86) The probability of current smokers having increased risk of greater disease severity (RR ≥1.1) compared with never smokers was 80% Risk of severe disease among former smokers compared with never smokers: RR 1.52, 95% CI 1.12-2.06 (heterogeneity τ 0.29, 95% CI 0.05-0.65) The probability of former smokers having increased risk of greater disease severity (RR ≥1.1) compared with never smokers was 98% **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Meta-analysis across 13 studies 'fair' quality	on smoking status. Research shows large discrepancies between EHRs and actual behaviour.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Current smokers risk of in-hospital mortality from COVID-19 compared with never smokers: RR1.05, 95% CI 0.71-1.49 (heterogeneity τ 0.45, 95% CI 0.17-0.85) The probability of current smokers being at greater risk of in-hospital mortality (RR ≥1.1) compared with never smokers was 39% Former smokers risk of in-hospital mortality from COVID-19 compared with never smokers: RR 1.39, 95% CI 1.16-1.69 (heterogeneity τ 0.23, 95% CI 0.05-0.44) The probability of former smokers being at greater risk of in-hospital mortality (RR ≥1.1) compared with never smokers was 99%.		
2. Kunchok, D. and K. Hyunju (2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis." medRxiv***** Available here Supplementary material here	This systematic review investigated risk of severe disease or death in hospitalised COVID-19 patients. Forty-four studies comprising 20,594 hospitalised patients met inclusion criteria; 12,591 from the US-Europe and 7,885 from China. 22 studies reported outcomes relating to smoking history; 13 studies about current smokers (19 from China, 7 from USA, 1 each from Italy and Poland) 25 were retrospective, 2 were prospective (from USA and China), and one cross-sectional). The outcome 'severe disease' was defined as any of the following: 1) the study classified COVID-19 disease as severe or critical (defined by studies as respiratory rate≥30 per minute, oxygen saturation≤93%, and PaO2/FiO2<300 and/or lung infiltrates>50% within 24-48 hours. Critical illness was defined as respiratory failure, shock and/or multiple organ dysfunction or failure) 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** The outcome of severe disease was defined by a composite measure Risk of severe COVID-19 disease: Smoking history compared to never smokers sRR (fixed effects) 1.33, 95% CI 1.16-1.54 (I^2 42%; n=15) sRR (random effects) 1.38, 95% CI 1.16-1.63, (I^2 42%; n=15) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** 27% (95% CI 18-41%) of COVID-19 patients who died had a smoking history. For patients with smoking history, the case fatality rate was 22% (95% CI: 11-42%, five studies) Compared to never smokers, patients with smoking history risk of death: sRR (fixed effects) 1.87; (95% C: 1.05-3.33; I^2 80%; 6 studies: 4 x China, 1 x USA, 1x Italy) sRR (random effects) 1.89 (95% CI 1.03-3.44; I^2 80%; 6 studies: 4 x China, 1 x USA, 1x Italy)	Note different results from Search conducted to 22nd May 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratios presented here are largely calculated from unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700. Included studies predominantly from China – may not be relevant to Wales/UK. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals. Also in the meta-analysis for death 8 of the 10 Chinese studies were either from Wuhan or included patients from Wuhan. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals.	Search terms were not sufficiently sensitive. Three databases searched. No preprint or COVID-19 specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was undertaken for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	21% (95% CI 13-37%) of COVID-19 patients who died were current smokers. For current smokers the case fatality risk was 21% (95% CI 5-56%, 3 studies). Compared to never smokers, current smokers risk of death: sRR (fixed effects) 2.20 (95% CI 1.16-4.16, 4 studies, I^2 78%) sRR (random effects) 2.51 (95% CI 1.30-4.86, 4 studies, I^2 78%). Most studies appear to be from China, but it was not possible to ascertain which countries the 4 included studies originated. Sensitivity analysis excluded outliers (1 study from China with a sample size of 108 reporting unadjusted risk, excluded as it showed a significantly higher risk compared to others), but the risk of death for smoking history (sRR 1.59; 95% CI 1.01-2.49) remained significant.		

Reference	Relevant findings	Things to consider	Limitations of systematic review
Alcohol			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Above vs within guidelines alcohol consumption: Low certainty evidence of no important association (OR or RR ≤1.70) with an increased risk of hospitalisation in community samples (2 large prospective cohort studies, both fair quality, both from UK). One study showed a significant difference and one did not.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Physical activity			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. * Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Below vs above guidelines of physical activity: 2 studies of fair quality including 728,075 participants from the UK provided low certainty evidence of no important association (OR or RR ≤1.70) with an increased risk of hospitalisation. Mixed effects were observed.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Education			*Back to Table 1*
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. The certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Education: Lower education vs university degree 1 study of fair quality including 340,966 participants from the UK provided low certainty evidence for no important (OR or RR ≤1.70) association with increased risk of hospitalisation in a community sample. The increased risk observed was not statistically significant.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	There are some limitations of this systematic review, however, the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Place of residence			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** **Living in a low income area**: 1 study involving 3,481 participants from the US provided low certainty evidence for no important (OR or RR ≤1.70) association with an increased risk of hospitalisation in people positive for COVID-19. **Homelessness**: 1 study involving 1,052 participants from the US provided low certainty evidence for a large association (OR or RR ≥2.00) with increased risk of hospitalisation in people positive for COVID-19 compared to people who have a home (1 study, n=1,052). PHW reviewers noted this study is likely underpowered as though the effect size was large, the confidence interval is extremely wide and crosses the line of no effect.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where

Reference	Relevant findings	Things to consider	Limitations of systematic review
	1,3 or 4 household members compared with 2: 1 study involving 340,966 participants from the UK provided low certainty evidence for no important (OR or RR ≤1.70) association with increased risk of hospitalisation compared to households of 2 members in a community sample. Adjusted odds ratio became statistically significant as household members increased to 4 (OR 1.58, 95% CI 1.26 to 2.01).	Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Socioeconomic status			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?**	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity).	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality)

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Highest vs. lowest quintile of social deprivation (using Townsend Index): 1 study of fair quality including 340,966 participants from the UK provided low certainty evidence of a moderate (OR or RR 1.71-1.99) association with increased risk of among a community sample. Q5 vs Q1 OR 1.67 (95%CI 1.3, 2.16). **Income ≤25th vs. >50th or 75th percentile**: 1 study of good quality including 1052 participants from the US provided low certainty evidence of an important (OR or RR ≥2.00) association with an increased risk of hospitalisation in people positive for COVID-19. **≥Average vs. below average income:** 1 study of fair quality including 418,794 participants from the UK provided low certainty evidence of no important association (≤1.70) with an increased risk of hospitalisation among a community sample. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** **Highest vs. lowest quintile of social deprivation (using index of multiple deprivation):** 1 study of fair quality including 130,091 hospitalised participants from the UK provided moderate certainty evidence of no important (≤1.70) association with increased risk of mortality. Q5 vs. Q1 aHR 1.32 (95%CI1.15, 1.52).	Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	(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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Co-morbidities

Reference	Relevant findings	Things to consider	Limitations of systematic review
Cardiovascular disease (CVD)			*Back to Table 1*
11. Hessami, A., et al. (2020). "Cardiovascular Diseases and COVID-19 Mortality and Intensive Care Unit Admission: A Systematic Review and Meta-analysis." medRxiv. ***** Available here There are two versions of this paper – the most recent (posted 10 July has been extracted here but an earlier version was appraised). Supplementary materials available here	Sixteen papers including 3,473 participants in meta-analysis for ICU admission and mortality. Fifty-nine papers including 9,509 patients for descriptive outcomes. Included cohort, case series, case control and cross-sectional designs. The majority of studies were from China, but also included European countries, USA, Israel, Brazil, Korea and one cohort study was international including data from USA, France, Italy, Germany and Singapore (n=27,584 participants). NB results in bold are were the meta-analysis was not predominantly studies from China. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Meta-analysis association with ICU admission Acute cardiac Injury; OR 15.58, 95% CI 5.15 to 47.12, I^2 61.73%. Five studies from China and one from South Korea Arrhythmia; OR 7.03, 95% CI 2.79 to 17.69, I^2 32.22%. Two studies from China **Coronary heart disease; OR 2.61, 95% CI 1.09 to 6.26, $I^2$77.65%. Three studies from China, three from the USA and two from Italy** Cardiovascular disease; OR 3.11, 95% CI 1.59 to 6.09, I^2 71.01%. Nine studies from China, one each from the USA, Germany and South Korea Hypertension; OR 1.95, 95% CI 1.41 to 2.68, I^2 67.62%. 12 studies from China, six studies from the USA, two from Italy and one from South Korea **Heart failure was not statistically significantly; OR 2.44, 95% CI 0.67 to 8.79, I^2 not reported. Two studies from theUSA and one from China** **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Meta-analysis association with mortality: Acute Cardiac Injury; OR 13.29, 95% CI 7.35 to 24.03, I^2 74.26%. 12 studies conducted in China Coronary Artery Disease; OR 3.78 95% CI 2.42 to 5.90, I^2 76.2%. 14 studies from China, one Italy, one in USA Arrhythmia; OR 2.75, 95% CI 1.43 to 5.25, I^2 0%. Three studies conducted in China	Search was conducted up to 27th May 2020 in several databases Most data was from studies in China, the results in bold are were the meta-analysis was not predominantly Chinese studies. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Analyses do not appear to include adjustments for potential confounders. Confounding effects of other co-morbidities in ICU admission and mortality were not considered. SR authors noted that cardiovascular complications could be pre-existing in patients or caused by the infection making it difficult to determine if the relationship is causal. Authors reported high heterogeneity of included study populations. Population size of individual studies varied widely.	Review authors noted the following limitations: heterogeneity of studies in population

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Hypertension; OR 2.60, 95% CI 2.11 to 3.19, I^2 73.92%. 26 studies from China, two from Italy, one each from Iran, USA and UK Heart Failure; OR: 6.72, 95% CI 3.34 to 13.52, 86.78% six studies from China, one from Italy and one from the USA Cardiovascular diseases; OR 2.61, 95% CI 1.89 to 3.62, I^2 55.49%. 10 studies from China, one each from Iran, Italy and the UK.		
2. Kunchok, D. and Hyunju, K (2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis." medRxiv. ***** Available here Supplementary material here	Forty-four studies comprising 20,594 hospitalised patients met inclusion criteria; 12,591 from the US-Europe and 7,885 from China. Looked at risk of severe disease or death in hospitalised COVID-19 patients. Defined outcome as severe disease for any of the following 1) the study classified COVID-19 disease as severe or critical, 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. Severe disease was defined by studies as respiratory rate≥30 per minute, oxygen saturation≤93%, and PaO2/FiO2<300 and/or lung infiltrates>50% within 24-48 hours. Critical illness was defined as respiratory failure, shock and/or multiple organ dysfunction or failure. Studies were conducted in; China (n=31), USA (n=8), Italy (n=2), UK (n=1), Iran (n=1) and Singapore (n=1). Two studies were prospective, one cross sectional and remaining retrospective design (assume case series). Median age was 57 years; 65 years for the US and Europe and 54 years for China. Heart disease prevalence (16%) among COVID-19 patients in the US were substantially higher than the general US population. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** The outcome of severe disease was defined by a composite measure Patients with heart disease relative risk 1.67, 95% CI 1.42 to 1.96 I^2 83% n = 20 (China n=16, USA n=4) Patients with hypertension relative risk 1.61, 95% CI 1.36 to 1.92 I^2 80% n= 22 (China n=19, USA n=3) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** From Forest plot in paper: Relative risk of death for patients with heart disease RR 1.99 95% CI 1.66 to 2.38, I^2 33%, n = 16 (China n=10, USA n=2, Italy, Iran, Poland, UK n=1 each)	Note different results from Search conducted to 22nd May 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratios presented here are largely calculated from unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700. Included studies predominantly from China – may not be relevant to Wales/UK. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals. Also in the meta-analysis for death 8 of the 10 Chinese studies were either from Wuhan or included patients from Wuhan. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals.	Search terms were not sufficiently sensitive. Three databases searched. No preprint or COVID-19 specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was undertaken for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Relative risk of death for patients with hypertension RR 1.84 95% CI 1.84, 95% CI 1.61 to 2.10 I^2 41%, n = 15 (China n=8, USA n=3, Italy, Poland, Iran, UK n=1 each) Summary relative risk of death from table 2 in the paper Cardiovascular disease sRR: 1.99; 95% CI: 1.72 to 2.38; $I^2$33%; n=16 Hypertension sRR 1.84 95% CI 1.66 to 2.03, I^2 0%, n=14 After sensitivity analysis Cardiovascular disease sRR 1.99, 95% CI 1.69 to 2.33 Hypertension sRR 2.02, 95% CI 1.70 to 2.38.		
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv.***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Heart failure; low certainty evidence for a large (OR or RR ≥2) association with increased risk of hospitalisation in people having confirmed COVID-19 Coronary artery disease, hypertension and hyperlipidaemia, composite outcomes; moderate certainty evidence for no important association (OR or RR ≤1.70) for increased risk of hospitalisation for community samples or people positive for COVID-19	Registered on PROSPERO This is a good review and included relevant countries. Data is reported in the supplementary file but there is no meta-analysis (on grounds of heterogeneity). This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Searches were conducted up to 15th June 2020 Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ.	Searching, study selection and data extraction were undertaken by a single reviewer, with uncertainties resolved with a second reviewer. However, methodology has been reported with great transparency. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection? Heart failure; no data is reported for ICU admission, mechanical ventilation or severe disease in people positive for COVID-19 Heart failure; Low certainty evidence of a moderate association with severe disease in people positive for COVID-19 (OR or RR 1.71 to 1.99) Coronary heart disease, hypertension, hyperlipidaemia, composite outcomes; uncertain evidence for ICU admission and mechanical ventilation in community samples or those positive for COVID-19 Coronary heart disease, hypertension, hyperlipidaemia, composite outcomes; low certainty evidence of no important association (OR or RR ≤ 1.70) with severe disease in community samples or those positive for COVID-19 **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Heart failure; low certainty evidence of no important association (OR or RR ≤1.70) with mortality for people positive for COVID-19 Coronary heart disease, hypertension, hyperlipidaemia, composite outcomes; low certainty evidence of no important association (OR or RR ≤1.70) with mortality for people positive for COVID-19	Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	were rated fair. A second reviewer was consulted in the case of uncertainty about the assessment of any individual study. A single reviewer assessed the certainty of the evidence for each association considering relevant components of GRADE.
12. Chang, R., et al. (2020). "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." medRxiv. ***** Available here Supplementary table here	This systematic review and meta-analysis investigated COVID-19 ICU and mechanical ventilation patient characteristics and outcomes among 28 retrospective cohort studies. Data from 12,437 COVID-19 ICU admissions (28 studies) between December 2019 and May 2020 were from USA (n=9), China (n=13), UK (n=2), and one each from Italy, Spain, France and Mexico. All included studies are described as observational, case series were excluded. 15 studies were assessed as good quality and 13 as fair quality. Of note, 14 studies had over 20% of patients with an unknown outcome at endpoint, of which eight had a fair quality assessment assigned to them. Prevalence of CVD among included studies was 0.13 (95% CI 0.104-0.170, I^2 0%, three studies) **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Pooled ICU admission rate among 17,639 hospitalised COVID-19 patients meta-analysed from eight studies (four from China, three from the USA and one from the UK) but data is not presented and findings are not discussed. Pooled IMV rate was analysed in 18 studies (eight from China, six from the USA, one each from Mexico, UK, France and Italy) but data is not reported and findings are not discussed. **Q4. Which population groups are at higher risk of dying from COVID-19 infection?**	This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Search conducted to 1st May 2020 using search terms only. This review was reported in accordance with PRISMA guidelines. Two authors independently screened at title, abstract, full text, data extraction and quality assessment. Studies with overlapped patients, but distinct outcome measures were meta-analysed, otherwise only larger outcome samples were used in studies that overlapped. No information on which countries the data on CVD originates, but they reported high heterogeneity between the studies (I^2 89.74%).	It is not possible to ascertain which countries included studies originate in the meta-analyses, so we cannot be sure the results are generalisable. It is not possible to ascertain what quality rating was assigned to the studies in the meta-analysis. This study looked at multiple co-morbidities, so specific studies may have been missed in the search. In addition, the search was not sensitive enough. Quality of included studies was not discussed (all rated good or fair in the meta-analysis).

