Evidence review

Assessment of COVID-19 in primary care:

the identification of symptoms, signs, characteristics, comorbidities and clinical signs in adults which may indicate a higher risk of progression to severe disease

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Contents

Introduction

The purpose of this rapid review is to provide NHSScotland with advice on assessment of patients with COVID-19 in primary care.

This guidance is for: general practitioners and primary care teams involved in the assessment of patients presenting with potential COVID-19.

Since the outbreak of coronavirus, there has been an abundance of rapid and systematic reviews published on the diagnosis and management of people with symptoms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), known as COVID-19, mostly from a secondary care (hospital) perspective. About 80% of people with COVID-19 have symptoms which are mild (no pneumonia manifestations) or asymptomatic.[1] Others develop severe disease (defined as requiring admission to an intensive care unit (ICU)). The challenge for primary care practitioners is to identify and triage patients presenting with potential COVID-19, a disease in which the pattern and duration of symptoms is heterogeneous. This is compounded by the need to conduct consultations via telephone or video. In addition, the evidence-base is not robust and is subject to change as new evidence emerges.

The COVID-19 Scottish Primary Care Hub Triage Guide lists the common symptoms, and provides red flags for those requiring immediate assessment and yellow flags for those at a higher risk of deterioration (eg with certain comorbidities). We conducted a search for new evidence on prognostic indicators, risk factors and clinical measures to identify people self-managing symptoms of COVID-19 in the community whose symptoms may change or worsen, and therefore may require monitoring or clinical intervention after their initial presentation to primary care. The research question and methodology can be found in section 6.

KEY FINDINGS

Primary care clinicians should consider using the COVID-19 Scottish Primary Care Hub Triage Guide to inform initial consultations with patients presenting with potential COVID-19.

Symptoms, characteristics, comorbidities and clinical signs in adults which may indicate a higher risk of progression to severe disease:

- The only symptom identified which may distinguish severe disease is shortness of breath/dyspnoea. *(Table 1)*
- Characteristics which have been associated with severe disease are older age, male sex and Asian ethnicity. Older age is the strongest predictor. *(Table 2)*
- Comorbidities/risk factors most associated with severe disease are hypertension, cardiovascular disease, diabetes, obesity, stroke, chronic pulmonary disease, chronic kidney disease and cancer. *(Table 2)*
- No significant associations were found for chronic liver disease. Most studies have found no association between smoking and severe disease. There was no evidence of any association between steroids and immunosuppressant medication or angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor (AT1) antagonists but very few studies have investigated this. *(Table 2)*
- No studies investigated the impact of socioeconomic status or frailty. *(Table 2)*
- Clinical signs which have been found to be associated with severe disease are low oxygen saturation levels, low blood pressure and high respiratory rate. Of these, the strongest evidence relates to oxygen saturation levels. *(Table 3)*
- The evidence base is too weak and emergent to make definitive recommendations.

1. Signs and symptoms

The intention of this evidence review was to identify any evidence of symptoms in adults which may differ between mild, moderate and severe disease. The initial scoping of the evidence identified a COVID-19 signs and symptoms tracker which presents severe and non-severe symptoms based on early data from China, https://www.cebm.net/covid-19/covid-19-signs-and-symptoms-tracker/. This was produced by The Centre for Evidence-Based Medicine at the University of Oxford and was based on an unpublished systematic review and meta-analysis.[2] Unpublished studies have not been subject to peer review. We identified a published systematic review and meta-analysis which included 43 studies and 3,600 patients mostly from China.[3] Details of the prevalence of symptoms found in this study are given in Table 1. A review, which includes data from the United Kingdom, found little evidence to differentiate between mild and moderate symptoms and those in a severe condition.[1]

