Guideline Audit and Research Recommendations

This is a summary of the recommendations made in respiratory guidelines from the BTS and NICE. The intention is for this to be updated as guidelines are added or revised, and expanded to include other guidelines from other organisations in future.
It is presented to direct trainees towards topics where important unanswered questions exist and therefore to provide inspiration for project proposals.

The following guidelines have been reviewed:

British Thoracic Society (BTS)

Topic	Title	Date
Acute Respiratory Distress Syndrome	FICM/ICS Guidelines on the Management of ARDS, supported by BTS	2018
Asthma	BTS/SIGN Guideline for the management of asthma	2019
Bronchiectasis in Adults	BTS Guideline for Bronchiectasis in Adults	2018
Emergency Oxygen	BTS Guideline for oxygen use in healthcare and emergency settings	2022
Home Oxygen	BTS Guidelines for Home Oxygen Use in Adults	2015
Long Term Macrolide Use	BTS Guideline for Long Term Macrolide Use	2020
Mesothelioma	BTS Guideline for the Investigation and Management of Pleural Mesothelioma	2018
NIV	BTS/ICS Guideline for the Ventilatory Management of Acute Hypercapnic Respiratory Failure in Adults	2016
NTM	BTS Guideline for the Management of Non-Tuberculous Mycobacterial Pulmonary disease	2017
Pneumonia	BTS Guidelines for the Management of Community Acquired Pneumonia in Adults: update 2009	2015
Pulmonary Embolism	BTS Guideline for the outpatient management of pulmonary embolism	2018
Pulmonary Nodules	BTS Guidelines for the investigation and management of pulmonary nodules	2015

National Institute for Health and Care Excellence (NICE)

Topic	Title	Date
Asthma	Asthma: diagnosis, monitoring and chronic asthma management; NICE guideline [NG80]	2017
OSA/OHS	Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s; NICE guideline [NG202]	2021
COPD	Chronic obstructive pulmonary disease in over 16s: diagnosis and management; NICE guideline [NG115]	2018
COPD	Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing; NICE guideline [NG114]	2018
COVID-19	COVID-19 rapid guideline: managing the long-term effects of COVID-19; NICE guideline [NG188]	2020
COVID-19	COVID-19 rapid guideline: managing COVID-19; NICE guideline [NG191]	2021
Cystic Fibrosis	Cystic fibrosis: diagnosis and management; NICE guideline [NG78]	2017
Lung Cancer	Lung cancer: diagnosis and management; NICE guideline [NG122]	2019
Pneumonia	Pneumonia (community-acquired): antimicrobial prescribing; NICE guideline [NG138]	2019
Pneumonia	Pneumonia (hospital-acquired): antimicrobial prescribing; NICE guideline [NG139]	2019
Pulmonary Fibrosis	Idiopathic pulmonary fibrosis in adults: diagnosis and management; Clinical guideline [CG163]	2013

Tuberculosis	Tuberculosis; NICE guideline [NG33]	2016

FICM/ICS Guidelines on the Management of ARDS supported by BTS

- The use of corticosteroids in established ARDS should be the subject of a suitably powered, multicentre RCT with long-term follow-up
- The use of ECCO2 R in established ARDS should be the subject of a suitably powered multicentre RCT with long term follow-up and economic analysis

BTS/SIGN Guideline for the management of asthma

- Clinical prediction models for quantifying risk need to be developed and prospectively validated in adults, children aged 5–12 and children under five years of age. Does risk assessment based on these factors improve outcomes when used prospectively in routine clinical practice?

- In monitoring asthma, what level of risk is associated with factors where evidence is currently limited or equivocal?

- Does incorporation of assessment of risk of future asthma attacks (potentially using a risk score) into routine care improve outcomes?

- What is the utility of FeNO measurement in guiding asthma treatment to improve asthma outcomes, such as reduced asthma attacks or increased asthma control, in different patient groups?

- What is the impact of poverty, urban/rural living and ethnicity on asthma outcomes in the UK setting?

- In children under five years of age, what factors are associated with increased risk of acute asthma/wheezing attacks? Do risk factors in this age group differ from those in older children?

- What features of available apps lead to improvements in adherence to medication and which have any impact on clinical outcomes?

- Which approaches to improving medication adherence are most effective and sustainable in patients with asthma?

- How effective are house dust mite and other allergen reduction measures in asthma? A systematic review/meta-analysis is required including only high-quality trials that i) use interventions that are documented to reduce allergen exposure, ii) follow up participants for a sufficient time for important clinical 151 outcomes to become apparent, iii) provides separate analyses for children and adults, and iv) accounts for any changes in asthma medication over the course of the trial.