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Pooled ICU mortality rate of 12,437 patients from 20 studies was 28.3 % (eight from the USA, seven from China, one each from Mexico, Spain, Italy, UK, and France). CVD was associated with ICU mortality (pOR 2.77, 95% CI 1.76 – 4.37, I^2 44.87%, six studies)	Not all included studies were peer reviewed (16 were peer reviewed, 11 were preprints, and one was an online report). Authors could not adjust for confounders of potentially related variables in an analysis of survival vs. non-survival based on the studies Authors reported significant regional discrepancies in outcomes. Fixed effects meta-analysis unless there was evidence of heterogeneity (was considered significant if the P-value of the Q test is <0.1 and/or I^2 >50%) when random effects model was used.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
Diabetes			*Back to Table 1*
1. Wingert, A et al. (2020). “Risk factors for severe outcomes of COVID-19: a rapid review.” medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known.	There are some limitations of this systematic review, however, the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality were (a) the extent of adjustment for relevant covariates (i.e., basic adjustment for age and sex, versus more extensive

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Two studies involving 6,331 participants from the USA and the UK provided low certainty evidence for important/large associations with increased risk of hospitalisation (OR or RR ≥2.00) in people having confirmed COVID-19 among people with diabetes. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Uncertain evidence for intensive care admission (1 small study) Low certainty evidence of no increased risk of mechanical ventilation (OR or RR ≤1.70) was found among diabetic patients positive for COVID-19 (study information not reported). **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Four studies involving 23,315 participants from the USA and the UK found low certainty evidence of no increased risk for mortality (OR or RR ≤1.70) was found among diabetic patients positive for COVID-19.	Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	adjustment for numerous potential confounders including comorbidities), (b) follow-up duration and extent of censorship for some outcomes (e.g., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.
13. Palaiodimos, L., et al. (2020). "Diabetes is associated with increased risk for in-hospital mortality in patients with COVID-19: a systematic review and	Authors systematically reviewed and meta-analysed available observational studies reporting the effect of diabetes in mortality among hospitalised patients with COVID-19. They identified 18,506 patients (3713 with diabetes and 14, 793 non-diabetics) from fourteen observational studies (twelve retrospective and two prospective). Five studies in Asia, five in the United States and four in Europe. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?**	Search conducted to May 2020. Authors have assessed all included studies as being of low risk of bias. This is surprising given the estimated association is not adjusted for important covariates (with the exception of three studies – meta-analysis of which showed no association between diabetes and in-hospital mortality). Some of the meta-analyses of unadjusted risk estimates were limited by significant heterogeneity (I^2 77.4%).	Search strategy provided in supplementary material suggests the search may not have been sufficiently sensitive. SR authors did not state which study designs the included studies used.

Reference	Relevant findings	Things to consider	Limitations of systematic review
meta-analysis." Hormones. Available here Supplementary material here	Of hospitalised patients, those with diabetes were associated with a higher risk of death compared to patients without diabetes, but with significant heterogeneity (OR: 1.65; 95% CI: 1.3 to 1.96; I^2 77.4%) (based on meta-analysis of 14 studies assessed as being at low risk of bias). Sensitivity analysis were conducted, and found similar risk estimates among studies in the United States (OR: 1.34; 95% CI: 1.04 to 1.85; I^2 73.7%) Europe or the USA (OR: 1.60; 95% CI: 1.27 to 1.93; I^2 82.8%). **From the published paper analysis of only the studies that provided adjusted estimates diabetes vs no diabetes in-hospital mortality OR 1.29 95% CI 0.87 to 1.71 I^2 0% n=3, one UK study, two USA**	Sensitivity analyses by country and age was performed, but the results for age do not appear to be available. Authors acknowledge a lack of data on glucose control prior or during hospitalisation, which limits their ability to differentiate estimates between controlled and uncontrolled diabetes. Guzman, Cummings and Palaiodimos were the only studies that provided adjusted estimates all rated at low risk of confounding however, six studies that did not provide adjusted estimates were also assessed as being at low risk of confounding (fig 2 in published paper). Authors made efforts to exclude duplicated or overlapping patient populations.	
14. Mantovani, A., et al. (2020). "Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies." Nutrition, Metabolism and Cardiovascular Diseases 30(8): 1236-1248. Available here Supplementary material here	Estimated the association between diabetes and clinical severity and in-hospital mortality associated with COVID-19. Included 83 observational studies involving 78,874 hospitalised patients with laboratory-confirmed COVID-19 from China, France, Israel, and the USA were included. Subsets of these studies contributed to meta-analyses of the risk conferred by diabetes on intensive care admission or mortality. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Pre-existing diabetes was associated with an approximate twofold higher risk of having severe/critical COVID-19 (defined as requiring intensive care treatment) (OR 2.10, 95% CI 1.71 to 2.57; I^2=41.5%) (based on random effects model of 22 studies; China x 16, USA x 3, France x 2, Israel x 1) compared to those without diabetes. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Pre-existing diabetes was associated with an approximate threefold increased risk of in-hospital mortality (n=15 studies all but one from China; random-effects OR 2.68, 95% CI 2.09 to 3.44; I^2=46.7%) This analysis supports an adverse effect of pre-existing diabetes on these two clinical outcomes, irrespective of sex. There was a clearer effect of increasing age (p Z 0.05) on the association between pre-existing diabetes and severity of COVID-19. Conversely, age did not appear to exert any significant effect on the association between pre-existing diabetes and risk of in-hospital mortality.	Search conducted to May 2020 for observational studies. All studies were rated as being at a high risk of bias and systematic review authors noted the lack of adjustment of effect sizes for other confounding variables such as age, sex, obesity and other comorbidities in most studies. The majority of patients (i.e., ~85% of total) included in the meta-analysis were of Asian ancestry (mostly Chinese population). The few eligible studies that adjusted results for age, sex, obesity and other relevant comorbidities showed that pre-existing diabetes was independently associated with poorer in-hospital outcomes, and that diabetic patients with better-controlled blood glucose had a less severe COVID-19 illness and lower mortality rate compared to those with poorly controlled blood glucose during hospitalisation. However, these studies were conducted in China, so may not be generalisable to the UK. Diagnosis of diabetes was not always consistent among the included studies, some inaccuracy in the estimated prevalence of diabetes and the identification of diabetic sub-types may not be excluded, although the vast majority of diabetic cases were likely to be type 2. Majority of included studies reported small numbers of participants with diabetes who contracted COVID-19. The overall quality of most included studies was low and are therefore at a high risk of bias.	Three databases searched, no preprint sources may have missed relevant studies. No information is available on the methodological design of included studies other than they were observational. Meta-analyses may have inappropriately pooled differing study designs and pooled unadjusted with adjusted estimates. Diagnosis of diabetes was not always consistent among the included studies; some inaccuracy in the estimated prevalence of diabetes and in the identification of diabetic sub-types may not be excluded, although the vast majority of diabetic cases were likely to be type 2. Authors did not define the term ‘severity’ in the illness outcome. Subgroup analysis by country/location was not performed (other than for pooled prevalence).

Reference	Relevant findings	Things to consider	Limitations of systematic review
15. Kow, C. S. and Hasan, S.S. (2020). "Mortality risk with preadmission metformin use in patients with COVID-19 and diabetes: A meta-analysis." Journal of Medical Virology. Available here	This letter to editor outlines a systematic review conducted that reported adjusted mortality estimates of metformin users in COVID-19, and included five observational studies with a total of 8,121 patients hospitalised for COVID-19. Of these, two were conducted in the USA (6,476 participants) and China (328 participants) and one study was conducted in France (1,317 participants). Authors report studies were of high quality. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Pooled analysis of all included studies showed significantly reduced odds for mortality with the use of metformin (OR 0.62, 95% CI 0.43 – 0.89) compared to non-use of metformin in COVID-19 patients with diabetes.	Search was conducted up to August 8th 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review compares outcomes in those who were treated pre-hospital admission with Metformin – this is reported to have anti-inflammatory effects in experimental studies so the hypothesis is that this might have an impact on COVID-19 related outcomes. Three of the five included studies involved relatively few participants, meaning those meeting the outcome may be small, although 95% CI do not suggest the studies are underpowered. Low heterogeneity was observed across the included studies (p=0.23; I^2 29%), but authors reported this may be due to only patients with COVID-19 and concurrent diabetes being included in the analyses. Authors commented on the possibility that adherence to metformin among users cannot be assured. PHW reviewers noted that there is no sub-analysis investigating the degree of control of diabetes.	Information on the search strategy indicates only keyword searches were undertaken, meaning some studies may have been missed. Strict inclusion criteria were used, so some relevant studies may have been missed. No information is available on whether quality assessment of the included studies was consistency checked. No information is available on the study design other than retrospective observational design. Meta-analyses of included studies used individual adjusted data; however, they adjusted for different potential confounders. No details are available of confounders adjusted for in the meta-analysis.

Reference	Relevant findings	Things to consider	Limitations of systematic review
COPD			*Back to Table 1*
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries.	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. This review combined respiratory conditions as a risk factor. Because of this PHW reviewers have only been able to extract data on the relevant included studies available and not use SR authors determinations on certainty in, and magnitude of effect. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Two studies were identified, one retrospective cohort study (good quality, US) and one large prospective cohort study (fair quality, UK). Both showed increased risk of hospitalisation, the UK study (n=418, 794) showing borderline significance UK study using a community sample aOR 1.51 (95% CI 1.00- 2.28). The US study using a sample that had tested positive for COVID-19 was not statistically significant. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Two good quality studies were identified, one prospective study (UK) and one small retrospective study (US). The UK study showed increased risk aHR 1.17 (95%CI 1.09-1.27, n=20,133), Findings from the other study had a larger effect size but a wider confidence interval leading to a non-statistically significant finding.	context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.
12. Chang, R, et al. “COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic	This systematic review investigated the patient characteristics of COVID-19 intensive care patients (ICU), rates and risks of invasive mechanical ventilation (IMV) and associated outcomes among 28 retrospective cohort studies. COVID-19 ICU patient clinical complications included acute kidney injury, the association with death was analysed in the meta-analysis. Data from 12,437 COVID-19 ICU admissions from USA (n=9), China (n=13), UK (n=2), and one each from Italy, Spain, France and Mexico. 12 studies reported on COPD and five were included in the analysis.	Search conducted to 1st May 2020 using search terms only. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Studies with overlapped patients, but distinct outcome measures were meta-analysed, otherwise, only larger outcome samples were used in studies that overlapped.	This study looked at multiple co-morbidities, so specific studies may have been missed in the search. In addition, the search was not sensitive enough. It is not possible to ascertain what quality rating was assigned to the studies in the meta-analysis. Quality

