

## Covid-19 Evidence Update

### Summarized and appraised resources

10/09/2021

*The following resources are available via electronically or in print. Please follow links to access full text online, or contact the library if you have any difficulties with the links.*

The resources included in this update are summaries or critically appraised articles. If you would like a more specific search conducted please email [kgh-tr.library.service@nhs.net](mailto:kgh-tr.library.service@nhs.net)

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## Royal College/Society Guidance and Point of Care Tools

### Latest information and guidance

|   |  |
|---|--|
| <p>NICE</p> <p><a href="#">COVID-19 rapid guideline: managing COVID-19 (NG191)</a> Published 23/03/2021 Last updated 10/08/2021</p> <p><a href="#">Rapid guidelines and evidence summaries</a></p> <p><a href="#">Speciality guides</a> (NHS England and NHS Improvement advice has moved here)</p> | <p>NHS England and NHS Improvement <a href="#">Secondary care</a> (Includes Prevention, Infection control, Assessment, Management, Discharge, Isolation, Estates and facilities, Finance, Workforce, Cancer ...)</p> |
| <p>Royal College of Emergency Medicine<br/><a href="#">Covid-19 resources</a></p>   | <p>Association for Palliative Medicine<br/><a href="#">Covid 19 and Palliative, End of Life and Bereavement Care</a></p>   |
| <p>Royal College of General Practitioners<br/><a href="#">COVID-19</a></p>  | <p>Royal College of Obstetrics &amp; Gynaecologists<br/><a href="#">Coronavirus (COVID-19), pregnancy and women's health</a></p>   |
| <p>Royal College of Paediatrics and Child Health<br/><a href="#">Key topics COVID 19</a></p>  | <p>Royal College of Pathologists<br/><a href="#">COVID-19 Resources Hub</a></p>  |
| <p>Royal College of Psychiatrists<br/><a href="#">COVID-19: Community mental health settings</a></p>  | <p>Royal College of Surgeons<br/><a href="#">COVID 19 Information Hub</a></p>  |
| <p>Royal Pharmaceutical Society<br/><a href="#">COVID-19</a></p>  | <p>British Society of Echocardiography<br/><a href="#">COVID-19 clinical guidance</a></p>  |
| <p>British Society of Gastroenterology<br/><a href="#">COVID 19 updates</a></p>   | <p>British Society for Haematology<br/><a href="#">COVID-19 Updates</a></p>  |

|   |   |
|---|---|
| <p>British Society for Rheumatology<br/> <a href="#">COVID-19 updates for members</a></p>   | <p>Combined Intensive Care Society, Association of Anaesthetists, Royal College of Anaesthetists, Faculty of Intensive Care Medicine guidance<br/> <a href="#">Clinical Guidance</a></p>  |
| <p>BMJ Best Practice<br/> <a href="#">Coronavirus disease 2019 (COVID-19) Management of coexisting conditions in the context of COVID-19</a></p>  | <p>DynaMed<br/> <a href="#">Covid 19 (Novel Coronavirus)</a><br/> <a href="#">Covid-19 and Pediatric Patients</a><br/> <a href="#">Covid 19 and Special Populations</a><br/> <a href="#">Covid-19 and Patients with Cancer</a><br/> <a href="#">Covid-19 and Cardiovascular Disease Patients</a><br/> <a href="#">Covid-19 and Patients with Chronic Kidney Disease and End-stage renal Disease</a><br/> <a href="#">Covid-19 and Pregnant Patients</a><br/> <a href="#">Covid-19-associated Coagulopathy</a></p> |
| <p>Don't forget the bubbles<br/> <a href="#">An evidence summary of paediatric Covid-19 literature</a><br/> <a href="#">Covid-19</a> – a seslection of evidence based summaries and articles.</p> |   |

## New Guidance and Reports

### NICE

#### [COVID-19 rapid guideline: managing COVID-19.](#)

National Institute for Health and Care Excellence (NICE); 2021.

<https://www.nice.org.uk/guidance/ng191>

[In September 2021, NICE added new recommendations on non-invasive respiratory support and doxycycline, and updated existing recommendations on heparins.]

*Freely available online*

### Other

#### [COVID-19 vaccination: blood clotting information for healthcare professionals.](#)

Public Health England (PHE); 2021.