- What are the potential beneficial effects of vitamin D supplementation in people with asthma, particularly children and people with frequent severe asthma exacerbations, with different baseline vitamin D levels?

- How effective are breathing exercises in children with asthma?

- What components of individualised multicomponent allergen reduction strategies are effective at improving asthma control and reducing exacerbations?

- Do strategies to reduce environmental allergens improve asthma control and reduce exacerbations in specific subgroups of people with asthma, eg children?

- How effective is montelukast in patients without allergic rhinitis and/or atopic dermatitis?

- Development of an agreed universal definition of 'asthma exacerbation' to allow comparison of this outcome between studies.

- Classification of asthma-related and non-asthma related adverse events to allow comparison of adverse events between studies.

- Which, if any, subgroups of children benefit most from addition of LTRA as compared with LABA as additional add-on therapy to ICS alone?

- What are the short- and long-term steroid-sparing effects of monoclonal antibody therapies in adults and children on different treatment regimens?

- Does the effectiveness of treatment with monoclonal antibodies decrease over time and/or does clinically relevant antibody sensitisation occur, and if so, at what point does/do these occur?

- What markers of response are there to enable targeting of monoclonal antibody therapy?

- Does suppression of IgE or IL-5 have any long-term effects on the recipient's immune function?

- What is the short- and long-term effectiveness and safety of subcutaneous and sublingual immunotherapy in asthma in studies with optimal design and patient-centric endpoints, such as asthma control and exacerbations? Does effectiveness differ between different products or between patients with different characteristics?

- Which patients with asthma might benefit most from bronchial thermoplasty and what are the long-term outcomes and safety of this treatment?

- What is the place of bronchial thermoplasty in the management of severe asthma compared with other options such as biological treatments?

- What is the relative clinical effectiveness and safety of bronchial thermoplasty compared with monoclonal antibody treatments?

- What is the role of non-invasive ventilation and high-flow oxygen therapy in treating children with severe exacerbations of asthma, and what is their effect on measurable outcomes including respiratory parameters, physiological variables and blood gases?

- In considering treatment with extracorporeal membrane oxygenation (ECMO) what is the definition of life-threatening or standard care?

- What is the clinical effectiveness and safety of ECMO treatment in patients with asthma taking anticoagulants?

BTS Guideline for Bronchiectasis in Adults

- Consensus criteria for diagnosis of ABPA need to be validated in bronchiectasis cohorts.
- Consensus criteria for definition of abnormal post pneumococcal test immunisation antibody responses need to be validated in bronchiectasis cohorts.
- Randomised controlled trials using clinically important outcome measures are required to assess the effectiveness of airway clearance techniques in varying severities of bronchiectasis.
- Randomised controlled trials are required to evaluate the effects of airway clearance techniques in patients who are undergoing an exacerbation.
- Randomised controlled trials are needed to assess the long term impact of muco-active therapies.
- Randomised controlled trials are needed to assess the long term impact of anti-inflammatory therapies.
- Long term randomised controlled trials of oral and inhaled antibiotics are needed to assess their efficacy and safety in patients with bronchiectasis who have frequent respiratory tract infections with recurrent P. aeruginosa infection or other potential pathogenic micro-organisms.
- Further interventional/randomised controlled trials needed to establish the role of any alternative therapies in the management of bronchiectasis.
- Studies assessing the benefits of nutritional supplementation in patients with bronchiectasis should be undertaken.
- The role of education, self management plans and who delivers the pulmonary rehabilitation needs to be explored.
- The role of pulmonary rehabilitation after exacerbations requiring hospital admission needs to be explored.
- The incidence of cross-infection of respiratory pathogens in the group exercise setting should be investigated in the bronchiectasis population.
- A randomised control trial of P. aeruginosa eradication therapy is needed to determine the microbiological and clinical outcomes of eradication therapy.
- Randomised controlled trials are needed to assess which patients with bronchiectasis would benefit from long term Immunoglobulin G replacement therapy alone or as an adjunct to long term antibiotic therapy- assessing the optimal dose of IgG replacement and identification of ideal trough IgG level to prevent recurrent infections.
- Large scale robust data that confirm or refute the transmissibility of key pathogens such as P. aeruginosa and non-tuberculous mycobacteria are needed.