Reference	Relevant findings	Things to consider	Limitations of systematic review
review and meta-analysis." medRxiv. ***** Available here Supplementary material here	**Q5. Which population groups are at higher risk of dying from COVID-19 infection?** COPD was associated with ICU mortality (pOR 3.22, 95% CI 1.03 – 10.09, I^2 55.03%, 5 studies)	Not all included studies were peer reviewed (16 were peer reviewed, 11 were preprints, and one was an online report). Authors could not adjust for confounders of potentially related variables in an analysis of survival vs. non-survival based on the studies Authors reported significant regional discrepancies in outcomes. Fixed effects meta-analysis was used unless there was evidence of heterogeneity (was considered significant if the P-value of the Q test is <0.1 and/or I^2 >50%). For such heterogeneity, random effects model was used.	of included studies was not discussed (all rated good or fair in the meta-analysis). No information on which countries the data on CVD originates. It is not possible to ascertain whether the results are generalisable.
2. Kunchok, D. and K. Hyunju (2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis." medRxiv. ***** Available here Supplementary material here	This systematic review investigated risk of severe disease or death in hospitalised COVID-19 patients. Forty-four studies comprising 20,594 hospitalised patients met inclusion criteria; 12,591 from the US-Europe and 7,885 from China. 27 studies reported outcomes relating to kidney disease, 17 from China, 7 from USA, 1 each from Italy, Iran and Poland. The outcome 'severe disease' was defined as any of the following: 1) the study classified COVID-19 disease as severe or critical (defined by studies as respiratory rate≥30 per minute, oxygen saturation≤93%, and PaO2/FiO2<300 and/or lung infiltrates>50% within 24-48 hours. Critical illness was defined as respiratory failure, shock and/or multiple organ dysfunction or failure) 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. 26 studies reported COPD as an epidemiological risk factor (15 from China, 8 from USA, and one each from Italy, Poland and the UK); nine were included in the analysis. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Patient's with COPD had a summary relative risk (sRR) of death of 2.80 (95% CI 1.69-4.66; I^2 82%; n=9) among patients hospitalised with COVID-19. Discrepancy in the discussion section notes risk of death in COPD is as sRR 2.0 (95% CI 1.6-2.4).	Search conducted to 22nd May 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratios presented here are largely calculated from unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700. Included studies predominantly from China – may not be relevant to Wales/UK. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals. Also in the meta-analysis for death, 8 of the 10 Chinese studies were from Wuhan or included patients from Wuhan.	Search terms were not sufficiently sensitive. Three databases searched. No preprint or COVID-19 specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was undertaken for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Asthma			*Back to Table 1*
16. Wang, Y., et al. (2020). "Does Asthma Increase the Mortality of Patients with COVID-19?: A Systematic Review and Meta-Analysis." Int Arch Allergy Immunol: 1-7. Available here	This review compared the clinical outcome of asthmatic patients with those of nonasthmatic patients diagnosed with COVID-19. It included five retrospective cohort studies including 9,001 patients (767 with asthma). The majority of data included was from patients living in the US. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** One study from the USA (n=1,526 (220 with asthma)) reported the risk of hospitalisation with asthma RR 0.96 (95% CI 0.77-1.19). Two included studies reported on duration of hospitalisation and one on prolonged hospital stay. None of the studies showed a significant difference between those with asthma and nonasthmatics. SR authors noted that data on the influence of asthma on the risk of hospitalisation is still too limited to draw any strong conclusions. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Two studies reporting on transfer to ICU reported no increased risk in those with asthma, one study from France (n=106 (23 with asthma)) gave an OR 1.06 (95% CI 0.27-3.52). Both these studies included fewer than 25 individuals with asthma in the sample so confidence intervals are wide. SR authors noted that the data for the influence of asthma on the requirement of ICU admission is still too limited to draw any strong conclusions. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** A meta-analysis of data from 744 asthmatic patients and 8,151 nonasthmatic patients indicated that the presence of asthma had no significant effect on mortality (OR 0.96; 95% CI 0.70–1.30; I^2 0%; p = 0.79, 4 studies: three studies from the USA and one from Spain). Results were stable in a sensitivity analysis involving singular exclusion of included studies.	Searches for studies conducted to June 2020. In two studies, all patients in both groups were hospitalised while in another two, both hospitalised and nonhospitalised patients were included in the study groups. SR authors noted that the influence of confounding variables like asthma severity and use of corticosteroids was not assessed. The risk estimates presented for mortality are also unadjusted for confounders such as age, sex or co-morbidities. The presence of asthma was self-reported in all studies. Asthma may not have been adequately recorded in the medical charts of all of the patients. In terms of risk of bias in the included studies, the two largest studies both had high risk with regard to selection of participants and all studies were at high risk from confounding variables.	PHW reviewers were unable to appraise the search for this systematic review as it was not provided. There is a lack of information about whether consistency checking was conducted at data extraction and quality assessment. SR authors did not discuss the implications of the quality of the included studies on their findings.
17. Wang, Y., et al. (2020). "The association between COVID-19 and asthma: A systematic review and meta-analysis." Clin. exp. allergy.	This systematic review investigated the association between severe or fatal COVID-19 and asthma. The SR included 14 studies, mostly retrospective, representing data from 17,694 participants. Five studies were performed in America, two in China and one each in Switzerland, Spain, Saudi Arabia and Kuwait. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** This SR did not report on intensive care admission but rather a composite outcome of severe COVID-19. This was determined by symptoms (e.g. patients with pulse oxygen saturation less	Searches for studies conducted to August 2020. SR authors noted that all studies were high quality. PHW reviewers found this surprising given SR authors were unable to assess whether all baseline characteristics were balanced across groups and that results provided unadjusted estimates that did not consider confounding variables. SR authors acknowledged that more accurate outcomes would result from adjustments for other confounders such as age, gender and co-morbidity.	The search for this systematic review was poorly reported therefore PHW reviewers were unable to assess whether it was likely to have missed relevant research. The paper was published as a letter to the editor and did not include a flow diagram documenting the screening process for inclusion of studies. SR authors combined results with different outcomes in the case of ‘severity’ and

Reference	Relevant findings	Things to consider	Limitations of systematic review
Available here	than 90% or required mechanical ventilation, or with acute respiratory distress syndrome, or admitted to intensive care unit.) Most studies involved admission to intensive care in the eleven studies pooled. Patients with severe COVID-19 disease were not associated with an increased risk of asthma than non-severe COVID-19 patients (OR 1.36; 95% CI 0.79-2.34; *p* = .27; I^2 77%; p-heterogeneity= <0.00001; 11 studies (n=14.148 (641 with asthma): four studies from America, two each from China and Mexico and one each from Switzerland, Kuwait, and Saudi Arabia). Sensitivity analyses by omitting each study at a time did not significantly alter the direction of the overall estimates. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Asthma was not associated with increased risk of mortality in patients with COVID-19 (OR 1.03; 95% CI 0.55-1.93; *p* = .92; I^2 76%; 5 studies (n=14,588 (616 with asthma): two studies from America, and one each from Mexico, Spain, and Kuwait). Sensitivity analyses by omitting each study at a time did not significantly alter the direction of the overall estimates.	SR authors noted that there was heterogeneity across results. PHW reviewers noted that confidence intervals for severity outcomes are extremely wide in most included studies.	potentially different study designs. The SR is unclear on study designs identified/ included. The SR did not discuss the heterogeneity observed nor investigate it in detail.
18. Wang, Y., et al. (2020) "The relationship between severe or dead COVID-19 and asthma: A meta-analysis." Clin. exp. allergy. Available here	This systematic review explored the association between severe or dead COVID-19 and asthma. The SR included 14 studies, most of them retrospective, representing data from 32,187 participants. Seven studies were from America, two studies from Spain and one each from Kuwait, Mexico, the UK, France and China. Asthma was mainly defined according to the patients' medical history. The overall quality of available literature was moderate with NOS scores ranging from 7 to 9. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** This SR did not report on intensive care admission but rather a composite outcome of severe COVID-19. This was determined by symptoms (eg patients required intubation and mechanical ventilation, with acute respiratory distress syndrome, hospitalisation or admitted to intensive care unit). The meta-analysis showed that asthma was not associated with an increased risk of severe COVID-19 disease (OR = 1.09, 95% CI: 0.79-1.51, P = .61; I^2 77%; 12 studies (n= 20,333 (6,029 with asthma): America (n=6), Spain (n=2) and one each from Kuwait, Mexico, France and China) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Asthma was not associated with increased risk of mortality in patients with COVID-19 (OR 0.84, 95% CI: 0.58-1.23, P = .37; I^2 54%; 10 studies (n= 19,367 (2,149 with asthma): America (n=4), Spain (n=2), one each from Kuwait, China, Mexico and France) The adjusted pooled analysis of only three studies showed as well that asthma was not associated with increased risk of mortality in patients with COVID-19 (OR 1.86, 95% CI: 0.74-4.64, P = .105; I^2 55.6%; 3 studies (n= 12,957): one each from the UK, America and Kuwait.	Search conducted to September 1st 2020. The sample size of patients ranged from 112 to 10,926. SR authors noted that there was heterogeneity across results and most of the studies were retrospective.	The search for this systematic review was poorly reported therefore PHW reviewers were unable to assess whether it was likely to have missed relevant research. The paper was published as a letter to the editor and did not include a flow diagram documenting the screening process for inclusion of studies. SR authors combined results with different outcomes in the case of 'severity' and potentially different study designs. The SR is unclear on study designs identified/ included. The SR did not discuss the heterogeneity observed nor investigate it in detail.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	The subgroup analysis based on countries indicated no significant relationship between asthma and risk of mortality in patients with COVID-19 from America (OR 0.73, 95% CI: 0.52-1.03, P = .08; I^2 0%). Sensitivity analyses by omitting each study at a time did not significantly change the results.		
19. Castro-Rodriguez, J. A. and Forno, E. (2020). "Asthma and COVID-19 in children: A systematic review and call for data." Pediatr. pulmonol. Available here	This SR aimed to ascertain whether asthma was a risk factor for SARS-CoV-2 infection or COVID-19 severity in children. It reports a lack of epidemiological evidence to determine whether or not asthma is a risk factor in children. No studies were included.	Last update of searches was May 1, 2020.	There was poor reporting of SR methods in this review. No detail of intended quality assessment, data extraction or analysis was provided. Searches involved trying to find relevant systematic reviews to collate included primary studies of relevance. Then follow-up searches of PubMed and two pre-print databases were conducted to find additional primary studies. Search strategy was limited.
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here. Supplementary data here.	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00)	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (c) inappropriate or large exclusions from the study and/or analysis (e.g., missing

Reference	Relevant findings	Things to consider	Limitations of systematic review
	In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. This review combined respiratory conditions as a risk factor. Because of this PHW have only been able to extract data on the relevant included studies available and not use SR authors' determinations on certainty in, and magnitude of effect. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** SR authors found one good quality retrospective cohort (n=1052) from the USA that reported an aOR= 1.52 (95%CI 0.89-2.58; p >0.05) for the risk of hospitalisation in asthmatic patients who were positive for COVID-19	Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Chronic Kidney disease (CKD)			*Back to Table 1*
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. Chronic kidney disease was identified in 5 studies with a community sample or those positive for COVID-19 (3 from USA and 2 from UK). All had a 'good' quality rating except one prospective cohort from the UK, rated as 'fair'. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Moderate certainty evidence for a large (OR or RR ≥2) association with increased risk of hospitalisation in people having confirmed COVID-19 (2 studies, UK [fair quality] and USA [good]). **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Severe disease as defined by study authors; for example, composite outcome of ICU transfer or death. Moderate certainty evidence of no important (OR or RR ≤1.70) association with increased risk of severe disease in people having confirmed COVID-19 (2 studies, n=2,922, both USA, both good quality). **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Moderate certainty evidence of no important (OR or RR ≤1.70) association with increased risk of mortality in people having confirmed COVID-19 (3 studies, n=23,058, USA x 2, UK, all good quality).	Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.
2. Kunchok, D. and K. Hyunju		Search conducted to 22nd May 2020.	Search terms were not sufficiently sensitive. Three databases searched. No

Reference	Relevant findings	Things to consider	Limitations of systematic review
(2020). "Epidemiological Risk Factors Associated with Death and Severe Disease in Patients Suffering From COVID-19: A Comprehensive Systematic Review and Meta-analysis." medRxiv. ***** Available here Supplementary material here	This systematic review investigated risk of severe disease or death in hospitalised COVID-19 patients. Forty-four studies comprising 20,594 hospitalised patients met inclusion criteria; 12,591 from the US-Europe and 7,885 from China. 27 studies reported outcomes relating to Kidney disease; 17 from China, 7 from USA, 1 each from Italy, Iran and Poland. The outcome 'severe disease' was defined as any of the following: 1) the study classified COVID-19 disease as severe or critical (defined by studies as respiratory rate≥30 per minute, oxygen saturation≤93%, and PaO2/FiO2<300 and/or lung infiltrates>50% within 24-48 hours. Critical illness was defined as respiratory failure, shock and/or multiple organ dysfunction or failure) 2) intensive care unit (ICU) admission 3) acute respiratory distress syndrome 4) mechanical ventilation. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** CKD patients had higher relative risk of severe disease [sRR: 1.67; 95% CI: 1.30- 2.16; I^2 90%; n=14] compared to non-CKD hospitalised patients (8 studies) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** CKD patients had higher relative risk of death [sRR: 2.17; 95% CI: 1.30-3.13; I^2 75%; n=8] compared to non-CKD hospitalised patients (8 studies) Sensitivity analysis was conducted by using counts only from one original study, rather than adjusted risk estimates. Results were similar (sRR 1.90, 95% CI 1.27-2.86).	This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. Authors noted that most studies reported frequencies of risk factor and did not present adjusted measures for disease severity or death. As such, the risk ratios presented here are largely calculated from unadjusted estimates. Funnel plots showed asymmetry plots suggesting publication bias or a systematic difference between studies of higher and lower precision (possibly small study effects). There was considerable variation in study size n=16 to n=5700. Included studies predominantly from China – may not be relevant to Wales/UK. There may be duplication of some patients included in the meta-analyses – some Chinese studies appear to have the same authors but are published in different journals. Also in the meta-analysis for death 8 of the 10 Chinese studies were either from Wuhan or included patients from Wuhan.	preprint or COVID-19 specific databases searched so may have missed most recent studies. There was a lack of information on whether consistency checking was undertaken for the selection of the studies, data extraction and quality assessment. The SR did not report the statistical significance values and the quality score for each of the included studies. Note different results from different sections of this paper – some are summary RR some just RR, not always clear what the differences are – although results are similar – not clear if there are errors in the paper. Also errors in labelling of tables. 95% confidence intervals for between-study heterogeneity using a method not described in the paper.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Liver disease			*Back to Table 1*
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone.	There are some limitations of this systematic review, however, the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt,

Reference	Relevant findings	Things to consider	Limitations of systematic review
Supplementary data here	considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE. Hepatic or liver disease, with or without cirrhosis was reported in 3 studies. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Low certainty evidence for no important (OR or RR ≤1.70) association with increased risk of hospitalisation in people positive for COVID-19. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Two studies, n=20,597 Low certainty evidence of a large association (OR or RR ≥2.00) of increased risk of mortality for people positive for COVID-19. Low certainty evidence of no important (OR or RR ≤1.70) association of increased risk of mortality among people hospitalised.	Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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. Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.	decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Neurological disease			Back to Table 1