Our rapid review *(see section 6)* identified 10 published studies and 11 preprints or preliminary reports that included data on signs and symptoms from mixed healthcare settings, primarily in the United States (US) and Italy. Most studies are retrospective, observational studies so are potentially biased and may not be easily generalisable to Scottish primary care practice. Preprint studies have not been subject to peer review. For these reasons, all evidence reported should be considered low quality and needs to be interpreted with caution. Table 1 includes the results of the review of published and preprint literature comparing symptoms of mild/moderate and severe disease from settings other than China. It compares them to the findings from the recently published systematic review of 43 studies and 3,600 patients mostly from China.[3] In Table 1 the symptoms listed are those which have been identified as associated with COVID-19. For some symptoms we found no evidence comparing that symptom in cases of mild/moderate and severe disease. This is noted in Table 1. It is not always clear in the literature how the authors define severe disease. For the purposes of this review we considered that disease was severe when a patient was admitted to ICU. In Table 1 'all cases' means all diagnosed cases and may include mild, moderate and severe disease. The severity of disease as a percentage of the diagnosed cases would be likely to vary depending on the testing policy in place in that setting at the time the data was collected. This may also result in a higher percentage of confirmed cases in subgroups believed to be at risk as they are more likely to have been tested.

The Chinese meta-analysis provides weak evidence that dyspnoea may be an indicator of severe disease as 49% of patients with severe disease experienced dyspnoea compared to 13% of patients with non-severe disease.[3] This finding is supported by evidence from outside China where 21 out of 24 patients (88%) in ICU in the US[4] experienced shortness of breath compared to 5% of the first 38 diagnosed cases (of any severity) from eight European countries[5] and 32% of cases confirmed after presenting at an Emergency Department in Italy.[6]

Table 1: Prevalence of symptoms in mild/moderate and severe COVID-19

Symptoms associated with COVID-19	Prevalence (% of cases - range) from studies outside China			Prevalence (% of cases) from meta-analysis – mainly China[3]	
	ICU	Hospitalised patients	All cases	Critical illness	Non-critical illness
Cough[4-9]	88	66–86	16–37	66	57
Fever > 37.8ºC[5-7,9-12]	28–73	24–85	20–84	81	71
Dyspnoea[4-7,9,13]	88	11–80	5–32	49	13
Fatigue[5,10]	-	33	21	42	34
Cough (sputum)	No evidence found comparing mild/moderate to severe disease			32	31
Delirium (confusion)	No evidence found comparing mild/moderate to severe disease.				
Diarrhoea[7,10]	-	17–27	-	8	4
Vomiting/nausea[6,7,10]	-	8–24	8	-	-
Myalgia[7,10,13]	-	34–42	16	18	21
Chest pain[6,8,13]	-	-	2–4	-	-
Anosmia/dysgeusia	No evidence found comparing mild/moderate to severe disease				
Headache[4-6,10]	8	17	2–16	11	12
Dizziness	No evidence found comparing mild/moderate to severe disease				
Abdominal pain[6,10]	-	17	1	-	-
Sore throat[4-10,13]	8	18–61	1–8	17	11

2. Prognostic Tools

A variety of risk prediction scores and tools have been developed, which may have use in the community. Further research is required for validation and to determine which would be most appropriate in a community setting. A summary is available here: https://www.cebm.net/covid-19/what-prognostic-clinical-risk-prediction-scores-for-covid-19-are-currently-available-for-use-in-the-community-setting/

As yet, no trials have been conducted to validate the use of the National Early Warning Score (NEWS) or NEWS 2 in the assessment of patients for COVID-19 in primary care.[14] However, it has been temporarily endorsed by the Royal College of General Practitioners as a response to COVID-19 https://elearning.rcgp.org.uk/mod/page/view.php?id=10568

Five studies of association between co-morbidities or risk factors and hospitalisation for COVID-19, severe illness or death were identified.[6,11,12,15] Table 2 shows the associations noted in these studies as well as ranges of co-morbidities/risk factors identified from the wider body of identified studies. A recent meta-analysis, available as a preprint, summarises findings of 63 association studies of which 57 were from China.[16] Relevant information from this study is also provided in Table 2. Not all variables are included in all studies and considerable risks of confounding remain, which may explain the variation in the results reported in these studies. The headings used for the comorbidities/risk factors are those cited in the studies and have not been recategorised for this review.