See also Appendix 8 of the Guideline which present the research recommendations in PICO format

BTS Guideline for oxygen use in healthcare and emergency settings

Clinical trials

1. Randomised trial of 'precautionary use' of oxygen in critical illness compared with a conservative policy of monitoring carefully and giving titrated oxygen therapy oxygen only if the saturation falls below the target range (and trials to determine the best target range to aim for).
2. RCTs of nasal high-flow humidified oxygen compared with NIV or high-concentration oxygen in critical illness.
3. The optimal oxygen target values and their feasibility during CPR and immediately after a restoration of spontaneous circulation in order to improve survival and neurological outcome.
4. Prospective studies of the effect of oxygen in non-hypoxaemic patients with major trauma and head injury.
5. Use of oxygen in myocardial infarction (at date of guideline publication, AVOID study is published in 2016 and DETO2X-AMI trial is ongoing).330–333
6. Use of oxygen in unstable coronary syndromes or type 2 myocardial infarction.
7. Use of oxygen in chest pain of presumed cardiac origin.
8. Studies to determine if different types of oxygen mask can affect clinical outcomes.
9. Use of oxygen in obstetric emergencies.
10. Prospective studies to determine the optimal target saturation range for patients not at risk of hypercapnia, for example, target range 92–96% vs 94–98%.
11. Use of nasal cannulae to deliver low-dose oxygen therapy (eg, nasal cannulae at 0.5–1.0 L/min compared with 24% and 28% face masks).
12. Prospective studies to establish the ideal target saturation range in patients with exacerbated COPD; for example, should the target range be 88–92% or slightly lower or slightly higher for optimal outcome?
13. RCTs of nasal high-flow (but low concentration) humidified oxygen compared with NIV in patients exacerbated COPD with hypercapnic respiratory failure and pH 7.30–7.35 following initial optimisation of treatment.
14. RCTs of titrated oxygen therapy in acute presentations of patients with conditions associated with chronic respiratory failure (eg, neuromuscular disease or obesity-associated hypoventilation).
15. RCTs of titrated oxygen therapy in patients presenting acutely with non-hypercapnic respiratory failure (eg, heart failure, pneumonia).
16. Randomised trials to determine if nitrous oxide is an effective analgesic agent and if the oxygen component affects clinical outcomes.
17. Randomised trials to determine if clinical outcomes can be improved by the use of Heliox mixtures and, if so, which conditions are likely to benefit.
18. Use of oxygen as required for relief or breathlessness in nonhypoxaemic patients with acute illness.
19. Effects of humidified high-flow oxygen on patient comfort.
20. Effects of increased flow rates from Venturi masks on patient comfort and oxygen saturation.
21. Further comparisons of high-flow nasal oxygen with reservoir masks and high-concentration Venturi masks.

Implementation studies

22. Benefits of alert cards and personalised oxygen masks for patients with prior hypercapnic respiratory failure.
23. Further studies of clinical outcomes of patients exposed to hyperoxia.
24. Relationship between oxygen levels and outcomes in a wide range of conditions.
25. Studies to determine if implementation of this guideline improves patient outcomes.
26. Studies to determine the best way to help clinicians to comply with guideline recommendations.

Systematic reviews

27. Outcomes from different levels of oxygen supplementation in AECOPD.
28. Updated review of oxygen therapy in myocardial infarction.
29. Review of oxygen therapy in stroke.

BTS Guidelines for Home Oxygen Use in Adults

1. Research to investigate which patients with particular disease phenotypes benefit from LTOT: for example smokers compared with ex-smokers, those with pulmonary hypertension, those with COPD-driven cachexia and frequent exacerbators.
2. Research to investigate long-term outcomes (survival) in diseases other than COPD such as CF, ILD and bronchiectasis.
3. Research to investigate delivery of oxygen during pulmonary rehabilitation and maintenance classes, assessing impact on outcomes such as exacerbations, exercise tolerance and quality of life.
4. Longitudinal studies to assess the impact of LTOT on pulmonary haemodynamics in COPD patients with pulmonary hypertension using both direct (eg, cardiac catheterisation) and indirect (eg, NT-proBNP, echocardiography) parameters, along with quality of life and exercise tolerance outcomes.
5. A robust assessment of risk assessment measures with the aim of developing an integrated pathway for home oxygen teams and oxygen provider services to manage patients who smoke.
6. Research to investigate the role of palliative oxygen in comparison with or used together with other measures such as opiates, fan therapy and cognitive behavioural therapy.
7. Research to investigate and compare the use of ABG and CBG in predicting need for LTOT and risk of hypercapnia.
8. Audit of assessment, ordering for and follow-up of home oxygen patients to improve and maintain standards of care from home oxygen assessment teams.