Reference	Relevant findings	Things to consider	Limitations of systematic review
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. * Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00) In determining the magnitude they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE Neurological disease (Alzheimer's, dementia or chronic neurological disorder) was identified in 4 studies within a community sample or hospitalised population (2 from Italy and 2 from the UK). All had a 'fair' quality rating except one prospective cohort from the UK, rated as 'good'. **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** There was low certainty of evidence for important/large associations with increased risk of hospitalisation in people having confirmed COVID-19. Dementia; low certainty evidence for a large (OR or RR ≥2) association with increased risk of hospitalisation in community people having confirmed COVID-19 (1 prospective cohort, n= 418,794, UK [fair quality]). **Q5. Which population groups are at higher risk of dying from COVID-19 infection?**	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known. Generalisations to other countries should be made with caution, as high risk groups in these populations may differ. Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity). Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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.	There are some limitations of this systematic review, however the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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., ≥2 weeks for mortality) (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 where assessment of any individual study was difficult. A single reviewer assessed the certainty of the evidence.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Alzheimer's disease or Dementia: low certainty evidence of no important (OR or RR ≤1.70) association with increased risk of mortality in community people having confirmed COVID-19 (1 prospective cohort and 2 retrospective cohorts, n= 20,829, 2 from Italy, one from UK [2 fair quality and 1 good quality]). Chronic neurological disorders: low certainty evidence of no important (OR or RR ≤1.70) association with increased risk of mortality in hospitalised people having confirmed COVID-19 (1 prospective cohort, n=20,133, UK [good quality]).	Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, 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 the hospitalisation outcome, the included study had significant missing data on risk factors from 2006-2010.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
Pregnancy			Back to Table 1
20. Allotey, J., et al. (2020). "Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis." BMJ 370: m3320-m3320. Available here	77 studies ((55 comparative, 22 non-comparative) were included; 26 (34%) were from the United States, 24 from China (31%), seven from Italy, six from Spain, three each from the United Kingdom and France, and one each from Belgium, Brazil, Denmark, Israel, Japan, Mexico, the Netherlands, and Portugal. Eight studies (9,5247 women) compared pregnant populations with non-pregnant populations, and four studies (2,230 women) compared pregnant women with COVID-19 versus pregnant women without COVID -19. Most of the included studies were deemed to have a low or medium risk of bias. Overall, 10% (95% CI 7% to14%; 28 studies, 11,432 women) of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed COVID-19 (laboratory confirmation). One in 20 asymptomatic mothers (5%, 95% CI 2% to 9%; 11 studies) attending or admitted to hospital had a diagnosis of COVID-19. Three quarters (74%, 95 CI 51% to 93%; 11 studies) of the 162 pregnant women with COVID-19 in the universal screening population were asymptomatic. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Compared with non-pregnant women of reproductive age with COVID-19, the odds of admission to the intensive care unit was OR 1.62 (95% CI 1.33 to 1.96; I^2 0%) and need for invasive ventilation (OR 1.88, 95% CI 1.36 to 2.60; I^2 0%; 4 studies, 91,606 women) in pregnant and recently pregnant women. Odds of admission to intensive care unit in pregnant and recently pregnant women, compared to pregnant women without COVID-19 OR 71.63 (95% CI 9.81 to 523.06, 1 UK study, historical controls). Compared to non-pregnant women of reproductive age with COVID-19 the odds of invasive ventilation among pregnant women with COVID-19 was OR 1.88 (95% 1.36 to 2.60, 1 study) Pre-existing maternal comorbidity was associated with admission to an intensive care unit (OR 4.21, 95% CI 1.06 to 16.72; I^2 0%; 2 studies; 320 women) and the need for invasive ventilation (OR 4.48, 95% CI 1.40 to 14.37; I^2 =0%; 2 studies; 313 women).	Searches conducted to 26 June 2020 in published version. This is a living systematic review and meta-analysis, so estimates may change as new data becomes available. Each cycle of the living systematic review involves weekly search updates (rounds), with analysis performed every 2-4 weeks for monthly reporting through a dedicated website, with early analysis if new definitive evidence emerges. This version was accepted for publication August 2020. A protocol was registered with the PROSPERO database. SR authors noted that all comparative findings are based on small numbers of studies, despite the large sample sizes. They added that substantial heterogeneity was observed in the estimates for rates of clinical manifestations and outcomes, which varied by sampling frames, participant selection, and risk status of the participants. Available research included women with suspected and confirmed COVID-19, and primarily reported on pregnant women who required visits to hospital, including for childbirth. SR authors noted this will affect the generalisability of the estimates. For some outcomes, the findings were influenced by a single large study.	SR authors did not provide a definition of severe COVID-19. Authors did conduct a sensitivity analysis based on the quality of the studies but did not discuss the implications of the quality on their findings extensively.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Increased maternal age (OR1.78, 1.25 to 2.55; I^2 =9%; 4 studies; 1,058 women), high body mass index (OR 2.38, 95% CI 1.67 to 3.39; $I^2$0%; 3 studies; 877 women) chronic hypertension (OR 2.0, 95% CI 1.14 to 3.48; $I^2$0%; 2 studies; 858 women), and pre-existing diabetes (OR 2.51, 95% CI 1.31 to 4.80; $I^2$12%; 2 studies; 858 women) were associated with the composite outcome of severe COVID-19 in pregnancy. Of these co-occurring factors, only chronic hypertension was associated with statistically significant increased risks for intensive care admission or mortality. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** All-cause mortality odds among pregnant women with COVID-19 compared to non-pregnant women of reproductive age with COVID-19: OR 0.81 (0.49 to 1.33, I^2 0%, 4 studies) Compared to pregnant women without COVID -19: OR 18.08 (95% CI 1.00 to 327.83, 1 UK study, historical controls).	SR authors noted that meta-analyses were restricted to cohort study data to minimise risk of bias. PHW reviewers have only extracted findings related to complications of COVID-19 rather than pregnancy outcomes. The paper includes some information on rates of adverse pregnancy outcomes in women with COVID-19 not extracted here.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
Cancer (non-specific)			Back to Table 1
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review." medRxiv. ***** Available here Supplementary data here	Rapid narrative review investigating the association between potential risk factors and the risk of severe outcomes (rate of hospitalisation, hospital length of stay, severe disease [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]) of COVID-19. 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) hospitalised with COVID-19, and d) with a risk factor of interest. Included 34 studies reporting on 32 unique populations. Prospective or retrospective cohort studies. Three UK studies used overlapping cohorts from a single database and were considered as a single population in the analysis. Another included UK study is also likely to overlap with these populations. Included studies were USA (n=17), Italy (n=8), Spain (n=1) and UK (n=7) and one study reporting data from 17 countries. 19/34 studies were rated as good quality 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 domains considered important for the review. Median study participant size of individual studies was 596 (range 44 to 418,794). Authors categorised associations as; Small/unimportant (odds ratio [OR] or risk ratio [RR] ≤1.70) Moderate (1.71 to 1.99), Large (≥2.00) Very large (≥5.00)	Searches were conducted up to 15th June 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article. The review was conducted to identify those who should be prioritised for vaccination. Authors considered the magnitude of the effect not statistically significance alone. Includes only those relating to OECD populations. 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) were included, but were considered to be less applicable to the Canadian context when interpreting the findings. In addition, three studies conducted in the United Kingdom (UK) used overlapping cohorts from a single medical/research database, and were considered as a single population in the analysis. Another large UK study is likely to also be overlapping with these populations, but the degree of overlap is not known.	There are some limitations of this systematic review, however, the methodology has been reported with great transparency. PHW reviewers consider it a good review, protocol registered on PROSPERO, which included research from relevant countries. Searching, study selection and data extraction were undertaken by a single reviewer. Where there was doubt, decisions were resolved with a second reviewer. No formal tool used for quality assessment. Key variables used to assess the quality 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),

<table>
<tr><th>Reference</th><th>Relevant findings</th><th>Things to consider</th><th>Limitations of systematic review</th></tr>
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In determining the magnitude, they compared findings across all relevant studies and often relied heavily on the findings of the largest and/or good quality studies. Certainty of the evidence for each association considering relevant components of GRADE.

Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?

SR authors reported moderate certainty for no important association between having cancer and increased risk of hospitalisation for COVID-19 in non-specific cancer (based on two studies (n= 6,331) from the USA, one prospective cohort and one retrospective cohort).
<table>
<tr><th>Outcome among population</th><th>Study</th><th>Total number of patients</th><th>Adjusted odds ratio*</th><th>95% CI lower bound</th><th>95% CI upper bound</th><th>p-value</th><th>Quality rating</th></tr>
<tr><td>positive for COVID-19</td><td>Azar K (USA; rc)</td><td>1,052</td><td>0.96</td><td>0.45</td><td>2.03</td><td>>0.05</td><td>Good</td></tr>
<tr><td>positive for COVID-19</td><td>Petrilli CM (USA; pc)</td><td>5,279</td><td>0.88</td><td>0.65</td><td>1.19</td><td>0.41</td><td>Good</td></tr>
</table>
Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?

Severe disease (Composite outcome)

SR authors reported moderate certainty for no important increase in severe disease of COVID-19 in nonspecific cancer (based on two studies (n= 2,769), one prospective cohort from the USA and one retrospective cohort from Italy).
<table>
<tr><th>Outcome among population</th><th>Study</th><th>Total number of patients</th><th>Adjusted odds ratio*</th><th>95% CI lower bound</th><th>95% CI upper bound</th><th>p-value</th><th>Quality rating</th></tr>
<tr><td>hospitalised with COVID-19</td><td>Petrilli CM (USA; pc)</td><td>2,725</td><td>1.3</td><td>0.95</td><td>1.8</td><td>0.1</td><td>Good</td></tr>
<tr><td>hospitalised with COVID-19</td><td>Colaneri M (Italy; rc)</td><td>44</td><td>22.199</td><td>0.826</td><td>596.152</td><td>0.0648</td><td>Good</td></tr>
</table>
Q5. Which population groups are at higher risk of dying from COVID-19 infection?

SR authors reported moderate certainty of no important increase in mortality for COVID-19 in non-specific cancer (based on three studies (n= 24,041), two studies from the UK and one from the USA, one retrospective cohort and two prospective cohorts). They added that moderate associations may exist for increased mortality with haematological malignancy (based on one retrospective cohort (n=1.,83) from the UK, low certainty).
</td>
<td>
Generalisations to other countries should be made with caution, as high risk groups in these populations may differ.

Data is reported in the supplementary file. There is no meta-analysis (on grounds of heterogeneity).

Authors excluded studies only examining patients with severe COVID-19 (i.e., in ICU settings), and therefore the 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 SR authors 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.

Authors focused the review on better quality studies that minimally controlled for age and sex, therefore, the strength of certain associations should be interpreted cautiously because there are likely to be multiple unmeasured confounders that have not been accounted for.
</td>
<td>
(b) follow-up duration and extent of censorship for some outcomes (e.g., ≥2 weeks for mortality)
(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 where assessment of any individual study was difficult.

A single reviewer assessed the certainty of the evidence.
</td>
</tr>
</table>

<table>
<tr><th>Reference</th><th>Relevant findings</th><th>Things to consider</th><th>Limitations of systematic review</th></tr>
<tr>
<td></td>
<td>
<table>
<tr><th>Outcome among population</th><th>Study</th><th>Total number of patients</th><th>Adjusted odds ratio*</th><th>95% CI lower bound</th><th>95% CI upper bound</th><th>p-value</th><th>Quality rating</th></tr>
<tr><td colspan="8">Cancer or tumour</td></tr>
<tr><td>hospitalised with COVID-19</td><td>Petrilli CM (USA; pc)</td><td>2,725</td><td>1.29</td><td>1.03</td><td>1.62</td><td>0.03</td><td>Good</td></tr>
<tr><td>hospitalised with COVID-19</td><td>Docherty AB (UK; pc)</td><td>20,133</td><td>aHR 1.13</td><td>1.02</td><td>1.24</td><td>0.017</td><td>Good</td></tr>
<tr><td>positive for COVID-19</td><td>Shah V (UK; rc)</td><td>1,183</td><td>aHR 1.74</td><td>1.12</td><td>2.71</td><td>0.014</td><td>Fair</td></tr>
<tr><td colspan="8">Haematological cancer - lymphoid</td></tr>
<tr><td colspan="8"></td></tr>
<tr><td>positive for COVID-19</td><td>Shah V (UK; rc)</td><td>1,183</td><td>aHR 1.75</td><td>1.07</td><td>2.87</td><td>0.026</td><td>Fair</td></tr>
<tr><td colspan="8">Haematological cancer - myeloid</td></tr>
<tr><td colspan="8"></td></tr>
<tr><td>positive for COVID-19</td><td>Shah V (UK; rc)</td><td>1,183</td><td>aHR 1.70</td><td>0.7</td><td>4.13</td><td>0.244</td><td>Fair</td></tr>
</table>
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<td></td>
<td></td>
</tr>
<tr>
<td>21. Giannakoulis, V. G., et al. (2020). “Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data.” JCO Global Oncology 6: 799-808.

Available here</td>
<td>Authors systematically reviewed and meta-analysed observational studies reporting the effect of cancer on mortality and ICU admission (including severe disease, such as invasive mechanical ventilation (IMV)) in patients with COVID-19. This systematic review included a total of 32 studies (19 peer-reviewed, 13 preprints) involving 46,499 patients (1,776 patients with cancer) with COVID-19 from Asia, Europe, and the United States. Most studies were retrospective cohort studies with three identified as prospective.

Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?

The need for ICU admission was also more likely in patients with cancer versus without cancer (3,220 events; RR 1.56; 95% CI, 1.31 to 1.87; p < .0001; I^2 = 53% p-heterogeneity = .0008). Based on a random effects meta-analysis of 26 studies with 15,375 patients (801 patients with cancer). 18 studies were from China, six from the US, and two from Italy.

Q5. Which population groups are at higher risk of dying from COVID-19 infection?

All-cause mortality was higher in patients with cancer versus those without cancer (2,034 deaths; RR 1.66; 95% CI 1.33 to 2.07; p < 0001; I^2 = 37%; p-heterogeneity = .13); Based on a random effects meta-</td>
<td>Search retrieved research made available between January 2020 and April, 2020.

