National Institute for Health and Care Excellence

Draft

Obstructive sleep apnoea/ hypopnoea syndrome and obesity hypoventilation syndrome in over 16s

Evidence review B: Assessment tools for people with suspected OSAHS, OHS or COPD-OSAHS overlap syndrome

NICE guideline

Diagnostic evidence review

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Contents

1 Assessment scales for suspected obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome

1.1 Review question: What assessment scales should be used if obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome is suspected (for example, the Epworth sleepiness scale, STOP-Bang sleep apnoea questionnaire or Berlin questionnaire)?

1.2 Introduction

Assessment scales are used to help with the identification of obstructive sleep apnoea/hypopnoea syndrome (OSAHS), obesity hypoventilation syndrome (OHS) and COPD-OSAHS overlap syndrome. These enable any healthcare professional assess patients in standardised way and help ensure only those most likely to have one of these conditions are referred onward to a sleep clinic for further investigation and diagnosis. Current assessment tools are usually the Epworth sleepiness score, the Stop Bang Questionnaire and the Berlin Questionnaire. There is no national guidance on which is the preferred option at the present time. This review aims to identify which, if any, of these should be used in practice.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People in whom OSAHS/OHS/ COPD-OSAHS overlap syndrome is suspected based on symptoms or co-existing conditions
Target condition	OSAHS/OHS/ COPD-OSAHS overlap syndrome
Index tests	Assessment scales including any one or more of the below: • Epworth sleepiness scale • STOP-BANG questionnaire • Berlin questionnaire
Reference standards	**Accuracy** For diagnosis of OSAHS reference standard will be AHI/RDI/ODI >5 by hospital polysomnography For diagnosis of OHS reference standard will be hypercapnia on arterial/capillary blood gases

	Test and treat Any strategy compared with any other
Statistical measures and Outcomes	**Accuracy outcomes**: • sensitivity • specificity • positive predictive value (PPV) • negative predictive value (NPV) **Test and treat outcomes:** **Critical** • mortality (dichotomous) • generic or disease specific quality of life (continuous) **Important** • sleepiness scores (continuous, e.g. Epworth) • apnoea-hypopnoea index or respiratory disturbance index (continuous) • oxygen desaturation index (continuous) • healthcare resource use (rates/dichotomous) • impact on co-existing conditions: o HbA1c for diabetes (continuous) o cardiovascular events for cardiovascular disease (dichotomous) o systolic blood pressure for hypertension (continuous)
Study design	Single gate cross-sectional study designs will be included in the accuracy review. Two gate study designs will be excluded from the accuracy review RCTs will be prioritised for test and treat comparisons, if insufficient RCTs are found, non-randomised studies will be considered if they adjust for key confounders (age, BMI, co-existing conditions)

1.4 Clinical evidence

1.4.1 Included studies

OSAHS

This review aimed to assess which assessment scales are most useful in identifying possible cases of obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome. Ten studies were included in the review.[18, 68, 93, 96, 108, 126, 164, 416, 480, 553] Evidence from these studies is summarised in the clinical evidence summary below (Table 2).

Three studies assessed the accuracy of the Berlin questionnaire, 4 studies assessed Epworth Sleepiness Scale (ESS), 7 studies assessed STOP BANG questionnaire, and one study assessed a combination of STOP BANG and Epworth Sleepiness Scale (ESS). Some studies assessed more than one questionnaire.

Studies using modified assessment scales and/or using assessment scales which were not in English, were not included in this review.

No test and treat studies were identified.

OHS

No studies were identified for people with suspected OHS.

COPD-OSAHS overlap syndrome

Two diagnostic accuracy studies in people with suspected COPD-OSAHS overlap syndrome were included in this review.[579, 582] One study assessed 3 questionnaires (Epworth Sleepiness scale, Berlin questionnaire and STOP-BANG questionnaire) and another study assessed 2 questionnaires (Berlin questionnaire and STOP-BANG questionnaire). No test and treat studies (RCTs) were identified.

Evidence from these studies is summarised in the clinical evidence summary below (Table 2).