BTS Guideline for Long Term Macrolide Use

Asthma

1. Further research, over a longer period, is needed to investigate the role of long-term macrolide therapy in reducing exacerbations of asthma.
2. Use of validated scoring systems and creation of a core outcome set should be considered in future trials of macrolide therapy in asthma to allow more accurate delineation of clinical response and comparison between studies.
3. Head to head comparisons of different macrolide therapy and of differing dose regimens for the same macrolide are required to optimise the use of macrolide therapy in asthma.
4. Research into the discrepancy between significant reductions in inflammation but minimal improvements in clinical parameters is required.
5. Research into the impact of macrolide therapy in different clinical phenotypes of asthma should be performed in order to assess whether greater benefit is seen in one phenotype over another.
6. Research into the overlap between asthma and bronchiectasis and the impact of this on response to macrolides may assist in identifying asthma phenotypes which may respond differently to macrolide therapy.

Bronchiectasis

1. Long-term studies of microbiological impact of prolonged macrolide therapy.
2. Head-to- head comparison of different dose regimens for the same macrolide (eg, 250 mg three times a week of azithromycin vs 500 mg three times a week).
3. Head-to- head comparisons of different macrolides (eg, azithromycin vs erythromycin).
4. Prolonged studies of benefit and risk beyond 12 months of use.
5. Studies assessing the effect of macrolides following re-introduction of therapy after a break.
6. Use of bronchiectasis specific QOL measures in macrolide trials.
7. Comparison of outcomes in patients with different baseline exacerbation rates when treated with macrolides.
8. Comparison of outcomes in patients with different baseline microbiological culture/microbiome profiles when treated with macrolides.
9. Comparison of outcomes in patients with different baseline QOL scores when treated with macrolides.
10. Comparison studies of long-term macrolides to other oral or inhaled prophylactic regimens.
11. Studies looking into the benefits of combined macrolide and Inhaled antibiotic regimens.

COPD

1. Long-term (>12 months) follow-up trials to evaluate impact of long-term macrolide therapy on mortality, antimicrobial resistance, long-term potential cardiac toxicity and disease progression.
2. Studies to evaluate the impact of short-term breaks in chronic therapy with long-term macrolide antibiotics are needed.
3. Studies phenotyping COPD in large trials where subgroup analysis can potentially identify groups of patients with COPD who will benefit most from long-term macrolide therapy.
4. Trials investigating head to head the benefits and adverse effects of oral agents that reduce acute exacerbations in patients with COPD (long-term, low-dose macrolides, carbocysteine, roflumilast).

British thoracic society Guideline for the investigation and management of malignant Pleural mesothelioma

Further research is required to identify biomarkers that reliably predict treatment response within clinical practice.

The role of VATS-PP and EPD in good prognosis patients should be examined further in clinical trials, which should include robust measurement of quality of life.

The role of immunotherapy in malignant pleural mesothelioma (MPM) should be further assessed in large phase III randomised controlled trials (RCTs).

Further randomised controlled trials of second-line therapy on MPM are required.

Prospective clinical trials of preoperative radiotherapy, postoperative radiotherapy after pleurectomy decortication and definitive radiotherapy after chemotherapy in MPM are required.

Further prospective randomised clinical trials are required to determine the role of radiotherapy for symptom control in MPM and the optimal dose fractionation.

BTS/ICS Guidelines for the Ventilatory Management of Acute Hypercapnic Respiratory Failure in Adults

This guidance does not state specific research recommendations. It states: "Important practical points that lack research evidence were highlighted as 'Good Practice Points'" but none are written as research questions

NIV monitoring: Further studies are needed to assess the role of transcutaneous CO2 monitoring.

Further evaluation of out-of-hospital NIV in acute hypercapnic respiratory failure is required.

British Thoracic Society Guidelines for the Management of Non-tuberculous Mycobacteria Pulmonary Disease (NTM-PD)

NTM epidemiology

1. What are the risk factors for developing NTM-pulmonary disease?
Why is this important? We need to understand who is at high risk of NTM infection in order (1) to alert clinicians to consider NTM-pulmonary disease in these groups and diagnose it promptly and (2) to evaluate the benefit of screening for NTM in high-risk groups.

2. What are the mechanisms contributing to patient-to-patient transmission of NTM?
Why is this important? Given the growing evidence supporting *M. abscessus* transmission between individuals with CF, it is essential that we evaluate whether person-to-person transmission can occur in different patient groups and with other NTM species, and define precisely the routes through which cross-infection can occur in order to minimise risk to individuals.