<https://www.gov.uk/government/publications/covid-19-vaccination-blood-clotting-information-for-healthcare-professionals>

[Information for healthcare professionals on blood clotting following COVID-19 vaccination. 23 August 2021: Updated guidance document.]

*Freely available online*

#### [COVID-19 vaccination: myocarditis and pericarditis information for healthcare professionals.](#)

Public Health England (PHE); 2021.

<https://www.gov.uk/government/publications/covid-19-vaccination-myocarditis-and-pericarditis-information-for-healthcare-professionals>

[Information for healthcare professionals on myocarditis and pericarditis following COVID-19 vaccination.]

*Freely available online*

**[JCVI statement, September 2021: COVID-19 vaccination of children aged 12 to 15 years.](#)**

Department of Health and Social Care (DHSC); 2021.

<https://www.gov.uk/government/publications/jcvi-statement-september-2021-covid-19-vaccination-of-children-aged-12-to-15-years/>

[Updated advice from the Joint Committee on Vaccination and Immunisation (JCVI) on vaccination of children aged 12 to 15.]

*Freely available online*

**[Third primary COVID-19 vaccine dose for people who are immunosuppressed: JCVI advice.](#)**

Department of Health and Social Care (DHSC); 2021.

<https://www.gov.uk/government/publications/third-primary-covid-19-vaccine-dose-for-people-who-are-immunosuppressed-jcvi-advice/>

[Statement from the Joint Committee on Vaccination and Immunisation (JCVI) on the benefits of a third primary COVID-19 vaccine dose in individuals aged 12 years and over with severe immunosuppression.]

*Freely available online*

**[COVID-19 and peripheral arterial complications in people with diabetes and hypertension: A systematic review.](#)**

Rastogi A. *Diabetes & Metabolic Syndrome* 2021;15(5):102204 .

[COVID-19 patients with diabetes or hypertension are susceptible for lower limb complications and require therapeutic anti-coagulation.]

*Freely available online*

**[Efficacy and Safety of Corticosteroid Use in Coronavirus Disease 2019 \(COVID-19\): A Systematic Review and Meta-Analysis.](#)**

Cui Y. *Infectious Diseases and Therapy* 2021;;doi.org/10.1007/s40121-021-00518-3.

[This meta-analysis indicated that corticosteroid use might cause a slight reduction in COVID-19 mortality. However, it could significantly reduce the MV requirement in patients with COVID-19 and restrict serious adverse events.

Additionally, the pulse dose of methylprednisolone for less than 7 days may be a good treatment choice for patients with COVID-19.]

*Freely available online*

**[Insulin Treatment May Increase Adverse Outcomes in Patients With COVID-19 and Diabetes: A Systematic Review and Meta-Analysis.](#)**

Yang Y. *Frontiers in Endocrinology* 2021;;doi.org/10.3389/fendo.2021.696087.

[Insulin treatment may increase mortality and severe/critical complications in patients with COVID-19 and diabetes, but more large-scale studies are needed to confirm and explore the exact mechanism.]

*Freely available online*

**[Ivermectin for the Treatment of Coronavirus Disease 2019: A Systematic Review and Meta-analysis of Randomized Controlled Trials.](#)**

Roman YM. *Clinical Infectious Diseases* 2021;;ciab591.

[Compared with the standard of care or placebo, IVM did not reduce all-cause mortality, LOS, or viral clearance in RCTs in patients with mostly mild COVID-19. IVM did not have an effect on AEs or SAEs and is not a viable option to treat patients with COVID-19.]

*Freely available online*

## [Covid-19 Evidence Alerts from McMaster Plus](#)

COVID-19 Evidence Alerts to current best evidence for clinical care of people with threatened, suspected or confirmed COVID-19 infection. Reports are critically appraised for scientific merit, and those with acceptable scientific merit are appraised for relevance and importance by frontline clinicians. The studies listed below meet their criteria for quality. The site also lists other studies published which do not meet their criteria, or do not belong to a study category they appraise. ([More information available](#)).