Table 2: Comorbidities and risk factors associated with COVID-19

Comorbidity/risk factor	
Age Older age significantly associated with severe disease.	Older age was reported as significantly associated with severe disease in 47 out of 54 studies (87%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] The average age for hospitalisation reported in studies from the US and Italy was 53–68 years, for ICU admission was 63–70 years and for death was 77–81 years.[4,6,11,12,17-22] An unpublished study examining associations in 4,103 confirmed cases in New York found that older age was the strongest predictor of hospitalisation. Age ≥75 years (odds ratio (OR) 66.8, 95% confidence interval (CI) 44.7 to 102.6) and age 65–74 (OR 10.9, 95% CI 8.3 to 14.3). The association was retained albeit weakly for critical illness after blood test results on admission were included in the analysis: age ≥75 years (OR 2.6, 95% CI 1.6 to 4.1) and age 65-74 (OR 1.9, 95% CI 1.2 to 2.9).[11] Other studies of association for settings outside China (all unpublished) found mixed results. A study of 585 cases in US veterans aged 54–75 found age significantly associated with hospitalisation but not ICU admission when laboratory findings were included in the analysis.[12] A study of 2,653 cases in Italy found that age was significantly associated with both hospitalisation and death.[15] A smaller Italian study of 411 cases found that older age was significantly associated with death but not admission to ICU.[6] A small US study (n=54) found that older age was significantly associated with hospital admission and pneumonia but not if oxygen saturation levels were included in the analysis.[22]
Sex Male sex significantly associated with severe disease.	Male sex was reported as significantly associated with severe disease in 16 out of 45 studies (36%) which reported on sex in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] In studies from Korea, Europe, Italy, USA and Bolivia, males accounted for 38–67% of cases, 50–63% of hospital admissions, 63–93% of severe disease and 56–74% of deaths.[4,6,11,17-22] An unpublished study examining associations in 4,103 confirmed cases in New York found that there was a significant association between male sex and hospitalisation (OR 2.8, 95% CI 2.4 to 3.3) but not critical illness once laboratory results were included in the analysis.[11] Two other unpublished studies from settings outside China were identified. A study of 2,653 cases in Italy found that male sex was significantly associated with both hospitalisation and death.[15] Another Italian study, of 411 cases at a single hospital, found that male sex was significantly associated with admission to ICU but not death.[6]

Ethnicity Asian ethnicity significantly associated with severe disease in the US.	There is no mention of ethnicity as a variable of interest in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] An unpublished study of 4,103 cases in New York found a significant association between Asian ethnicity and both hospitalisation (OR 1.44, 95% CI 1.04 to 1.98) and critical illness (OR 1.91, 95% CI 1.09 to 3.37). The same study found no association between African American ethnicity and hospitalisation and a negative association with critical illness (ie African Americans were less likely to experience critical illness), OR 0.6, 95% CI 0.4 to 0.9.[11] A further preprint study of 585 cases in a US cohort of veterans aged 54–75 found that black ethnicity was significantly associated with testing positive for COVID-19 but was not associated with hospitalisation or admission to intensive care.[12]
Socioeconomic status	None of the included studies reported any measure of socioeconomic status. However, an ongoing national audit of patients critically ill with confirmed COVID-19 in NHS ICUs (not including Scotland) has reported a higher proportion of patients from more deprived areas than those from less deprived areas.[23] These findings require further investigation and verification.
Obesity Significantly associated with severe disease.	Body mass index (BMI) was reported as significantly associated with severe disease in 6 out of 11 studies (55%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] One US study (n=4,103) found that obesity was the most important factor for hospitalisation after age; BMI>40 kg/m^2 (OR 6.2, 95% CI 4.2 to 9.3) and BMI 30-40 kg/m^2 (OR 4.3, 95% CI 1.9 to 9.2).[11] BMI was also associated with critical illness; BMI>40 kg/m^2 (OR 1.7, 95% CI 1.0 to 2.9) and BMI 30–40 kg/m^2 (OR 1.4, 95% CI 1 to 1.8).[11] An Italian study including 2,653 cases found that obesity was not associated with either hospitalisation or death.[15]
Smoking Evidence of association is unclear.	Being a current smoker was reported as significantly associated with severe disease in one out of 11 studies (9%) in the unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] In the association studies identified for settings outside China two studies considered smoking. One study of 585 cases in US veterans found no association with hospitalisation or ICU admission.[12] A study of 4,103 cases in New York found a negative association with hospitalisation (OR 0.71, 95% CI 0.57 to 0.87) and no association with critical illness.[11] A systematic review including 28 studies concluded that there was low quality evidence that current and former smoking compared to never smoking is associated with greater disease severity.[24]