NTM microbiology

1. Can we develop more rapid identification of NTM species from respiratory samples?
Why is this important? There are currently significant delays in identification and speciation of mycobacteria from respiratory samples, which delay the diagnosis, and consequently the treatment, of NTM-pulmonary disease. The development and rigorous validation of non-culture-based detection and speciation methods would greatly impact on the management of NTM infection.

2. Can we better understand the role of DST in predicting treatment outcomes?
Why is this important? We currently do not understand the significance of *in vitro* susceptibility testing for most antibiotics inmost NTM species in predicting clinical response to antibiotics. This potentially means we are prescribing ineffectual or inappropriate antibiotics and failing to give optimal drug regimens.

NTM treatment

1. Can we better understand the pathogenicity of specific NTM species and subspecies to facilitate treatment decision-making?
Why is this important? It is recognised, although incompletely understood, that the pathogenic potential of different NTM species varies considerably. A comprehensive analysis of the likelihood that an isolated NTM species or subspecies might cause progressive inflammatory lung disease would allow a more nuanced approach to the diagnosis of NTM-pulmonary disease and the decision about when and how to treat patients.

2. Are there more effective and more tolerable NTM treatment regimens?
Why is this important? We currently use combination antibiotic regimens that are often associated with significant toxicity, require prolonged administration, and particularly in the case of *M. abscessus* frequently fail. There remain considerable challenges in coordinating and funding multicentre studies of novel drugs or new combinations of existing drugs for NTM infections.

BTS Guidelines for the Management of Community Acquired Pneumonia in Adults: update 2009

No specific research recommendations made; the following areas were identified as particularly lacking in evidence:

- Data are lacking about the prevalence of CAP in COPD, alcoholic patients and in patients on long term oral steroids
- It is usual practice to arrange ''routine'' hospital clinic follow-up and repeat the chest radiograph at around 6 weeks after discharge. However, there is no evidence on which to base a recommendation regarding the value of this practice in patients who have otherwise recovered satisfactorily
- Re: IV antibiotics - There can be no rigid recommendation concerning the timing of transfer to oral therapy and further studies of this area are needed
- The precise duration of antibiotic therapy for the management of microbiologically documented and non-documented CAP is not supported by robust evidence
- There are no robust trials comparing the efficacy of different antibiotics for treating Legionnaires' disease,
- Further studies are indicated in the optimal treatment of high severity legionella pneumonia; there are no robust data on the use of combination antibiotics in this setting
- Lung abscess: there is a lack of evidence on which to base firm recommendations regarding the optimum duration of antimicrobial therapy.

BTS Guideline for the outpatient management of pulmonary embolism

- Re: outpatient management of low-risk PE: Research is required to enhance the evidence base regarding patient experience and cost effectiveness
- Prospective randomised comparison of (s)PESI against Hestia rules out criteria to determine proportion of patients who can be managed as OPs, including safety outcome. One study is currently running which will address this issue (NCT02811237).
- Further studies evaluating the role of technology for remote monitoring, such as virtual consultations and data gathering, are needed.
- Studies addressing the safety and efficacy of OP care pathways for pregnant and postpartum patients with suspected or confirmed PE are needed.
- Further studies are needed to validate risk stratification tools specific to patients with cancer.

BTS Guidelines for the investigation and management of pulmonary nodules

- Nodule malignancy risk prediction models should be validated in patients with known extra pulmonary cancer
- Further analysis of variation in volumetry measurements by different software packages should be undertaken and methods developed for standardisation
- Further research is needed into the most effective follow-up pathway in low to medium risk patients and for those with pGGNs
- Further research should be undertaken into the use of PET-CT in the evaluation of pGGNs using lower SUV cut-off values
- Research should be undertaken into the application of new and existing tumour markers in the evaluation of pulmonary nodules
- Prospective trials should compare complications and oncological outcomes from lobectomy versus anatomic segmentectomy in appropriately selected patients
- Prospective randomised trials of local treatments for pathologically proved or clinically diagnosed early-stage lung cancer and pulmonary oligometastases should be considered
- Prospective randomised trials of interventions for pathologically proved or clinically diagnosed early-stage lung cancer should include assessment of harms.

Asthma: diagnosis, monitoring and chronic asthma management; NICE guideline [NG80]

- What is the acceptability and diagnostic accuracy of objective tests that could be used to comprise a diagnostic pathway for asthma in children and young people aged 5 to 16 (for example, exercise challenge, direct bronchial challenge with histamine or methacholine, indirect bronchial challenge with mannitol and peripheral blood eosinophil count)?