|   |
|---|
| <b>Diagnosis</b>  |
| <a href="#">A Comparison of Lung Ultrasound and Computed Tomography in the Diagnosis of Patients with COVID-19: A Systematic Review and Meta-Analysis.</a><br><i>Wang M, Luo X, Wang L, et al. <b>Diagnostics (Basel)</b></i>   |
| <a href="#">Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis.</a><br><i>BrÄ¼mmer LE, Katzenschlager S, Gaeddert M, et al. <b>PLoS Med</b></i>   |
| <a href="#">Clintest rapid COVID-19 antigen test for the diagnosis of SARS-CoV-2 infection: A multicenter evaluation study.</a><br><i>Merino-Amador P, Gonzalez-Donapetry P, Dominguez-Fernandez M, et al. <b>J Clin Virol</b></i>  |
| <a href="#">Clinical Evaluation of Sofia Rapid Antigen Assay for Detection of Severe Acute Respiratory Syndrome Coronavirus 2 among Emergency Department to Hospital Admissions.</a><br><i>Smith RD, Johnson JK, Clay C, et al. <b>Infect Control Hosp Epidemiol</b></i>                              |
| <a href="#">"The effectiveness of rapid antigen test-based for SARS-CoV-2 detection in nursing homes in Valencia, Spain".</a><br><i>Escriva BF, Mochon MDO, Gonzalez RM, et al. <b>J Clin Virol</b></i>   |
| <a href="#">AGA Rapid Review and Guideline for SARS-CoV2 Testing and Endoscopy Post-Vaccination: 2021 Update.</a><br><i>Sultan S, Siddique SM, Singh S, et al. <b>Gastroenterology</b></i>  |
| <a href="#">Performance of Repeat BinaxNOW SARS-CoV-2 Antigen Testing in a Community Setting, Wisconsin, November-December 2020.</a><br><i>Shah MM, Salvatore PP, Ford L, et al. <b>Clin Infect Dis</b></i>   |
| <b>Clinical Prediction Guide</b>  |
| <a href="#">The usefulness of Shock Index and Modified Shock Index in predicting outcome of COVID-19 patients.</a><br><i>Kurt E, Bahadirli S <b>Disaster Med Public Health Prep</b></i>   |
| <a href="#">Analysis of Oxygen Blood Saturation/Respiratory Rate Index, NEWS2, CURB65, and quick Sequential Organ Failure Assessment Scores to Assess Prognosis in Patients with Mild Coronavirus Disease 2019.</a><br><i>Piombi-Adanza SN, Baretto MC, Echaide FA, et al. <b>Rev Invest Clin</b></i> |
| <a href="#">Usefulness of Easy-to-Use Risk Scoring Systems Rated in the Emergency Department to Predict Major Adverse Outcomes in Hospitalized COVID-19 Patients.</a><br><i>Gonzalez-Flores J, Garcia-Avila C, Springall R, et al. <b>J Clin Med</b></i>  |
| <a href="#">ABC(2)-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores.</a><br><i>Marcolino MS, Pires MC, Ramos LEF, et al. <b>Int J Infect Dis</b></i>  |
| <b>Etiology</b>   |
| <a href="#">Risk of thrombocytopenia and thromboembolism after covid-19 vaccination and SARS-CoV-2 positive testing: self-controlled case series study.</a><br><i>Hippisley-Cox J, Patone M, Mei XW, et al. <b>BMJ</b></i>  |
| <b>Primary Prevention</b>   |
| <a href="#">Systematic review of empirical studies comparing the effectiveness of non-pharmaceutical interventions against COVID-19.</a><br><i>Mendez-Brito A, Bcheraoui CE, Pozo-Martin F <b>J Infect</b></i>  |
| <b>Prognosis</b>  |
| <a href="#">Clinical Features and Outcomes of Coronavirus Disease 2019 Among People With Human Immunodeficiency Virus in the United States: A Multicenter Study From a Large Global Health Research</a>   |

