Table 21: Review protocol: When to suspect

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	When to suspect
2.	Review question	In whom should obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome be suspected (for example, based on symptoms or coexisting conditions)?
3.	Objective	To identify people who should be formally assessed for the presence or absence of OSAHS/OHS/ COPD-OSAHS overlap syndrome by finding markers (co-existing conditions or symptoms/signs) that are either strongly associated with OSAHS/OHS/ COPD-OSAHS overlap syndrome or that predict the presence of OSAHS/OHS/ COPD-OSAHS overlap syndrome.
4.	Searches	The following databases (from inception) will be searched: • Embase • MEDLINE Searches will be restricted by: • English language studies The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Obstructive sleep apnoea/hypopnoea syndrome is the most common form of sleep disordered breathing. The guideline will also cover obesity hypoventilation syndrome and COPD-OSAHS overlap syndrome (the coexistence of obstructive sleep apnoea/hypopnoea syndrome and chronic obstructive pulmonary disease).
6.	Population	Inclusion: • People without a diagnosis of OSAHS/OHS/ COPD-OSAHS overlap syndrome Stratification by setting – primary care vs specialist care

7.	Intervention/Exposure /Test	Predictors:
		• Symptoms & signs
		  ○ Snoring
		  ○ Witnessed apnoea
		  ○ Unrefreshing sleep
		  ○ Somnolence during waking hours

		○ Nocturia ○ Tiredness ○ Insomnia ○ Headaches ○ Sleep fragmentation ○ Ankle swelling ○ Unexplained elevated Hb ○ Cognitive dysfunction/memory impairment • Co-existing conditions ○ Treatment resistant hypertension ○ Nocturnal non-dipping hypertension ○ Treatment resistant arrhythmias ○ Atrial fibrillation ○ T2DM ○ Diabetic macular oedema ○ Aortic aneurysms ○ Chronic heart failure ○ Cardiovascular events ○ Stroke ○ Down's syndrome ○ Acromegaly ○ BMI over 30 kg/m^2 Any of the above, alone or in combination
8.	Comparator/Reference standard/Confounding factors	Any of the above vs an absence of risk factors
9.	Types of study to be included	• Prospective cohort studies • Retrospective cohort studies will be included only if no sufficient prospective cohort studies are identified • Including studies with cross-sectional assessment of presence or absence of the relevant diagnosis (i.e. all participants must be tested for presence or absence of OSAHS/OHS/OS) Studies will only be included if all the key confounders have been accounted for in a multivariate analysis
10.	Other exclusion criteria	• Non-English language studies. • Conference abstracts • Studies not adjusted for pre-specified key confounders.
11.	Context	-
12.	Primary outcomes (critical outcomes)	• Association data ○ Adjusted RR or OR (adjusted for key confounders of age, sex, BMI, co-morbidities) • Accuracy data ○ SN, SP, PPV, NPV Stratified by prediction of OSAHS or OHS or COPD-OSAHS overlap syndrome
13.	Secondary outcomes (important outcomes)	Not applicable
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the

		searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).	
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. The methodological quality of each study will be assessed using the QUIPS checklist. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	• Meta-analyses will be performed if possible, using Cochrane Review Manager (RevMan5) depending on the appropriateness of data. • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/	
17.	Analysis of sub-groups	Not applicable	
18.	Type and method of review	☐	Intervention
		☒	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☒	Diagnostic association/prediction review

19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	NA
22.	Anticipated completion date	NA
23.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail SleepApnoHypo@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
24.	Review team members	From the National Guideline Centre: Carlos Sharpin, Guideline lead Sharangini Rajesh, Senior systematic reviewer Audrius Stonkus, Systematic reviewer Emtiyaz Chowdhury (until January 2020), Health economist David Wonderling, Head of health economics Agnes Cuyas, Information specialist (till December 2019) Jill Cobb, , Information specialist
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website:

		https://www.nice.org.uk/guidance/indevelopment/gid-ng10098
28.	Other registration details	NA – not registered
29.	Reference/URL for published protocol	NA – not registered
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
31.	Keywords	-
32.	Details of existing review of same topic by same authors	NA
33.	Additional information	-
34.	Details of final publication	www.nice.org.uk