Studies reported in preprints were included in the meta-analysis.

Pre-specified subgroup analyses by type of cancer (solid-tumour vs haematological malignancy) and country could not be performed because of unavailability of relevant data.

SR authors suggested that the observed absence of increase mortality risk in older individuals implies that the presence of cancer may not further affect the already burdened prognosis among individuals age>65.

SR authors noted the concern for duplicate publications however they attempted to minimise this</td>
<td>The search conducted for this systematic review could have been more sensitive.

SR authors could have provided a fuller discussion on the quality of included studies. The paper tabulated critical appraisal findings but did not discuss the implications of these. However they did conduct a sensitivity analysis for mortality outcomes from low risk studies.</td>
</tr>
</table>

Reference	Relevant findings	Things to consider	Limitations of systematic review
	analysis of eight studies with 37,807 patients (1,428 of which had cancer). Three studies from the US, two from Italy, and one each from the UK, Iran and China. In the sensitivity analysis of four studies with low risk of bias (8,804 total patients, 694 with cancer), all-cause mortality was higher in patients with versus without cancer (856 deaths; RR 1.47; 95% CI 1.04 to 2.09; p = .03). Of these four studies, two were conducted in Italy and were prospective and two were retrospective cohort studies conducted in the UK and the US. Sensitivity analyses by excluding each study and recalculating the RR also showed all-cause mortality being higher in patients with versus without cancer. However, in a pre-specified subgroup analysis of patients > 65 years of age, all-cause mortality was comparable between those with versus without cancer (915 deaths; RR 1.06; 95% CI 0.79 to 1.41; p = .71; I^2 = 27%; p-heterogeneity = .21). The analysis was based on 8 studies with 5,438 patients (of which 505 had cancer). The studies were two of each from the US, Italy and China and one each from the UK and Iran.	by excluding studies on mortality conducted in the same region with overlapping enrolment dates and included only the results of the largest cohort. By comparing the risk of bias table with the critical appraisal tool, PHW reviewers noted that many of the included studies did not adjust for confounding in an adequate way and some studies also had inadequate follow-up. This analysis was based on unadjusted risk ratios.	
22. Liu,Y., et al. (2020). "Clinical risk factors of mortality in patients with cancer and COVID-19: a systematic review and meta-analysis of current observational studies." Expert Review of Anticancer Therapy. Available here Supplemental material here	The main purpose of this systematic review (SR) was to identify research reporting on characteristics or comorbidities in cancer patients to identify if these were additional risk factors to having cancer. The SR and meta-analysis included 17 studies involving 3,268 patients with both cancer and COVID-19. Most included studies were retrospective cohort designs though meta-analyses did include one case control study and one cross sectional study. Eight studies were performed in China, two in the UK, and one of each in France, Spain and the USA, and four were international multicentre studies. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** In patients with cancer: Pooled mortality across 17 studies included in a random effects meta-analysis was 24.8% with a high and significant heterogeneity among studies (RR 0.25; 95%CI 0.20, 0.30; I^2= 89.7%; p-heterogeneity= .000; 17 studies n= 3.268 (743 deaths)). Eight studies were performed in China, four were international multicentre, two in the UK, and one each in the USA, France and Spain. **Characteristics** Male gender was associated with a higher risk of death (RR 1.16; 95% CI 1.04–1.28; Z=2.27; p =0.006, I^2=42% (low heterogeneity) but significant (p-heterogeneity=0.05)). Based on a random effects meta-analysis of 14 studies including 2.946 patients (1653 males and 1293 females). Six studies were from China, four were international multicenter, two from the UK and one each from Spain and the USA. Age older than 65 years was another risk factor for higher mortality (RR 1.27; 95% CI 1.08–1.49; p= .004; I^2= 56% (moderate heterogeneity). Based on a random effects meta-analysis of six studies including 1580 patients (897 patients >65 years). Three studies were from China and three were international multicenter studies. **Comorbidities** Having a comorbidity increased the probability of death in both the low heterogeneity subgroup (RR 1.12; 95% CI 1.04–1.2; p= 0.002, I^2= 40% (low heterogeneity); p-heterogeneity= 0.10, subgroup analysis of 9 studies (n=2.592 (106 with comorbidities); five studies from China, three international multicenter, and one from the UK) and the overall group (RR 1.15; 95% CI 1.03–1.27; p <0.0001, I^2= 68% (moderate heterogeneity); p-heterogeneity= 0.0009; based on a random effects meta-analysis of 10 studies	Search included studies published up to July 2020. For some risk factors heterogeneity (I^2) was higher, limiting conclusions. Also for some analyses in relation to treatment, results were pooled from a few trials. No subgroup analysis by countries was performed therefore the meta-analyses included data from participants both in OECD and non-OECD countries SR authors postulated that it is possible that comorbidities increase the complexity and difficulty of treatment after the onset of COVID-19, thereby seriously affecting prognosis. SR authors also speculated that tumours in thyroid cancer and breast cancer present lower risks of death potentially due to the location of the cancer (away from vital organs). No comment was made by SR authors on the distribution of these cancers by sex.	The search for this systematic review may have missed some relevant papers. It was not reported whether screening was conducted in duplicate or whether a percentage of records were consistency checked. SR authors acknowledged that they were unable to control for some potential confounders. Lack of control for confounding variables in the included studies appears to be the primary reason for lower scores during quality assessment. SR authors did not discuss the implications of confounding extensively; no adjusted effect sizes are reported. Limitations of the included studies are not discussed narratively and sensitivity analyses are conducted. The meta-analyses on occasion combined studies with different methodological design.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	(n=2.651 (126 with comorbidities); five studies from China, three international multicenter, and one each from the UK and France). Patients in this analysis above might suffer from multiple comorbidities simultaneously. Some studies reported the effect of a specific comorbidity. The most common concurrent disease was hypertension 36.67% (741/2021), followed by diabetes (15.79%, 319/2020). The effects of hypertension (RR 1.23; 95% CI 1.09–1.38; Z=3,40; p= 0.0007, I^2= 41% (low heterogeneity); p-heterogeneity=0.07; 11 studies) and chronic obstructive pulmonary disease (COPD) (RR 1.47; 95% CI 1.09–1.98; Z= 2.54; *P*= 0.01; I^2= 0% (low heterogeneity); 7 studies) on mortality in patients with cancer were significant. The effects of diabetes, heart disease, cerebrovascular disease, chronic renal failure, smoking history and obesity did not reach statistical significance in patients with cancer. **Recent anti-cancer treatment (infection within one month)** Recent anti-cancer treatment were not clearly associated with mortality rates: Rates of **surgery** were similar in non-survivors (3.79%, 16/422) and survivors (3.66%, 63/1722), with 16 deaths, and surgery itself did not increase the risk of death (RR 1.15, 95% CI 0.69–1.94, I^2=0%; 7 studies (n=2.144 (79 patients with surgery): four from China, and one each from the UK, France and an international multicenter study). **Radiotherapy** did not increase the risk of death (RR 0.86, 95% CI 0.55–1.34, I^2=0%; 4 studies (n= 1.152 (102 with radiotherapy): two from China and one each from the UK and France)). **Chemotherapy** did not increase the risk of death (RR 0.86, 95% CI 0.55-1.34, I^2=67%; 9 studies (n= 2,387 (623 with chemotherapy)), **targeted therapy** did not increase the risk of death (RR 0.93, 95% CI 0.60-1.45, I^2=58%; 4 studies (n= 1,152 (107 with targeted therapy) and neither did i**mmunotherapy** (RR 1.01, 95% CI 0.66-1.54, I^2=34%; 8 studies (n=2,368 (1,122 with immunotherapy). A lack of anti-cancer therapy did not change the risk of death (RR 0.93, 95% CI 0.74-1.15, I^2=61%; P-heterogeneity= 0.01; 8 studies (n=2,368 (1,122 without anti-cancer therapy: three from China, two each from the UK and international multicenter and one from France) **Effects of cancer type and stage on mortality** The mortality rate for patients with solid cancers (19%, 328/1726) was lower than that for patients with hematological malignancies (27.78%, 110/396). Malignancies in the hematological system significantly increased the risk of death with low heterogeneity (RR 1.50; Z=3.96; 95% CI 1.23-1.83; *P*<0.001; I^2=47%; P-heterogeneity= 0.08; 7 studies). With respect to solid cancers, the risk of death was low in patients with breast (RR=0.55, 95% CI 0.38–0.8, *P*=0.0002; I^2= 0%, 6 studies) and thyroid carcinoma (RR=0.23, 95% CI 0.07–0.74, *P*=0.01; I^2= 0%, 4 studies). There was not sufficient evidence to determine whether lung, gastrointestinal, ovarian, liver, and cervix tumors are independent risk factors (*P*>0.05). In addition, limited data showed that the tumor stage did not affect the prognosis of patients with COVID-19 (*P*>0.05).		
23. Wang, B., and Huang, Y. (2020). "Immunotherapy or other anti-cancer treatments and risk of exacerbation and	This SR aimed to explore whether COVID-19 patients with recent immunotherapy or other anti-cancer treatments had more severe symptoms and higher mortality. The SR included a total of 17 studies (15 retrospective studies and two prospective studies) comprising 3,581 cancer patients with COVID-19 that were included in the meta-analysis. Seven studies were performed in China, five in the USA, two in Spain, one in France, and the other two in Italy.	Sources searched to June 2020 Included studies had small samples such that results could be underpowered.	The search for this SR was not well reported and many studies may have been missed. Consistency checking for inclusion of studies was not reported.

Reference	Relevant findings	Things to consider	Limitations of systematic review
mortality in cancer patients with COVID-19: a systematic review and meta-analysis." OncoImmunology, 9:1, 1824646 Available here Supplemental material here	**Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** This SR did not report on intensive care admission but rather on the composite outcome of risk of exacerbation. Authors did not define the composite outcome risk of exacerbation. Therefore, it is not possible to ascertain which severe events are included under the; it could have included hospitalisation, ICU admissions, IMV, ARDs and others. No correlations were observed between anti-cancer therapy (all types combined) and the risk of exacerbation (OR 1.54, 95% CI 0.96–2.49, *P* = .074, I^2= 22.3%) 5 studies (n=482): all from China). The different types of therapy were analysed separately and it was found that surgery (4 studies (n=965): three from China and one from the USA), chemotherapy (5 studies (n=875): three from China, and one each from the USA and Spain), and immunotherapy (6 studies (819): three from China, two from the USA and one from Spain) were not associated with severe events in cancer patients infected by SARS-CoV-2 (All *P*-value >0.05). A subgroup analysis was conducted for immunotherapy within 90 d and an increased risk of exacerbation was found (OR 2.53, 95% CI 1.30–4.91, *P* = .006, *p*-value = 0.170 for test of interaction; I^2= 0%, 2 studies). No increase in the risk of exacerbation was found when comparing chemotherapy within 28 days vs 40 days. **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** No significant correlation was found between anti-cancer therapy (all types combined) and the risk of mortality in cancer patients with COVID-19 (OR 1.33, 95% CI 0.84–2.10, *P* = .229, I^2=68.3%, 9 studies (n= 2,459): three from China, two each from the USA and Italy, and one each from Spain and France) Analysing therapies separately, no statistically significant correlation was shown between anti-cancer therapy (including **surgery** (4 studies (n=2,038): two each from China and the USA), chemotherapy (7 studies (n=2,574): two each from the USA and Italy, and one each from Spain, France and China), **targeted therapy** (5 studies (n=1.365): two from China and one each from the USA, Italy and France), **immunotherapy** (9 studies (n=1,740): three from the USA, two each from Italy and China, and one each from Spain and France), and **radiotherapy** (4 studies (n=1,328): two each from the USA and China)) and the risk of death events in cancer patients with COVID-19 (All *P*-value >0.05). In subgroup analysis examining time since treatment for the different therapies no difference was found for surgery, targeted therapy, immunotherapy and radiotherapy. Chemotherapy within 28 d increased the risk of death events (OR 1.45, 95% CI 1.10–1.91, *P* = .008, *p*-value = 0.015 for test of interaction; I^2= 6.5%, 6 studies).	SR authors cautioned that time interval delimitations may not be precise and uniform due to insufficient information in the included studies.	Authors did not report the methodological designs of included studies but only whether they were prospective or retrospective. Meta-analysis may have combined studies with different designs and different outcomes Authors did not consider the implications that the quality of the research may have on their findings. The SR did not define the composite outcome risk of exacerbation.
24. Qian, W., et al. (2020). "Immune checkpoint inhibitors use and effects on prognosis of	This SR aimed to assess the safety of Immune checkpoint inhibitors (ICI) in COVID-19 patients. It included 18 studies (consisted of nine cohort studies, five case series and four case reports) that reported on ICI use in cancer patients and prognosis of COVID-19. Only six of these studies (n=2,944 patients (185 with ICI)) were included in the meta-analyses on hospitalisation, severe outcomes or mortality. From these six studies, two were prospective cohorts and four were retrospective cohort studies. Three studies were performed in the USA, two in the UK and one in China.	Sources searched to August 2020. This paper is a pre-print and has not been subject to peer-review. If published, feedback during the peer-review process could lead to differences in the final article.	No mention of consistency checking when screening records for inclusion. SR authors only conducted quality assessment for studies included in the meta-analysis.