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| <p><a href="#">Network (TriNetX).</a><br/>Yendewa GA, Perez JA, Schlick K, et al. <b>Open Forum Infect Dis</b></p>   |
| <p><a href="#">Outcomes of COVID-19 in patients with rheumatoid arthritis: A multicenter research network study in the United States.</a><br/>Raiker R, DeYoung C, Pakhchanian H, et al. <b>Semin Arthritis Rheum</b></p>                  |
| <p><a href="#">Rate and severity of suspected SARS-Cov2 reinfection in a cohort of PCR-positive COVID-19 patients.</a><br/>Slezak J, Bruxvoort K, Fischer H, et al. <b>Clin Microbiol Infect</b></p>                                       |
| <p><a href="#">Mortality in Cancer Patients With COVID-19 Who Are Admitted to an ICU or Who Have Severe COVID-19: A Systematic Review and Meta-Analysis.</a><br/>Nadkarni AR, Vijayakumaran SC, Gupta S, et al. <b>JCO Glob Oncol</b></p>  |
| <p><b>Treatment</b></p>  |
| <p><a href="#">Metformin Use Is Associated with Decreased Mortality in COVID-19 Patients with Diabetes: Evidence from Retrospective Studies and Biological Mechanism.</a><br/>Poly TN, Islam MM, Li YJ, et al. <b>J Clin Med</b></p>       |
| <p><a href="#">fficacy and safety of Sofosbuvir plus Daclatasvir or Ravidasvir in patients with COVID-19, A Randomized Controlled Trial.</a><br/>Abbass S, Salama M, Salman T, et al. <b>J Med Virol</b></p>                               |
| <p><a href="#">Response to SARS-CoV-2 vaccination in immune mediated inflammatory diseases: Systematic review and meta-analysis.</a><br/>Jena A, Mishra S, Deepak P, et al. <b>Autoimmun Rev</b></p>                                       |
| <p><a href="#">SARS-CoV-2-neutralising monoclonal antibodies for treatment of COVID-19.</a><br/>Kreuzberger N, Hirsch C, Chai KL, et al. <b>Cochrane Database Syst Rev</b></p>   |
| <p><a href="#">Steroids Use in Non-Oxygen requiring COVID-19 Patients: A Systematic Review and Meta-analysis.</a><br/>Sahu AK, Mathew R, Bhat R, et al. <b>QJM</b></p>   |
| <p><a href="#">What Is the Role of Therapeutic Plasma Exchange as an Adjunctive Treatment in Severe COVID-19: A Systematic Review.</a><br/>Krzych LJ, Putowski Z, Czok M, et al. <b>Viruses</b></p>  |
| <p><a href="#">Janus kinase inhibitors and major COVID-19 outcomes: time to forget the two faces of Janus! A meta-analysis of randomized controlled trials.</a><br/>Patoulas D, Doumas M, Papadopoulos C, et al. <b>Clin Rheumatol</b></p> |
| <p><a href="#">Ciclesonide Inhaler Treatment for Mild-to-Moderate COVID-19: A Randomized, Open-Label, Phase 2 Trial.</a><br/>Song JY, Yoon JG, Seo YB, et al. <b>J Clin Med</b></p>  |
| <p><a href="#">Evaluation of adalimumab effects in managing severe cases of COVID-19: A randomized controlled trial.</a><br/>Fakharian A, Barati S, Mirenayat M, et al. <b>Int Immunopharmacol</b></p>                                     |
| <p><a href="#">Statins reduce mortality in patients with COVID-19: an updated meta-analysis of 147,824 patients.</a><br/>Diaz-Arocutipa C, Melgar-Talavera B, Alvarado-Yarasca A, et al. <b>Int J Infect Dis</b></p>                       |
| <p><a href="#">Interventions for palliative symptom control in COVID-19 patients.</a><br/>Andreas M, Piechotta V, Skoetz N, et al. <b>Cochrane Database Syst Rev</b></p>   |
| <p><a href="#">Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial.</a><br/>Ehrmann S, Li J, Ibarra-Estrada M, et al. <b>Lancet Respir Med</b></p>   |
| <p><a href="#">Convalescent Plasma for COVID-19: A Meta-analysis of Clinical Trials and Real-World Evidence.</a><br/>Kloypan C, Saesong M, Sangsuemoon J, et al. <b>Eur J Clin Invest</b></p>  |
| <p><a href="#">Effect of Anticoagulant Administration on the Mortality of Hospitalized Patients With COVID-19: An Updated Systematic Review and Meta-Analysis.</a><br/>Jiang L, Li Y, Du H, et al. <b>Front Med (Lausanne)</b></p>         |
| <p><a href="#">The effects of hyperbaric oxygen therapy (HBOT) on coronavirus disease-2019 (COVID-19): a systematic review.</a><br/>Oliaei S, SeyedAlinaghi S, Mehrtak M, et al. <b>Eur J Med Res</b></p>                                  |
| <p><a href="#">Efficacy and Safety of Azithromycin for the Treatment of COVID-19: A Systematic Review and Meta-analysis.</a><br/>Mangkuliguna G, Glenardi, Susanto N, et al. <b>Tuberc Respir Dis (Seoul)</b></p>                          |