Cancer Significantly associated with severe disease.	Cancer was reported as significantly associated with severe disease in 5 out of 19 studies (26%) in a recent unpublished meta-analysis including 17,648 COVID-19 patients, mostly in China.[16] Four of the association studies identified from settings outside China included cancer in their analysis. Three studies found no association with hospitalisation, admission to ICU or death.[6,11,12] One study of 2,653 cases in Italy found that cancer was associated with both hospitalisation (hazard ration(HR) 1.4, 95% CI 1.1 to 1.7) and death (HR 1.4,95% CI 1 to 2).[15]
Cardiovascular disease Significantly associated with severe disease.	*Cardiovascular disease* Cardiovascular disease (CVD) was reported as significantly associated with severe disease in 16 out of 25 studies (64%) in a large unpublished meta-analysis of mostly Chinese studies.[16] After age and 'at least one comorbidity', CVD and hypertension had the strongest association. An Italian study of 411 cases found CVD had a significant association with death but not with ICU admission.[6] *Hypertension* Hypertension was reported as significantly associated with severe disease in 22 out of 33 studies (67%) and coronary vascular disease in 16 out of 25 studies (64%) in the large unpublished meta-analysis of mostly Chinese studies.[16] After age and any comorbidity these two conditions had the strongest association. Two US studies (n=4,103 and n=585) did not find any significant association between hypertension and hospitalisation or critical illness.[11,12] Two Italian studies (n=2,653 and n=411) found that hypertension was significantly associated with both hospitalisation and death.[6,15] A fifth study (n=54) found hypertension significant for hospitalisation and ARDS but that the significance disappeared if oxygen saturation was included in the analysis.[22] *Stroke* Stroke was also reported as significantly associated with severe disease in five out of 12 studies in the systematic review of Chinese studies (42%).[16] *Heart failure* One Italian (n=2,653) and one US study (n=4,103) found significant associations between heart failure and hospitalisation, critical illness or death.[11,15] *Coronary artery disease* A US study (n=4,103) found no association between coronary artery disease and hospitalisation or critical illness.[11] *Ischaemic heart disease* One Italian study (n=2,653) found a significant association between ischaemic heart disease and both hospitalisation and death.[15]