Reference	Relevant findings	Things to consider	Limitations of systematic review
COVID-19 infection: A systematic review and meta-analysis." Research Square* Available here	**Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** Patients with prior ICI treatment exhibited a higher rate of hospitalisation (OR 2.6; Z=3.2; 95% CI 1.45-4.68; p=0.001; I^2=0%, 3 studies 9 (n= 12,592 (79 with ICI)): all from the USA) **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Patients with prior ICI treatment exhibited a higher rate of severe disease (e.g., admission to the intensive care unit (ICU), development of severe or critical symptoms, and utilisation of invasive mechanical ventilation) (OR 1.98; Z=2.43; 95% CI 1.14-3.43; p=0.015; I^2=35%; p-heterogeneity=0.203; 4 studies (n= 1.254 (85 with ICI): three from the USA and one from China) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Mortality in ICI-exposed cases was similar to non-ICI exposed patients (OR 0.90; Z=-0.52; 95% CI 0.60-1.34, p= 0.60; I^2 49%, p-heterogeneity= 0.253; five studies (n= 2.521 (154 with ICI)): one each from China, the UK, the USA and one European multicentre study). No statistically significant difference in mortality was observed between patients exposed to ICI and other antitumor treatment ICI and chemotherapy (OR 1.06; Z=0.26; 95% CI 0.67-1.67, p= 0.80; I^2= 3%; 4 studies (n= 653 (78 with ICI)): one each from China, the UK, the USA and one European multicentre study), hormone therapy (OR 1.26; Z=0.43; 95% CI 0.44-3.59, p=0.67; I^2 59%; p-heterogeneity= 0.09; 3 studies (n= 273 (37 with ICI)): one each from the UK, the USA and one European multicentre study), radiotherapy (OR 1.44, 95% CI 0.67-3.07, p= 0.35; I^2 46%; p-heterogeneity= 0.15; 3 studies (n= 156 (28 with ICI): one each from China, the UK, and the USA), surgery (OR 1.21; Z=0.42; 95% CI 0.50-2.98; p= 0.67; I^2 0%; 3 studies (n= 106 (17 with ICI)): one each from China, the USA, and the UK), or targeted therapy (OR 1.53; Z=1.53; 95% CI 0.89-2.63; p= 0.13; I^2 0%; 4 studies (n= 296 (37 with ICI)): one each from China, the UK, the USA and one European multicentre study).	Most of the included studies did not adjust for confounding such as age, sex, smoking, pulmonary disease, hypertension or CHD. Meta-analyses reported are for unadjusted ORs. Authors were unable to evaluate the effects of ICI subclasses or their role in individual tumours due to small number of studies. Median age of included participants was 64 to 69 years old. Findings from meta-analyses have included studies with a range of intervals since last dose of ICI. The number of patients receiving ICI was very small in the included studies (6-56) leading to wide 95% confidence intervals. Pooled analysis on hospitalisation included 609 cancer patients, for severe disease included 714 cancer patients and for mortality included 1,983 cancer patients. Cancer outcomes in patients who had delayed or interrupted ICI treatment could not be assessed due to the short follow-up times available.	SR authors have not discussed the implications of the quality of the included studies on the results.
25. Park, R., et al. (2020). "Sex-bias in COVID-19-associated illness severity and mortality in cancer patients: A systematic review and meta-analysis." EClinicalMedicine 26: 100519-100519. Available here.	This SR aimed to evaluate the sex-difference in the risk of adverse outcomes associated with COVID-19 in the cancer population. The outcomes of interest were severe illness, all-cause death, and the composite of severe illness and death. The searches were conducted in four bibliographic databases and several websites with conference proceedings. The SR included 17 retrospective studies with a total of 3,968 COVID-19 patients with cancer from the USA (n=3), China (n=7), France (n=1), the UK (n=2), Italy (n=1), Spain (n=1) and two studies were multi-national including patients from European and American countries. Supplementary material lists study designs as 16 case control and one cohort. **4. Which population groups are at higher risk of needing treatment in intensive care because of COVID19 infection?** <u>Severe illness</u> The severe illness was defined as either illness requiring ICU admission or based on the WHO criteria for severe COVID-19	Searches to June 2020 The authors highlighted that all the included studies were retrospective. Few studies reported multivariate adjusted ORs and there were overlaps in the outcomes studied. The definition of severe illness varied among the studies. Some of them included death as severe illness; therefore, the effect of male gender on severe illness excluding death is unclear.	The search was not provided, therefore PHW researchers were not able to assess the quality. No protocol registration. There was a lack of information for the consistency checking during the data extraction and quality assessment. The SR did not report the methodologic design of the included studies, significance value (p-value) or the proportion of males for each included study.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	The meta-analysis for severe illness showed that male COVID-19 patients with cancer had an increased risk for severe illness (OR 1.47, 95% CI, 1.16-1.85, I^2 0% 10 studies with 1,529 patients, China n=5, USA n=2, UK n=1, Spain n=1, European countries n=1) Subgroup analysis with the studies conducted in European or North American countries observed that male gender had an effect increasing the risk for severe illness in COVID-19 patients with cancer (OR 1.22, 95%CI 0.88-1.68, I^2= 0%, P(heterogeneity)= 0.54, 4 studies including 655 patients UK n=1, USA n=2, Spain n=1) **5. Which population groups are at higher risk of dying from COVID19 infection?** <u>Death</u> Univariate analysis The meta-analysis indicated that male gender increased the risk of death in COVID-19 patients with cancer (OR 1.58, 95% CI, 1.18-2.13, I^2 36%, 10 studies with 2,565 patients. China n=4, USA n=2, UK n=1, Spain n=1, Italy n=1, Spain and North America n=1) Subgroup analysis with the studies conducted in European or North American countries observed that male gender had an effect on increasing the risk of death in COVID-19 patients with cancer. The heterogeneity among the studies was moderate but not significant (OR 1.43, 95%CI 1.00-2.03, I^2= 51%, *p* heterogeneity=0.54, 6 studies including 2,136 patients. Spain and North America n=1, UK n=1, USA n=2, Spain n=1, Italy n=1) Multivariate analysis The multivariate analysis noted that male patients had an increased risk of death compared with the female patients (OR 1.72 95%CI 1.09-2.71, I^2= 36%, *p* heterogeneity=0.20, 4 studies with 1,596 patients. China n=1, Spain and North America n=1, Europe n=1, Spain n=1)		The quality of the included studies was not considered for the results. The SR did not undertake sensitive analysis or subgroup analysis to check the effect of possible confounders such as age or type of cancer.

Treatments for co-morbidities

Reference	Relevant findings	Things to consider	Limitations of systematic review
Angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) use			*Back to Table 1*
26. Hasan, S. S., et al. (2020). "Mortality and Disease Severity Among COVID-19 Patients Receiving Renin-	A total of 59 studies comparing mortality and/or severity outcomes between COVID-19 patients receiving an ACEI/ARB and their counterparts not receiving an ACEI/ARB were evaluated for the qualitative synthesis. Of the 59 studies, 32 were from OECD countries (USA = 10, Italy = 9, South Korea = 4, France = 3, Spain = 2, Belgium = 1, Denmark = 1, Turkey = 1, UK = 1) and 26 were from non-OECD countries (China = 23, Hong Kong = 1, Kuwait = 1, Singapore = 1). One prospective study included data from 38 countries, with 324 participants (no detail as to which countries provided data). Eleven studies were preprints (n=5 China, and one each from (Belgium n=299, France n=187, Hong Kong n=976, South Korea n= 8,266, UK n= 311, and USA n= 1,129). All but four included studies were described as retrospective (single or multicentre), three were prospective and one described as ambispective (China, n=548).	Search conducted to 19th August 2020. SR authors reported that most of the included studies did not adequately adjust for all confounders. Issues around inadequate adjustment for confounders that may influence the estimated risk of mortality associated with the use of ACEIs/ARBs in 21 studies. SR authors	Two authors conducted search independently, but it is unclear if screening was conducted by two reviewers; it looks likely as methods section mentions differing decisions being resolved by mutual consensus.

Reference	Relevant findings	Things to consider	Limitations of systematic review
Angiotensin System Inhibitors: A Systematic Review and Meta-analysis." American journal of cardiovascular drugs: drugs, devices, and other interventions. 1–20. Available here	There were 24 studies that exclusively included hypertensive patients. One study providing mortality estimates was excluded from the meta-analyses due to very wide confidence intervals **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?** Sixteen studies provided adjusted estimates for severe/critical disease with the use of an ACEI/ARB relative to the non-use of an ACEI/ARB and were included in the meta-analyses. Two studies were deemed 'good' quality and the remaining 22 were deemed as 'fair' quality. A pooled analysis of 13 studies providing adjusted ORs (7,446 COVID-19 patients) Odds of developing severe/critical disease: Use of an ACEI/ARB compared to the non-use of an ACEI/ARB: OR 0.91 (95% CI 0.75–1.10) A separate pooled analysis of three studies (6,325 patients) provided adjusted HRs. Risk of developing severe/critical disease: Use of an ACEI/ARB compared to the non-use of an ACEI/ARB: HR 0.73 (95% CI 0.33–1.66) Funnel plot asymmetry indicated risk of publication bias. A subgroup analysis was limited to six studies providing adjusted mortality estimates for exclusively hypertensive patients with COVID-19. Odds of developing severe/critical disease: **Hypertensive users of ACEIs/ARBs compared to non-hypertensive patients: pooled OR 0.63 (95% CI 0.41–0.96)** A subgroup analyses based on the region where studies were performed compared the risk of developing severe/critical disease among users of ACEIs/ARBs compared to non-users. Odds of developing severe/critical disease among East Asian countries: pooled OR 0.70 (95% CI 0.52–0.93) Odds of developing severe/critical disease among European countries: pooled OR 1.02 (95% CI 0.61–1.70) Odds of developing severe/critical disease among studies from the USA: pooled OR 0.80 (95% CI 0.40–1.61) Another subgroup analysis examined respective estimates for severe/critical outcomes (adjusted OR) for ACEIs and ARBs respectively among five studies compared to the non-use of an ACEI and an ARB, respectively, among patients with COVID-19. **Odds of development of severe/critical illness with the use of an ACEI: pooled OR 1.50 (95% CI 1.04–2.14)**	noted that as most of the included studies did not provide adjusted estimates, only a small sample were included in the meta-analyses. Among the studies included in the meta-analysis, only two studies properly adjusted for major confounders, and coincidentally these two studies also reported a significantly reduced risk of mortality from COVID-19 with the use of RAS inhibitors. Some included studies were pre-prints and have not been peer reviewed. SR authors noted issues around the inability to ascertain exposure to ACEIs/ ARBs during the course of illness in 19 studies, where a possibility of ACEIs/ARBs discontinuation upon COVID-19 diagnosis could not be ruled out based on the study design. SR authors also noted issues with assessing representativeness of the exposed cohort. In many studies, it was unclear whether the entire included cohort of patients was followed until discharge/death. SR authors noted that there was a risk that the duration of follow-up may not have been long enough for the outcomes of interest (mortality and/or severe/critical illness) to occur in some studies. If a study reported estimates from different multivariable models, the most extensively adjusted estimate in terms of the number of covariates was extracted. However, when different multivariable models adjusted for the same number of covariates, the model containing the most clinically meaningful covariates was extracted for the pooled analysis.	Data extraction was conducted by one author and verified by a second. Unclear whether quality assessment of included studies was consistency checked. Methodological design of included studies is unclear as authors only reported if study was prospective or retrospective. SR authors noted that there was a risk that the duration of follow-up may not have been long enough for the outcomes of interest (mortality and/or severe/critical illness) to occur in some studies.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Odds of development of severe/critical illness with the use of an ARB: OR 0.98 (95% CI 0.67–1.44) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** Twelve studies provided adjusted ORs (18,749 COVID-19 patients) on mortality risk. Odds of mortality: **Use of an ACEI/ARB compared to non-use of an ACEI/ARB: pooled OR 0.73 (95% CI 0.56–0.95)** A separate pooled analysis of 11 studies providing adjusted HRs (26,598 COVID-19 patients) Risk of mortality: **Use of an ACEI/ARB compared to the non-use of an ACEI/ARB: pooled HR 0.75 (95% CI 0.60–0.95)** One subgroup analysis was limited to studies providing adjusted mortality estimates for exclusively hypertensive patients with COVID-19. Odds of mortality: Use of ACEIs/ARBs compared to the non-users: pooled OR 0.73 (95% CI 0.52– 1.02; six studies) Risk of mortality: **Use of ACEIs/ARBs compared to the non-users: pooled HR 0.39 (95% CI 0.20–0.77; five studies)** Another subgroup analysis was based on the region where the studies were performed. Odds of mortality among East Asian studies: Use of ACEIs/ARBs compared to the non-users: pooled OR (0.76, 95% CI 0.44–1.31) Odds of mortality among European studies: Use of ACEIs/ARBs compared to the non-users: pooled OR 0.51 (95% CI 0.21–1.25) Odds of mortality among USA studies: Use of ACEIs/ARBs compared to the non-users: pooled OR 0.89 (95% CI 0.66–1.21) A final subgroup analysis examined the risk of mortality for ACEIs and ARBs respectively. Odds of mortality among users of ACEI: Use of ACEIs compared to non-use of ACEI: pooled OR 0.46 (95% CI 0.18– 1.17, 4 studies) Odds of mortality among users of ARBs: Use of ARBs compared to non-use of ARBs: pooled OR 1.18 (95% CI 0.99–1.42; 3 studies)	Systematic review authors could not establish with certainty whether RAS inhibitors were continued during the course of the disease in COVID-19 patients, as the use of RAS inhibitors was only established via medical record review or medical database review in majority of the studies included.	