[Early Convalescent Plasma for High-Risk Outpatients with Covid-19.](#)

*Korley FK, Durkalski-Mauldin V, Yeatts SD, et al. N Engl J Med*

[Effect of Azithromycin and Hydroxychloroquine in Patients Hospitalized with COVID-19: Network Meta-Analysis of Randomized Controlled Trials.](#)

*Chi G, Memar Montazerin S, Lee JJ, et al. J Med Virol*

[Effect of anakinra on mortality in patients with COVID-19: a systematic review and patient-level meta-analysis.](#)

*Kyriazopoulou E, Huet T, Cavalli G, et al. Lancet Rheumatol*

## Cochrane Systematic Reviews

### [Cochrane Evidence on COVID-19: a roundup](#)

#### [SARS-CoV-2-neutralising monoclonal antibodies for treatment of COVID-19](#)

Kreuzberger, N et al

#### **Implications for practice**

The evidence for each comparison results from one study only, and we rated certainty in the evidence as low due to very serious imprecision for all comparisons except casirivimab/imdevimab versus usual care in hospitalised individuals (moderate certainty evidence). Therefore, the identified evidence is mostly insufficient to draw meaningful conclusions regarding treatment with any specific monoclonal antibody (mAb), and the disease stage in which mAbs should be used.

For non-hospitalised participants (asymptomatic or mild disease), we are uncertain about the effectiveness and safety of bamlanivimab, the combination of bamlanivimab/etesevimab, casirivimab/imdevimab, sotrovimab, and regdanvimab compared to placebo. Information on patient-relevant outcomes such as mortality, quality of life, and serious adverse events is either inconclusive or entirely lacking, although bamlanivimab alone and in combination with etesevimab, as well as casirivimab/imdevimab, sotrovimab, and regdanvimab may reduce the occurrence of hospital admission or death. Data on adverse events (AEs) vary for the substances, doses and even type of AE (all grades, grades 3-4, serious adverse events). For all comparisons, the 95% confidence interval includes both benefit and harm and our certainty in the evidence is low. We acknowledge that the true effect may substantially vary from the reported effects.

For hospitalised participants (moderate-to-severe disease), bamlanivimab may have little to no effect on efficacy outcomes when compared to placebo, but it may increase the occurrence of severe symptoms and grade 3 to 4 adverse events. Casirivimab/imdevimab has probably no effect on mortality, progression to invasive mechanical ventilation (IMV), and hospital discharge alive by day 30. Unfortunately, we are lacking important information on AE and SAE for this comparison. Subgroup analyses within the studies suggest that it could be worth examining the subgroup of participants who have not developed antibodies at baseline.

## Evidence Aid

<https://evidenceaid.org/evidence/coronavirus-covid-19/>

This evidence collection contains plain-language summaries of high-quality research which are available in English, and translated into French, Spanish, Portuguese, Arabic and Chinese (simplified and traditional).

The collection includes summaries of systematic reviews that might be relevant to the direct impact of COVID-19 (including reviews of emerging research, as well as existing reviews of relevant interventions) on health and other outcomes, the impact of the COVID-19 response on other conditions, and issues to consider for the recovery period after COVID-19.

*Nothing added that hasn't already been reported.*

## Dynamed - [COVID-19 \(Novel Coronavirus\)](#)

### Latest updates

**Evidence** Updated 7 Sep 2021

BNT162b2 (Pfizer-BioNTech) vaccine associated with increased risk of myocarditis in persons  $\geq 16$  years old in Israel who were not healthcare workers or long-term care facility residents, but this increase in risk was greater with SARS-CoV-2 infection (N Engl J Med 2021 Aug 25 early online)

[View in topic](#)

**Evidence** Updated 1 Sep 2021

postdischarge cardiac abnormalities (including nonischemic and ischemic heart disease) reported in 54% of adults who had abnormal high-sensitivity troponin levels at time of hospital admission for severe COVID-19 (Eur Heart J 2021 May 14)