- What is the clinical and cost effectiveness of using an indirect bronchial challenge test with mannitol to diagnose asthma in adults (aged 17 and over)?

- What is the clinical and cost effectiveness of using electronic alert systems designed to monitor and improve adherence with regular inhaled maintenance therapy in people with asthma?

- What is the current frequency and the current method being used to check the inhaler technique of people with asthma? What is the optimal frequency and the best method of checking inhaler technique to improve clinical outcomes for people with asthma?

- What is the long-term (more than 12 months) clinical and cost effectiveness of using tele-healthcare as a means to monitor asthma control in adults, young people and children? Methods of tele-healthcare can include telephone interview (with healthcare professional involvement) and internet or smartphone-based monitoring support (no healthcare professional involvement).

- For children and young people with asthma that is managed in primary care, is there an advantage to increasing the inhaled corticosteroid (ICS) dose when asthma control has deteriorated compared with using the usual dose in a self-management programme?

- In adults, young people and children with asthma who have not been treated previously, is it more clinically and cost effective to start treatment with a reliever alone (a short-acting $beta_2$ agonist [SABA]) or with a reliever (a SABA) and maintenance therapy (such as ICS)? Are there specific prognostic features that indicate that one of these treatment options may be more appropriate for some groups?

- Is maintenance therapy more effective with a paediatric low dose of ICS plus a leukotriene receptor antagonist (LTRA) or with a paediatric low dose of ICS plus a long-acting $beta_2$ agonist (LABA) in the treatment of asthma in children and young people (under 16) who have uncontrolled asthma on a paediatric low dose of ICS alone?

- What is the clinical and cost effectiveness of offering additional maintenance therapy to adults, young people and children with asthma that is uncontrolled on a moderate dose of ICS plus LABA with or without LTRA?

- In adults, young people and children with well-controlled asthma, what are the objective measurements and prognostic factors that indicate that a decrease in regular maintenance treatment is appropriate?

- What are the most clinically and cost-effective strategies to improve medicines adherence in adults, young people and children with asthma who are non-adherent to prescribed medicines?

Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s; NICE guideline [NG202]

- What is the clinical and cost effectiveness of auto- and fixed-level continuous positive airway pressure (CPAP) for managing mild obstructive sleep apnoea/hypopnoea syndrome (OSAHS)?

- What is the clinical and cost effectiveness of auto- and fixed-level continuous positive airway pressure (CPAP) for managing moderate and severe OSAHS?

- Which interventions, including behavioural interventions, are most clinically and cost effective to improve adherence to CPAP in people with OSAHS, obesity hypoventilation syndrome (OHS) and COPD–OSAHS (chronic obstructive pulmonary disease–OSAHS) overlap syndrome who have difficulty using CPAP?
- In mild symptomatic OSAHS, which clinical and physiological phenotypes predict treatment response to customised mandibular advancement splints?
- In moderate OSAHS, which clinical and physiological phenotypes predict treatment response to customised mandibular advancement splints?
- What is the clinical and cost effectiveness of mandibular advancement splints for managing severe OSAHS?
- What is the optimal treatment for people with COPD–OSAHS overlap syndrome: non-invasive ventilation or CPAP?
- What is the clinical and cost effectiveness of upper airway surgical interventions for people with OSAHS who are unable to tolerate or adhere to CPAP?
- What is the clinical and cost effectiveness of nocturnal oxygen compared with placebo in people with OSAHS who are unable to tolerate CPAP?

Chronic obstructive pulmonary disease in over 16s: diagnosis and management; NICE guideline [NG115]

- In people with COPD, does pulmonary rehabilitation during hospital admission for exacerbation and/or in the early recovery period (within 1 month of an exacerbation) improve quality of life and reduce hospitalisations and exacerbations compared with a later (defined as after 1 month) pulmonary rehabilitation programme, and in which groups is it most clinically and cost effective?
- How can the individual factors associated with COPD prognosis (collected from a range of sources including primary care, imaging and pulmonary rehabilitation results) be combined into a multidimensional analysis that provides accurate and useful information on prognosis?
- What is the clinical and cost effectiveness of inhaled therapies (bronchodilators and/or inhaled corticosteroids) in people with both stable COPD and asthma?
- What features predict inhaled corticosteroid responsiveness most accurately in people with COPD?
- Which subgroups of people with stable COPD who are at high risk of exacerbations are most likely to benefit from prophylactic antibiotics?
- What is the long-term clinical and cost effectiveness of prophylactic antibiotics for people with stable COPD who are at high risk of exacerbations?
- What is the comparative effectiveness of different antibiotics, doses and regimens of prophylactic antibiotics for people with stable COPD who are at high risk of exacerbations?
- What is the comparative effectiveness of seasonal versus continuous prophylactic antibiotics for people with stable COPD who are at high risk of exacerbations?
- What are the most clinical and cost-effective treatments for pulmonary hypertension in people with COPD?~
- In people with COPD, does mucolytic drug therapy prevent exacerbations in comparison with placebo and other therapies?

Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing; NICE guideline [NG114]

- Within COPD exacerbations subgroups there was no evidence as to which groups may benefit most from antibiotics
- Many health professionals may not be aware of the limited benefit of antibiotics and there is an education need

COVID-19 rapid guideline: managing the long-term effects of COVID-19; NICE guideline [NG188]

- What are the most clinically effective interventions (including social prescribing and structured community support) for managing post-COVID-19 syndrome?
- Does effectiveness vary for different population groups (for example, sex, age, socioeconomic group, black, Asian and minority ethnic group communities or people with a learning disability)?
- Do any symptoms of post-COVID-19 syndrome predict the need for specialist intervention?
- Are there clusters of symptoms that identify response to interventions in post-COVID-19 syndrome?
- What is the clinical effectiveness of different service models of multimodality/multidisciplinary post-COVID-19 syndrome rehabilitation in improving patient-reported outcomes (such as quality of life)?
- What is the clinical effectiveness of exercise interventions for people with post-COVID-19 syndrome? Does effectiveness vary for different population groups (for example, sex, age, socioeconomic group, black, Asian and minority ethnic group communities or people with a learning disability)?
- Does early exercise rehabilitation assist in improving symptoms of post-COVID-19 syndrome?
- What is the prevalence and incidence of post-COVID-19 syndrome in people who have received single, double or boosted doses of the approved vaccinations in the UK? Does this vary across different population groups (for example in black, Asian and minority ethnic group communities)?
- What is the clinical effectiveness of D-dimer and other blood tests and clinical features as prognostic markers of developing post-COVID-19 syndrome?
- Presentation of post-COVID-19 syndrome in children, young people, pregnant women and older people
- What symptoms do children, young people, pregnant women and older people with suspected post-COVID-19 syndrome present with?
- What is the natural history of post-COVID-19 syndrome?
- What pathophysiological mechanism(s) underlie the most common presentations of post-COVID-19 syndrome? For example, generalised fatigue, breathlessness and ‘brain fog’?
- Develop and validate new and existing screening tools (including physical, psychological and psychiatric aspects) for post-COVID-19 syndrome in a UK population.
- What tools are validated for screening for post-COVID-19 syndrome, which are the most accurate at identifying post-COVID-19 syndrome in a UK population and what is their effectiveness in guiding management?

COVID-19 rapid guideline: managing COVID-19; NICE guideline [NG191]

This NICE guideline contains research questions but also provides possible/example frameworks that could be borrowed to answer the research question i.e. has already written the target population, intervention and outcome measures

- What is the effectiveness and safety of standard-dose compared with intermediatedose pharmacological venous thromboembolism (VTE) prophylaxis for people with COVID-19, with or without additional risk factors for VTE?

- What is the effectiveness and safety of extended pharmacological venous thromboembolism (VTE) prophylaxis for people who have been discharged after treatment for COVID-19?

- What is the effectiveness and safety of a treatment dose with a low molecular weight heparin (LMWHs) compared with a standard prophylactic dose for venous thromboembolism (VTE) prophylaxis in young people under 18 years with COVID-19?

- Does early review and referral to specialist palliative care services improve outcomes for adults with COVID-19 thought to be approaching the end of their life?

- Is high-flow nasal oxygen effective in reducing breathlessness compared with standard care or conventional oxygen therapy for people in hospital with COVID-19 and respiratory failure when it is agreed that treatment will not be escalated beyond non-invasive respiratory support or palliative care is needed?

- Does a multidisciplinary team agreed approach to weaning from continuous positive airway pressure improve weaning times and result in stopping continuous positive airway pressure for people with COVID-19 and acute respiratory failure?

- What is the effectiveness, cost effectiveness and safety of using a combination of casirivimab and imdevimab at doses other than 8 g for treating COVID-19?

- What is the effectiveness, cost effectiveness and safety of the combination of casirivimab and imdevimab for treating COVID-19 in people with particular clinical characteristics (for example, people who are seropositive, of unknown serostatus, immunocompromised, or with specific comorbidities and within both the seropositive and seronegative groups, according to vaccination status or history of natural infection)?