	Arrhythmia One Italian study (n=2,653) found a significant association between arrhythmia and both hospitalisation and death.[15] *Vascular disease* Two studies (Italy, n=2,653; US, n=585) found no associations between vascular disease and death.[12,15] *Hyperlipidaemia* One study (US, n=4,103) found hyperlipidaemia had a negative association with hospitalisation but found no association with critical illness.[11] Another found no association between dyslipidaemia and hospitalisation or death.[15] *ACE inhibitors and AT1 antagonists* Four of the association studies identified for settings outside China included ACE-I and AT1 antagonists in their analysis. Three studies found no association with either hospitalisation or severe disease.[6,12,22] One study (Italy, n=2,653) found that the medication was associated with hospitalisation but not death.[15]
Chronic kidney disease Significantly associated with severe disease.	Chronic kidney disease (CKD) was reported as significantly associated with severe disease in four out of 14 studies (29%) in a recent unpublished meta-analysis including 17,648 COVID-19 patients, mostly in China.[16] Four of the association studies identified from settings other than China included CKD in the analysis. All found some evidence of association with hospitalisation but the picture relating to severe disease and death was more mixed. A study of 4,103 confirmed cases in New York found that CKD had the strongest association with hospitalisation (OR 3.1, 95% CI 1.8 to 5.5) after age, obesity and heart failure. However, the study found no association for critical illness. Similarly, a study of 2,653 cases in Italy found that CKD was associated with hospitalisation (HR 1.9, 95% CI 1.3 to 2.9) but not death.[15] A US study of 585 cases in veterans aged 54–75 found a significant association for both hospitalisation and ICU admission in univariate analyses which was no longer significant when laboratory results were added to the analysis.[12] An Italian study of 411 cases found renal insufficiency to be associated with both death and ICU admission.[6]
Chronic liver disease Has not been associated with severe disease.	Hepatitis or cirrhosis was reported as significantly associated with severe disease in none of the 14 studies in a recent unpublished meta-analysis including 17,648 COVID-19 patients, mostly in China.[16]

Chronic respiratory disease Evidence of association is unclear.	Chronic obstructive pulmonary disease (COPD) was reported as significantly associated with severe disease in six out of 19 studies (32%) which reported the variable in a recent unpublished meta-analysis including 17,648 COVID-19 patients, mostly in China.[16] Other respiratory disease was reported as significantly associated with severe disease in two out of seven studies (29%) in the same meta-analysis. In unpublished studies from Korea and the USA, the prevalence of chronic respiratory disease was 7% in cases, 7–15% in hospital admissions, 11–21% in ICU admissions and 17% in patients who died.[7,11,17,25] Four of the association studies identified from settings other than China included pulmonary disease in their analysis. Results of the analysis were mixed. Two studies found no associations. A study of 4,103 confirmed cases in New York found no association between pulmonary disease and hospitalisation or critical illness.[11] A study of 411 cases from one hospital in Italy found pulmonary diseases not to be associated with death or admission to ICU.[6] Two studies (US, n=585; Italy n=2,653) found associations with hospitalisation but not severe disease or death.[12,15] No associations were found for asthma in the single study which looked at this separately.[12]
Diabetes Significantly associated with severe disease.	Diabetes was reported as significantly associated with severe disease in 13 out of 32 studies (41%) in the unpublished meta-analysis including 17,648 COVID-19 patients, mostly in China.[16] A US study with 4,103 participants found a significant association between diabetes and hospitalisation (OR 2.8, 95% CI 2.1 to 3.7) but not critical illness.[11] Another US study (n=585) found a significant association for hospitalisation but not critical illness.[12] An Italian study (n=2,653) found that diabetes was significantly associated with death but not admission to ICU.
Frailty	No evidence was identified relating to frailty.
Steroids or other Immuno-suppressants Evidence of association is unclear.	Immunocompromise was considered in only two out of 63 studies of association reported in a recent meta-analysis of 17,648 COVID-19 cases, mostly in China.[16] Neither of the studies found that it was significantly associated with severe disease. In two studies from the USA (n=2,026,227 and n=5,143) patients on immunosuppressant medications accounted for 3–5% of cases, 6% of hospital admissions and 6–9% of severe disease.[12,25] None of the identified association studies from settings outside China included steroids or immunosuppressants in the analysis.[6,11,12,15,22]