[View in topic](#)

**Evidence** Updated 1 Sep 2021

Pfizer-BioNTech RNA vaccine (BNT162b2) associated with reduced SARS-CoV-2 infection in nursing home residents and staff and healthcare workers and with reduced COVID-19-related hospitalization and mortality in nursing home residents in Catalonia, Spain (BMJ 2021 Aug 18)

[View in topic](#)

**Drug/Device Alert** Updated 30 Aug 2021

FDA supports extension of shelf-life of Pfizer-BioNTech COVID-19 vaccine (Comirnaty) from 6 months to 9 months (stored in ultra-low temperature freezer); extension of shelf-life to 9 months also applies to batches that might have expired prior to extension, provided they have been stored in ultra-low temperature freezer (FDA Press Release 2021 Aug 24)

[View in topic](#)

**Guideline Summary** Updated 30 Aug 2021

United States Department of Health and Human Services issues joint statement on COVID-19 booster doses (FDA Press Release 2021 Aug 18)

[View in topic](#)

**Evidence** Updated 27 Aug 2021



in adolescents aged 12-17 years, Moderna (mRNA-1273) vaccine may have favorable safety profile, and similar immune response compared to adults  $\leq 25$  years old (N Engl J Med 2021 Aug 11 early online)

[View in topic](#)

**Evidence** Updated 26 Aug 2021

overall mortality 22% in adults presenting to hospital with vaccine-induced immune thrombocytopenia and thrombosis (VIITT) after first dose of ChAdOx1 nCoV-19 vaccine (N Engl J Med 2021 Aug 11 early online)

[View in topic](#)

**Evidence** Updated 25 Aug 2021

clear mask worn by surgeon during new patient visit may increase patient trust and improve patient perceptions of surgeon's ability to communicate and express empathy compared to standard surgical mask (JAMA Surg 2021 Apr 1)

[View in topic](#)

## **BMJ Best Practice**

02 Sep 2021

### **Covid -19**

[What's new at this update](#)

FDA authorises booster dose for immunocompromised people

- The US Food and Drug Administration has authorised an additional (third) dose of the Pfizer/BioNTech and Moderna vaccines in moderately to severely immunocompromised people at least 28 days after the completion of their initial vaccine series.
- See the Prevention section for more information.

MHRA authorises monoclonal antibody for post-exposure prophylaxis

- The UK's Medicines and Healthcare products Regulatory Agency has issued a conditional marketing authorisation to casirivimab/imdevimab for post-exposure prophylaxis in adults and children  $\geq 12$  years of age and older and weighing  $\geq 40$  kg. The US Food and Drug Administration has also authorised casirivimab/imdevimab for this indication in select people. Casirivimab/imdevimab is also authorised for the treatment of COVID-19.
- The US National Institutes of Health recommends casirivimab/imdevimab for post-exposure prophylaxis in people who are at high risk for progression to severe disease and who are not fully vaccinated (or who are fully vaccinated but are not expected to mount an adequate immune response) and who meet certain exposure criteria.
- See the Emerging section for more information.

CDC recommends mRNA vaccines in people with a history of Guillain-Barre syndrome

- The US Centers for Disease Control and Prevention recommends that people with a history of Guillain-Barre syndrome should consider an mRNA vaccine instead of adenovirus-vector vaccines, which have been linked to cases of Guillain-Barre syndrome.
- See the Prevention section for more information.

01 Sep 2021

[Guidelines recommend measures to manage acute and chronic conditions during the COVID-19 pandemic: updated](#)

Further guidelines have been published to inform the management of patients with coexisting conditions during the COVID-19 pandemic.

New this update:

- Considerations for perinatal care (updated)
- Considerations for the mental health of adults (updated)
- Mental health of children and adolescents (updated)
- Asthma (updated)
- Cholestasis of pregnancy (new)
- Chronic congestive heart failure (updated)
- Chronic kidney disease (updated)
- Chronic obstructive pulmonary disease (COPD) (updated)
- Diabetes (type 2) (updated)
- HIV infection (updated)
- Idiopathic pulmonary fibrosis (updated)
- Substance use disorders (updated)

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