Reference	Relevant findings	Things to consider	Limitations of systematic review
	Risk of mortality among users of ACEIs: Use of ACEIs compared to non-use of ACEIs: pooled HR 1.03 (95% CI 0.85,1.23; five studies) Risk of mortality among users of ARBs: Use of ARB compared to non-use of ARB: pooled HR 0.82 (95% CI 0.55,1.24; five studies)		
27. Caldeira, D., et al. (2020). "Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers and the risk of COVID-19 infection or severe disease: Systematic Review and meta-analysis." International journal of cardiology. Heart & vasculature 31: 100627. Available here	Twenty seven studies were included in this review (RCT = 1, case-control = 4, cohort/nested case-control = 22). Fifteen of the included studies were conducted in OECD countries. One study included data from 11 countries in Asia, Europe, and North America (most of the data were collected from OECD countries). Study methodology included one randomised controlled trial (Spain), four case-control studies (Italy and Spain), with the remaining being cohort/nested case-control studies (China, France, Italy, Israel, South Korea, the UK, the USA and one multi-national) and included a total of 119,656 participants. Six studies were unpublished (16,112 participants). Study populations varied and included those hospitalised, those admitted to intensive care, positive COVID-19 patients, symptomatic COVID-19, and those with symptomatic COVID-19 presenting to emergency departments. **Q1. Which population groups are most likely to test positive for COVID-19?** Six cohorts examined the risk of COVID-19 infections associated with use of ACEi/ARB. COVID-19 infection was defined as being documented by nasopharyngeal or oropharyngeal swab tests or reported by authors as having COVID-19. These include adjusted and unadjusted estimates. Risk of having a positive test for COVID-19 infection among ACEi/ARB exposure: OR 0.99 (95% CI 0.89–1.11; I^2 36%; 5 studies, GRADE confidence moderate) Risk of having a positive test for COVID-19 infection among ACEi exposure: OR 0.94 (95% CI 0.87–1.02; I^2 0%; 7 studies) Risk of having a positive test for COVID-19 infection among ARB exposure: OR 1.01 (95% CI 0.93–1.10; I^2 11%; 6 studies) The analysis of five studies with adjusted estimates only. Association between ACEi/ARB and risk of infection among patients with COVID-19: OR 0.99 (95%CI 0.89–1.11, I^2 35%, 5 studies) Analyses of only hypertensive patients. Risk of developing the infection in patients treated with ACEi/ARB compared to non users: OR 0.97 (95% CI 0.85–1.11; I^2 38%). **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?**	Search conducted to 8 June 2020. A protocol was published on OSF registries in May 2020. Risk of bias was independently evaluated by three authors. SR authors noted that the results only reflect the impact of ACEi and/or ARB. Other modulators of the renin-angiotensin-aldosterone system such renin inhibitors (aliskiren), mineralocorticoid receptor antagonists (spironolactone or eplerenone), or even sacubitril were not evaluated in this review. The majority of studies included are observational studies, making it difficult to infer accurate causation. SR authors in discussing the limitations of their work noted that in some studies, the risk of severe/critical disease was retrieved from specific outcomes such as the need of mechanical invasive ventilation or acute respiratory distress syndrome. This could explain the heterogeneity found in this outcome.	Two reviewers screened at title and abstract. It is unclear if two reviewers screened at full text and data extraction. The meta-analyses combined studies with different study designs.

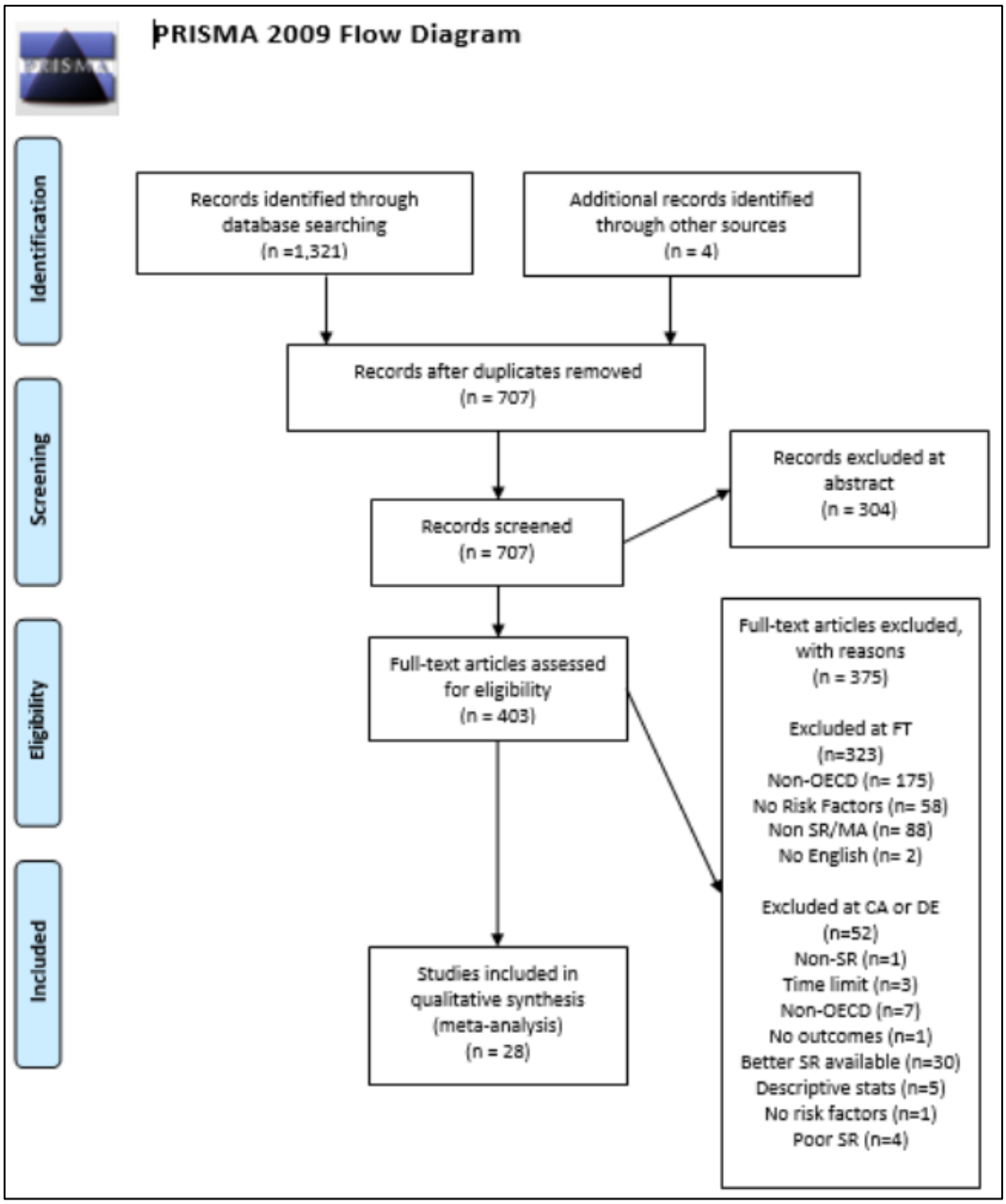
Reference	Relevant findings	Things to consider	Limitations of systematic review
	The outcome of severe/critical disease was defined according to the World Health Organization and Chinese Centre of Disease Control. The risk of severe COVID-19 disease associated with ACEi/ARB: OR 0.90 (95% CI 0.74–1.11; I^2 55%; 17 studies; GRADE confidence very low) The risk of severe COVID-19 disease associated with ACEi: OR 1.05 (95% CI 0.64–1.70; I^2 63%; 4 studies) The risk of severe COVID-19 disease associated with ARB: OR 1.32 (95% CI 0.75–2.30; I^2 86%; 6 studies) Analysis of studies examining the risk of severe COVID-19 disease and ACEi/ARB. Risk of severe/critical disease: OR 0.88 (95% CI 0.63–1.22, I^2 68%) Analysing only the data from hypertensive patients and the risk of developing severe COVID-19 disease. Risk of severe/critical disease: OR 0.91 (95% CI 0.69–1.21; I^2 64%) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** The risk of all-cause mortality with exposure to ACEi/ARB among patients with COVID-19: OR 0.91 (95% CI 0.74–1.11; I^2 20%; 17 studies; GRADE confidence low) The risk of all-cause mortality with exposure to ACEi among patients with COVID-19: OR 0.85 (95% CI 0.40–1.78, I^2 0%, 4 studies) The risk of all-cause mortality with exposure to ARB among patients with COVID-19: OR 0.80 (95% CI 0.47–1.35, I^2 0%, 3 studies) Analysis examining the association between ACEi/ARB and mortality among patients with COVID-19 in studies with adjusted estimates only. Risk of mortality: OR 0.90 (95% CI 0.68–1.18, I^2 27%) Analysing only the data from hypertensive patients: **Risk of mortality: OR 0.76 (95%CI 0.59–0.98; I^2 0%)**		
28. Asiimwe, I.G, et al. Cardiovascular drugs and COVID-19 clinical outcomes: a living systematic review and	175 (of a total of 178) studies were included in the quantitative element of this review. Most studies (n= 163, 92%) were cohort/case series studies, and 14 (8%) were case-control studies. Included studies were conducted in China (n=43), USA (n=39), Italy (n=27), Spain (n=13), UK (n=12), France (n=11), South Korea (n=9), Germany (n=3), two each from Belgium, Denmark, Israel, Kuwait, Netherlands and Turkey, and one each from Australia, Finland, Iran, Japan, South Africa, Switzerland and Thailand. Two studies were multi-national. The most commonly reported drug exposure was with angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) (ACEI/ARB). 'Severe' was defined as:	Latest search to 31 July 2020 This is a living review which is planned to be updated regularly. After each monthly search, new evidence will be briefly summarized unless it changes the nature or strength of the conclusions, in which case a major update will be performed. Protocol published on PROSPERO (CRD42020191283)	Studies that could potentially be eligible for inclusion may have been missed. Screening at title and abstract was conducted by two reviewers independently. No information available on full text screening. Data extraction conducted by one reviewer. As a quality control

Reference	Relevant findings	Things to consider	Limitations of systematic review
meta-analysis. MedRxiv. * Available here	"adults who met any of the following criteria: (1) respiratory rate ≥30 breaths/min; (2) oxygen saturation ≤93% at rest state; and (3) arterial PO2/oxygen concentration ≤300 mm Hg. Patients with pulmonary lesion progression >50% within 24–48 hours on radiologic imaging were treated as severe cases." OR Critical ("patients that met any of the following criteria: (1) occurrence of respiratory failure requiring mechanical ventilation; (2) presence of shock; and (3) other organ failure that requires monitoring and treatment in the intensive care unit.") OR those with acute respiratory disease syndrome, or those being taken to intensive care units and/or requiring oxygen/intubation/any form ofventilation/continuous renal-replacement therapy **Q1. Which population groups are most likely to test positive for COVID-19?** After removal of seven studies, to minimise overlapping data, the primary meta-analysis included 24 studies reporting count data and/or crude odds ratios (OR). **Risk of testing positive for COVID-19 and ACEIs/ARBs: pooled unadjusted OR: 1.15 (95% CI 1.02 to 1.30; I^2 93%, p < 0.01)** Analysis restricted to only studies from OECD countries. **Risk of testing positive for COVID-19 and ACEIs/ARBs: OR 1.19 (95% CI 1.06 to 1.35; I^2 93%, p<0.01)** Analysis restricted to only cohort studies from OECD countries. **Risk of testing positive for COVID-19 and ACEIs/ARBs: OR 1.33 (95% CI 1.15 to 1.55; I^2 89%, p<0.01)** Analysis restricted to only OECD studies reporting adjusted estimates. Risk of testing positive for COVID-19 and ACEIs/ARBs: pooled adjusted OR 1.01 (95% CI 0.93 to 1.10, I^2 0%, p= 0.71, 6 studies) **Q3. Which population groups are at higher risk of being hospitalised because of COVID-19 infection?** After excluding three studies to reduce potentially overlapping data, 23 studies explored the association between being hospitalised and being on ACEIs/ARBs. **Risk of hospitalisation and ACEIs/ARBs: pooled unadjusted OR 2.25 (95% CI 1.70 to 2.98, I^2 91%, p<0.01)** Analysis restricted to only studies reporting adjusted estimates. Risk of hospitalisation and ACEIs/ARBs: OR 1.16, 95% CI 0.80 to 1.68, I^2 53%, p= 0.06) All studies included in these analyses were conducted in OECD countries. **Q4. Which population groups are at higher risk of needing treatment in intensive care because of COVID-19 infection?**	Data has been extracted on a pre-print version posted on October 9 2020, which has not been peer-reviewed. Several included studies were preprints and had not been peer-reviewed The strength of the body of evidence and quality and strength of recommendations was assessed according to GRADE criteria. All studies had serious risks of bias, mainly driven by confounding and inappropriate selection of participants into the study. For most of the meta-analyses, heterogeneity in effect estimates was high. The authors stated that they tried to exclude potentially overlapping data but may have missed some overlapping data or inadvertently excluded non-overlapping data. The overall low contributions/assigned weights of the individual studies make the reported estimates robust to these errors.	measure, a second reviewer independently extracted and evaluated half the records to ascertain consistency.

Reference	Relevant findings	Things to consider	Limitations of systematic review
	After excluding sixteen studies to reduce potentially overlapping data, 60 studies reported the association between ACEIs/ARBs and severity outcomes. **Risk of severe disease: pooled OR 1.50 (95% CI 1.27 to 1.77, I^2 81%,p<0.01)** Analysis restricted to only studies reporting adjusted odds ratios (n=18 studies). Risk of severe disease: pooled adjusted OR 1.04, 95% CI 0.76 to 1.42, I^2 65%, p<0.01) **Q5. Which population groups are at higher risk of dying from COVID-19 infection?** After removal of potentially overlapping data, 40 studies were included in the primary meta-analysis examining the association between ACEI/ARB exposure and all-cause mortality. Risk of all-cause mortality: pooled OR 1.25 (95% CI 0.98 to 1.58, I^2 85%, p<0.01) Analysis restricted to only studies reporting adjusted odds ratios (n=13) Risk of all-cause mortality: pooled OR 0.86 (95% CI 0.64 to 1.15, I^2 4%, p= 0.41)		

Appendix 1

Flow Diagram of Screening Process



Appendix 2

Systematic reviews for which data extraction has not been conducted

This rapid summary is aiming to provide access to findings from the most up-to-date, comprehensive, well-conducted systematic reviews for decision-makers to consider whilst planning COVID prevention. Some systematic reviews that are relevant to the questions have not been data extracted following critical appraisal. This is because PHW reviewers consider that one of the following apply:

- only descriptive statistics were reported
- the SR was poorly conducted
- majority of data from non-OECD countries
- more robust systematic reviews are available to answer the question with regard to a particular risk factor and these have been extracted
- a more focussed systematic review is available and has been extracted and this review does not add to the findings
- or because a more up-to date good quality systematic review, having a later search date and increased data, is available and has been extracted.

The references for these systematic reviews are listed below with reasons for why their findings have not been reported.