At least one comorbidity Associated with severe disease.	At least one comorbidity was reported as significantly associated with severe disease in 17 out of 23 (74%) studies which reported the variable in a recent unpublished meta-analysis including 17, 648 COVID-19 patients, mostly in China.[16] It was second only to age as the variable which was reported as significant in the highest percentage of studies. In studies from Singapore, Korea, Italy and USA patients reported as having at least one comorbidity accounted for 27–29% of cases, 71–89% of hospital admissions, 68–78% of severe disease and 95–99% of deaths.[4,6,11,17-22] Only one of the identified association studies included 'at least one comorbidity' as a variable. Three other studies looked only at individual comorbidities[11,12,22] and one used a composite score of comorbidity, the Charlson Comorbidity Index.[15] A study of 411 cases presenting at an emergency department in Italy found a significant association between any comorbidity and both ICU admission and death.[6] An Italian study including 2,653 cases found a significant association between the Charlson Comorbidity Index scores of 1 and death and scores of 2 and 3 or more with both death and hospitalisation.[15] A higher score represents a greater level of comorbidity with 0 representing no comorbid conditions.

3. Clinical measures

Table 3 details clinical measures that were investigated for association with disease severity identified in the studies within the review.

Table 3: Clinical measures considered for identifying symptoms of COVID-19

Oxygen saturation Significantly associated with severe disease.	Arterial oxygen saturation (SpO2) was reported as significantly associated with severe disease in four out of five studies (80%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] It was unclear whether this was a higher or lower oxygen saturation and what level was investigated. Saturation levels were not given, nor was it explicitly stated that lower oxygen saturation was associated with severe disease, this has been assumed. Three of the identified studies of association from settings outside China included oxygen saturation in their analysis. Results were mixed. One study examining associations in 4,103 confirmed cases of COVID-19 in New York found that oxygen saturation at levels <88% and 88–92% were strongly associated with critical illness compared to levels >92% (OR 6.99, 95% CI 4.5 to 11 at 88% and OR 1.48, 95% CI 1.09 to 2.01 at 88–92%).[11] A US study of 585 veterans aged 54–75 found that a 1% reduction in SpO2 was not associated with hospitalisation or admission to ICU.[12] The final study of 54 patients in California found that SpO2 was significantly associated with hospitalisation and development of pneumonia and ARDS but not admission to ICU.[22]

Respiratory rate Significantly associated with severe disease.	Respiratory rate was reported as significantly associated with severe disease in six out of 10 studies (60%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] It is unclear what level was investigated for significance. None of the identified studies of association from settings outside China included respiratory rate in their analysis.
Heart rate Evidence of association is unclear.	Heart rate was reported as significantly associated with severe disease in one out of seven studies (14%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] It is unclear what level of increase was investigated for significance. An Italian study of 2,653 cases found a small negative association with increased heart rate and hospitalisation but no association with admission to ICU.[15]
Systolic blood pressure Significantly associated with severe disease.	Systolic blood pressure (SBP) was reported as significantly associated with severe disease in two out of five studies (40%) in a recent unpublished meta-analysis including 17,648 patients with COVID-19, mostly in China.[16] It is unclear whether this was higher or lower SBP and what level was investigated for significance. Of the identified studies of association in settings outside China, one US study (n=585) found that a 5mm Hg decrease in SBP was associated with hospitalisation (OR 1.1, 95% CI 1 to 1.2) but not with ICU admission.[12]

4. Method of patient consultation

No validated method of measuring breathlessness via tele- or video consultations has been identified. A recommendation based on the consensus of 50 clinicians advises against using the Roth test.[26] Questions like those in the COVID-19 Scottish Primary Care Hub Triage Guide can be asked. Smartphone apps should not be used as oximeters.[27]

5. Sources of further information

For up-to-date information on signs, symptoms and prognosis of COVID-19, the following websites provide summaries of new evidence which are updated frequently:

BMJ Best practice: https://bestpractice.bmj.com/topics/en-gb/3000168/prognosis

Centre for Evidence-Based Medicine, University of Oxford, provides rapid reviews of research, categorised under 'Signs and Symptoms', 'Symptom Assessment' and 'Diagnostic Tests': https://www.cebm.net/oxford-covid-19-evidence-service/

National Institute for Health and Care Excellence (NICE): https://www.nice.org.uk/covid-19

UptoDate: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention#H3432457140

Guidance and further information on management, care and service delivery in relation to COVID-19 is signposted from the Scottish Intercollegiate Guidelines Network (SIGN) website: www.sign.ac.uk

6. Methodology

6.1 Key question

This rapid review is based on a structured key question that defines the target population, the intervention or exposure under investigation and the outcomes used to measure efficacy, effectiveness, or risk. This question formed the basis of the literature search.

In people presenting in primary care with potential COVID-19, which are the best predictors of adverse outcomes, such as hospitalisation and ventilation therapy?

Population	Interventions/Exposures	Outcomes	Notes
People in the community presenting to primary care with potential COVID-19 For search purposes include all people presenting with potential COVID19 including hospital-based studies given lack of studies in the population of interest.	Sociodemographic factors: age, gender, ethnicity, socioeconomic status. Health-related behaviours: smoking, alcohol intake Clinical information: comorbidities, current medications, previous medical history, BMI, blood pressure, signs on clinical examination (temperature, pulse, respiratory rate), onset of new symptoms (eg cough, temperature >37.8°C, fatigue, sputum, shortness of breath, muscle aches, sore throat, headache, chills, nasal congestion, nausea, diarrhoea) development of symptoms, symptom progression, symptom duration, combination of symptoms.	Disease severity Admission to hospital Admission to ICU Mechanical ventilation Mortality Duration of symptoms Disease progression	Consider method of consultation: telephone, video, face-to-face and whether different assessments need to be considered for each.

6.2 Literature review

A topic exploration was conducted to identify relevant guidance, systematic reviews and rapid reviews, using a broad internet search including, but not exclusively, the following websites:

BMJ Evidence, Center for Disease Control and Prevention, Cochrane Library, Dynamed, MAGICApp, McMasterforum, Medrxiv, National Institute for Health and Care Excellence, Oxford Centre for Evidence Based Medicine, TRIP database, Uptodate, World Health Organization.

A systematic search was conducted for primary sources of evidence using Medline and Embase. MedRXiv was searched for preprints added up to and including 24 April 2020. No quality assessment was carried out as all evidence is likely to be low quality given that only early data is available.

6.3 Updating the review

Scoping searches for new evidence will be conducted every two months. The review will be updated if new evidence emerges that changes the current conclusions.

6.4 Contributors

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Each contributor completed a declaration of interests form. No competing interests were identified.

6.5 Peer review

General practitioners, an epidemiologist, and a lay representative were invited to comment on a draft version of this report, to consider the interpretation of the evidence and feasibility for practice.

SIGN is grateful to these experts for their contribution.

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6.6 Editorial

As a final quality check, the guideline is reviewed by an editorial group, as follows:

Dr Roberta James	*Programme Lead, SIGN*
Dr Safia Qureshi	*Director of Evidence, Healthcare Improvement Scotland*
Professor Angela Timoney	*Chair of SIGN*

Abbreviations

ACE	angiotensin-converting enzyme
ARDS	acute respiratory distress syndrome
AT1	angiotensin-II receptor antagonists/angiotensin receptor blockers
BMI	body mass index
CI	confidence interval
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CVD	cardiovascular disease
HR	hazard ratio
ICU	intensive care unit

NEWS	National Early Warning Score
NICE	National Institute for Health and Care Excellence
OR	odds ratio
SaO_2	arterial oxygen saturation
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SBP	systolic blood pressure
SIGN	Scottish Intercollegiate Guidelines Network
US	United States

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