- What is the clinical and cost effectiveness of budesonide for treating COVID-19 in the community in adults, young people and children?

Cystic fibrosis: diagnosis and management; NICE guideline [NG78]

1. Liver disease
   Should all children with meconium ileus receive ursodeoxycholic acid from diagnosis?
2. Airway clearance techniques
   How effective are daily airway clearance techniques in maintaining lung function in infants and children with cystic fibrosis?
3. Monitoring pulmonary disease
   Is lung clearance index a useful and cost-effective tool for the routine assessment and monitoring of changes in pulmonary status in people with cystic fibrosis?
4. Psychological assessment
   What is the most effective measure of psychological functioning to use as a test for thresholds of concern in people with cystic fibrosis?
5. Monitoring for cystic fibrosis related diabetes
   What is the most effective strategy to detect diabetes in people with cystic fibrosis?

6. Mucoactive agents
   What is the most clinically and cost-effective dose of rhDNase (dornase alfa; recombinant human deoxyribonuclease) for people with cystic fibrosis?

Lung cancer: diagnosis and management; NICE guideline [NG122]

- What is the effectiveness and cost effectiveness of immunotherapy in people with stage IIIA-N2 non-small-cell lung cancer following multimodality treatment including surgery?

- What is the effectiveness and cost effectiveness of stereotactic ablative radiotherapy (SABR) compared with surgery (for example, sublobar, wedge resection, lobectomy) for people with non-small-cell lung cancer (stage I and IIA) in whom surgery is suitable?

- What is the effectiveness and cost effectiveness of routinely performing contrast-enhanced brain CT at the time of initial diagnosis and/or staging CT?

- What is the effectiveness and cost effectiveness of prophylactic cranial irradiation compared with routine MRI follow-up in people with extensive-stage small-cell lung cancer without brain metastases?

Pneumonia (community-acquired): antimicrobial prescribing; NICE guideline [NG138]

No explicitly stated research recommendations

Lack of evidence highlighted in the following areas:

- For hospitalised individuals, optimum timing of switch from intravenous to oral antibiotics
- Does the addition of a macrolide to amoxicillin in the treatment of moderate- to high-severity CAP in adults alter clinical outcomes?
- Is doxycycline as effective as levofloxacin in treating moderate- to high-severity CAP? ["The committee discussed the evidence that doxycycline is as effective as levofloxacin for adults with moderate- to high-severity community-acquired pneumonia. However, the evidence for doxycycline comes from 1 small study with a 0% mortality rate, suggesting this is not a high-severity population. Therefore, the committee agreed that there is insufficient evidence to recommend doxycycline for this population."]
- Is a high does strategy more effective than low dose for treatment of moderate- to high-severity CAP?
- What is the optimum duration of antibiotic treatment for CAP? [Some inconsistencies in evidence in adults and children].
- Is there difference in efficacy between oral and intravenous route of administration of antibiotics in treating adults with CAP?

Pneumonia (hospital-acquired): antimicrobial prescribing; NICE guideline [NG139]

No explicitly stated research recommendations

Lack of RCT/systematic review evidence highlighted for following question: Does antibiotic dose/route/treatment duration for treatment of HAP affect clinical outcomes?

Idiopathic pulmonary fibrosis in adults: diagnosis and management; Clinical guideline [CG163]

Does pulmonary rehab improve outcomes for people with idiopathic pulmonary fibrosis?

Does ambulatory oxygen improve outcomes for people with idiopathic pulmonary fibrosis?

Is anti-reflux therapy an effective treatment for people with idiopathic pulmonary fibrosis?

ATS/ERS ILD guideline

Is there a role for genetic counselling in familial IPF?

What is the optimal approach to excluding connective tissue disease/chronic HP- what is the role of measuring specific anti-bodies?

Should we actively screen for co-morbidities in IPF?

How should the natural disease course and behaviour be integrated in to the diagnostic algorithm for ILD?

Tuberculosis; NICE guideline [NG33]

In people with suspected TB what is the relative clinical and cost effectiveness of universal and risk based rapid nucleic amplification tests?

For isoniazid resistant TB what is the most effective regime to decrease morbidity and mortality?

What is the impact of isolation on people being treated for TB?

For people with active, drug susceptible TB who experience treatment interruptions because of adverse events, particularly hepatotoxicity, what approach to re-establishing treatment is most effective in reducing mortality and morbidity?