Reference	**Reason for non-extraction**
Male gender / Sex	
29. Kelada, M., et al. (2020). "The role of sex in the risk of mortality from COVID-19: a systematic review." Cureus. 12(8):e10114. Available here	Majority of sample from non-OECD countries
30. Flook, M., et al. (2020). "Informing the public health response to COVID-19 (and lessons learnt for future pandemics): a systematic review of risk factors for disease, severity, and mortality." ResearchSquare. Available here	Majority of sample from non-OECD countries

Reference	Reason for non-extraction
31. Lu, L., et al. (2020). "A Comparison of Mortality-related Risk Factors of COVID-19, SARS, and MERS: A Systematic Review and Meta-analysis." The Journal of infection 81(4): e18-e25. Available here	Majority of sample from non-OECD countries
32. Setiati, S., et al. (2020). "Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review." Acta Medica Indonesiana 52(3): 227. Available here	Majority of sample from non-OECD countries
Ethnicity	
33. Pan, D., et al. (2020). "The impact of ethnicity on clinical outcomes in COVID-19: A systematic review." EClinicalMedicine. Available here	More up-to-date good quality systematic review available
30. Flook, M., et al. (2020). "Informing the public health response to COVID-19 (and lessons learnt for future pandemics): a systematic review of risk factors for disease, severity, and mortality." ResearchSquare. Available here	More focussed systematic review available
34. Usher Institute (2020). "What is the evidence on ethnic variation on COVID-19 incidence and outcomes?." Summary available here Full review available here	More up-to-date good quality systematic review available
1. Wingert.,A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review (preprint)." medRxiv. Available here	More focussed systematic review available
Obesity BMI≥30Kg/m2	
35. Chang, T. H., et al. (2020). "Effect of obesity and body mass index on coronavirus disease 2019 severity: A systematic review and meta-analysis." Obesity reviews: an official journal of the International Association for the Study of Obesity. 21(11). Available here	More robust systematic review available
36. Fang, C., et al. (2020). "Body mass index associated with severity and mortality of patients with coronavirus disease 2019: A systematic review and meta-analysis." ResearchSquare. Available here	More robust systematic review available

Reference	Reason for non-extraction
37. Tamara, A., et al. (2020). "Obesity as a predictor for a poor prognosis of COVID-19: A systematic review." Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14(4): 655-659. Available here	More up-to-date good quality systematic review available
38. Colombera Peres, K., et al. (2020). "Body Mass Index and Prognosis of COVID-19 Infection. A Systematic Review." Frontiers in Endocrinology 11: 562. Available here	More robust systematic review available
39. Yang, J., et al. (2020). "Obesity aggravates COVID-19: a systematic review and meta-analysis." Journal of Medical Virology. Available here	More robust systematic review available
40. Vivek Singh, M., et al. (2020). "Higher Body Mass Index Is an Important Risk Factor in COVID-19 Patients: A Systematic Review." Environmental science and pollution research international 27(33): 42115-42123. Available here	More robust systematic review available
41. Seidu, S., et al. (2020). "The impact of obesity on severe disease and mortality in people with SARS-CoV-2: A systematic review and meta-analysis." Endocrinology, Diabetes & Metabolism: e00176. Available here	More robust systematic review available
42. Raeisi, T., et al. (2020). "The Negative Impact of Obesity on the Occurrence and Prognosis of the 2019 Novel Coronavirus (COVID-19) Disease: A Systematic Review and Meta-Analysis." ResearchSquare. Available here	Poorly conducted SR
43. Malik, P., et al. (2020). "Obesity a predictor of outcomes of COVID-19 hospitalized patients-A systematic Review and Meta-Analysis." Journal of Medical Virology. Available here	More robust systematic review available
44. Sales-Peres, S. H. C., et al. (2020). "Coronavirus (SARS-CoV-2) and the risk of obesity for critically illness and ICU admitted: Meta-analysis of the epidemiological evidence." Obesity research & clinical practice. Available here	More robust systematic review available
30. Flook, M., et al. (2020). "Informing the public health response to COVID-19 (and lessons learnt for future pandemics): a systematic review of risk factors for disease, severity, and mortality." ResearchSquare. Available here	More up-to-date good quality systematic review available
12. Raymond, C., et al. "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." Medrxiv. Available here	More focussed systematic review available
Smoking	

Reference	Reason for non-extraction
1. Wingert, A., et al. (2020). "Risk factors for severe outcomes of COVID-19: a rapid review (preprint)." MedRxiv. Available here	More focussed systematic review available
12. Raymond, C., et al. "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." MedRxiv. Available here	More focussed systematic review available
45. Tian, W., et al. (2020). "Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis." Journal of Medical Virology. Available here	More focussed systematic review available
32. Setiati, S., et al. (2020). "Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review." Acta Medica Indonesiana 52(3): 227. Available here	No smoking data reported
CVD	
45. Tian, W., et al. (2020). "Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis." Journal of Medical Virology. Available here	More focussed systematic review available
30. Flook, M., et al. (2020). "Informing the public health response to COVID-19 (and lessons learnt for future pandemics): a systematic review of risk factors for disease, severity, and mortality." ResearchSquare. Available here	More focussed systematic review available
32. Setiati, S., et al. (2020). "Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review." Acta Medica Indonesiana 52(3): 227. Available here	More up-to-date good quality systematic review available
46. Bajgain, K. T., et al. (2020). "Prevalence of Comorbidities Among Individuals With COVID-19: A Rapid Review of current Literature." American journal of infection control. Available here	More focussed systematic review available
47. Kunihiro Matsushita, et al. (2020). "The relationship of COVID-19 severity with cardiovascular disease and its traditional risk factors: A systematic review and meta-analysis." medRxiv. Available here	More up-to-date good quality systematic review available
Diabetes	

Reference	Reason for non-extraction
48. Kumar, A., et al. (2020). "Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis." Diabetes & Metabolic Syndrome: Clinical Research & Reviews. Available here	More up-to-date good quality systematic review available
49. Barrera, F. J., et al. (2020). "Prevalence of Diabetes and Hypertension and Their Associated Risks for Poor Outcomes in Covid-19 Patients." Journal of the Endocrine Society 4(9): bvaa102. Available here	More up-to-date good quality systematic review available
50. Almeida-Pititto, B., et al. (2020). "Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis." Diabetology & metabolic syndrome 12(1): 1-12. Available here	More focussed systematic review available
COPD	
46. Bajgain, K. T., et al. (2020). "Prevalence of Comorbidities Among Individuals With COVID-19: A Rapid Review of current Literature." American journal of infection control. Available here	Only descriptive data reported
32. Setiati, S., et al. (2020). "Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review." Acta Medica Indonesiana 52(3): 227. Available here	More focussed systematic review available
Asthma	
30. Flook, M., et al. (2020). "Informing the public health response to COVID-19 (and lessons learnt for future pandemics): a systematic review of risk factors for disease, severity, and mortality." ResearchSquare. Available here	More focussed systematic review available
Chronic kidney Disease (CKD)	

Reference	Reason for non-extraction
46. Bajgain, K. T., et al. (2020). "Prevalence of Comorbidities Among Individuals With COVID-19: A Rapid Review of current Literature." American journal of infection control. Available here	Only descriptive statistics reported
Liver disease	
12. Chang Raymond et al. "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." Available here Supplementary table here	Only descriptive statistics reported
Pregnancy	
51. Khalil, A., et al. (2020). "SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes." EClinicalMedicine 25: 100446. Available here	More robust systematic review available
52. Juan, J., et al. (2020). "Effects of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcomes: a systematic review." Ultrasound in Obstetrics & Gynecology. Available here	More robust systematic review available
Cancer (non-specific)	
46. Bajgain, K. T., et al. (2020). "Prevalence of Comorbidities Among Individuals With COVID-19: A Rapid Review of current Literature." American journal of infection control. Available here.	More focussed systematic review available
12. Raymond, C., et al. "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." Medrxiv. Available here	More focussed systematic review available
53. Yekedüz, E., et al. (2020). "A Systematic Review and Meta-Analysis: The Effect of Active Cancer Treatment on Severity of COVID-19." Eur J Cancer.141:92-104 Available here	Poorly conducted SR (This SR only searched one source to identify research studies)

ACE1/ARB use

54. Nunes, J.P.L. (2020). "Mortality and use of angiotensin converting enzyme inhibitors in Covid 19 disease - a systematic review." MedRxiv. Available here	Poorly conducted SR Lack of transparency in reporting of methods and consistency checking. Incomplete data provided for included studies
55. Grover, A. and Oberoi, M. (2020). "A systematic review and meta-analysis to evaluate the clinical outcomes in COVID-19 patients on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers." European heart journal. Cardiovascular pharmacotherapy. Available here	More robust systematic review available
56. Mohitosh, B. (2020). "Effects of ACEIs and ARBs on Clinical Outcomes in COVID-19 Patients: A Meta-Analysis." SSRN. Available here	More robust systematic review available
57. Ssentango A., et al. (2020). "Renin-angiotensin-aldosterone system inhibitors and mortality in patients with hypertension hospitalized for COVID-19: a systematic review and meta-analysis." medRxiv. Available here	More robust systematic review available
58. Zhang, X., et al. (2020). "ACEI/ARB use and risk of infection or severity or mortality of COVID-19: a systematic review and meta-analysis." Pharmacological Research: 104927. Available here	More robust systematic review available
59. Barochiner, J. and Martínez, R. (2020). "Use of inhibitors of the renin-angiotensin system in hypertensive patients and COVID-19 severity: A systematic review and meta-analysis." Journal of clinical pharmacy and therapeutics. Available here	More robust systematic review available
60. Baral, R., et al. (2020). "Effect of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with COVID-19: a Systematic Review and Meta-analysis of 28,872 Patients." Curr Atheroscler Rep 22(10): 61-61. Available here	More robust systematic review available
61. Diaz-Arocutipa C., et al. (2020). "Association Between ACEIs or ARBs Use and Clinical Outcomes in COVID-19 Patients: A Systematic Review and Meta-analysis." medRxiv. Available here	More up-to date good quality systematic review
62. Qu G., et al. (2020). "Association between angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers use and the risk of infection and clinical outcome of COVID-19: a comprehensive systematic review and meta-analysis." medRxiv. Available here (version 2)	More up-to date good quality systematic review

63. Alamer, A., et al. (2020). "Mortality, Severity, and Hospital Admission Among COVID-19 Patients with ACEI/ARB Use: A Meta-analysis Stratifying Countries Based on Response to the First Wave of the Pandemic." ResearchSquare. Available here	More up-to date good quality systematic review
64. Lo, K. B., et al. (2020). "Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers and Outcomes in patients with COVID-19: A Systematic Review and Meta-Analysis." Expert review of cardiovascular therapy: 1-12. Available here	More up-to date good quality systematic review
65. Flacco, M. E., et al. (2020). "Treatment with ACE inhibitors or ARBs and risk of severe/lethal COVID-19: a meta-analysis." Heart 106(19): 1519-1524. Available here	More up-to date good quality systematic review
HIV	
66. Maya Mellor et al. (2020). "Risk of adverse COVID-19 outcomes for people living with HIV: a rapid review and meta-analysis." medRxiv. Available here	Time limit for delivery of rapid summary expired
67. Ssentongo, P., et al. "Prevalence of HIV in patients hospitalized for COVID-19 and associated outcomes: a systematic review and meta-analysis." Available here	Time limit for delivery of rapid summary expired
Blood Group	
68. Golinelli, D., et al. (2020). "The association between ABO blood group and SARS-CoV-2 infection: A meta-analysis." PloS one 15(9): e0239508. Available here	Time limit for delivery of rapid summary expired
Transplants	
12. Chang, R., et al. "COVID-19 ICU and mechanical ventilation patient characteristics and outcomes - A systematic review and meta-analysis." Available here	Only descriptive statistics reported
69. Marinaki, S., et al (2020). "A Systematic Review of COVID-19 Infection in Kidney Transplant Recipients: A Universal Effort to Preserve Patients' Lives and Allografts." J. Clin. Med. 2020, 9(9), 2986. Available here	Only descriptive statistics reported
Excluded at Critical appraisal	
70. Tamirat Bekele, B., et al. (2020). "Effect of Renin-Angiotensin-Aldosterone System inhibitors on outcomes of COVID-19 patients with hypertension: Systematic review and Meta-analysis." medRxiv. Available here	Majority of sample from non-OECD countries

71. Bae, S., et al. (2020) "Impact of cardiovascular disease and its risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis." PROSPERO Available here	Majority of sample from non-OECD countries
72. Roya, G., et al. (2020). "The Role of Vitamin D in The Age of COVID-19: A Systematic Review and Meta-Analysis Along with an Ecological Approach." medRxiv. Available here	No risk factors
73. Romero Starke, K., et al. (2020). "The Age-Related Risk of Severe Outcomes Due to COVID-19 Infection: A Rapid Review, Meta-Analysis, and Meta-Regression." International journal of environmental research and public health 17(16): 5974. Available here	Majority of sample from non-OECD countries
74. Copat, C., et al. (2020). "The role of air pollution (PM and NO2) in COVID-19 spread and lethality: A systematic review." Environ Res 191: 110129-110129. Available here	Non Systematic Review
75. Yi, Z., et al. (2020). "Renin Angiotensin System Inhibition and Susceptibility and Outcomes from COVID-19: A Systematic Review and Meta-analysis of 69,200 COVID-19 Patients." medRxiv. Available here	Poorly conducted SR
76. Gomez-Ochoa, S.A., et al. (2020). "COVID-19 in Healthcare Workers: A Systematic Review and Meta-Analysis of Prevalence, Risk Factors, Clinical Characteristics, and Outcomes." SSRN. Available here	Only descriptive data reported
77. Sahu, A. K., et al. (2020). "COVID-19 in health care workers–A systematic review and meta-analysis." The American Journal of Emergency Medicine. Available here	Only descriptive data reported
78. Daniels, S., et al. (2020). "Precarious employment conditions as a risk factor for presenteeism and transmission of SARS-CoV-2: a rapid review". (Copy received from authors)	No comparison group for those testing positive for COVID to estimate differential risk, prevalence only
79. Abate, s., et al. (2020). "Postoperative mortality among surgical patients with COVID-19: A systematic review and meta-analysis." ResearchSquare. Available here	Only descriptive data reported
80. Gomez-Ochoa, S.A., et al. (2020). "COVID-19 in Healthcare Workers: A Living Systematic Review and Meta-analysis of Prevalence, Risk Factors, Clinical Characteristics, and Outcomes." American Journal of Epidemiology. Available here	Only descriptive data reported / Duplicate