See also the study selection flow chart in appendix C, sensitivity and specificity Forest plots in appendix E, and study evidence tables in appendix D.

1.4.2 Excluded studies

See the excluded studies list in appendix H.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Target condition	Assessment scale	Reference standard	Comments
Ahmadi 2008[18] Retrospective chart review Canada	N = 130 analysed People referred to sleep and alertness clinic Age: mean 42.2 (male), 45.1 (female) Male/female ratio: 70:60 Ethnicity not reported	Sleep apnoea/ hypopnoea syndrome	Berlin questionnaire	Laboratory PSG with a pre-specified diagnostic RDI of >5	Setting: Respiratory ward or sleep laboratory
Boynton 2013[68] Cross-sectional USA	N = 219 recruited and analysed People referred for diagnostic PSG with suspicion of OSA Age: mean 46.3 (SD 13.9) Male/female ratio: 91/74 of those identified as being high risk for OSA Ethnicity not reported	OSA	Self-reported STOP-BANG questionnaire, high risk if score of 3 or more	Single nocturnal lab based PSG, with a pre-specified diagnostic AHI of >5	Setting: Respiratory ward or sleep laboratory

Study	Population	Target condition	Assessment scale	Reference standard	Comments
Cowan 2014[93] Cross-sectional UK	N = 129 analysed People referred to sleep centre for assessment of possible OSA Age: mean 49 (11) Male/female ratio: 82/47 Ethnicity: not reported	Obstructive sleep apnoea	ESS (≥11/24), Berlin, STOP-BANG (≥3/8)	Home limited polygraphy with AHI ≥ 5	Setting: sleep centre
de Carvalho 2020[96]	N = 66 recruited and N = 60 analysed Adults with down syndrome attending Down Syndrome Reference Center of Hospital Regional da Asa Norte (HRAN) linked to Faculdade de Medicina da Escola Superior de Ciências da Sau´de (ESCS), Brası´lia, Federal District, Brazil. Age: mean 27.7 (SD 9.1) Male/female ratio: 33/27	Obstructive sleep apnoea	STOP-Bang questionnaire	Laboratory polysomnography with a prespecified diagnostic AHI ≥ 5	Setting: laboratory

Study	Population	Target condition	Assessment scale	Reference standard	Comments
	Ethnicity: not reported				
Duarte 2020[108]	N = 8138 recruited and N = 7377 analysed, patients grouped into two large and independent cohorts: derivation (N=3771) and validation (N=3606) People referred to specialist centre for suspected obstructive sleep apnoea Age: derivation cohort - mean 45.9 (SD 14.6) validation cohort – mean 45.7(14.6) Male/female ratio: Derivation cohort – 1983/1788 Validation cohort – 1961/1645 Ethnicity: not reported	Obstructive sleep apnoea	STOP-Bang questionnaire	Laboratory polysomnography with a prespecified diagnostic AHI ≥ 5	Setting: laboratory

Study	Population	Target condition	Assessment scale	Reference standard	Comments
Felfeli 2020[126]	N=27 patients analysed Consecutive adult patients with new diagnosis of retinal vein occlusion confirmed with intravenous fluorescein angiography were enrolled and screened for obstructive sleep apnoea. Age: mean 69.6 (SD 11.5) Male/female ratio: 11/16 Ethnicity: not reported	Obstructive sleep apnoea	Berlin and Stop-Bang questionnaires	Laboratory polysomnography with a prespecified diagnostic AHI ≥ 15	Setting: laboratory
Hesselbacher 2012[164] Cross-sectional USA	N = 2112 studied, 1900 analysed People referred to specialist centre for suspected obstructive sleep apnoea Age: mean 54 (SD 15) Male/female ratio: 109:81 Ethnicity	Obstructive sleep apnoea	Epworth Sleepiness Scale	PSG, RDI >15	Setting: sleep centre
Pereira 2013[416] Cross-sectional	N=128 recruited and analysed People undergoing screening for obstructive sleep apnoea	Obstructive sleep apnoea	Berlin questionnaire; ; Stop Bang questionnaire;	Laboratory polysomnography with no pre-specified diagnostic AHI, RDI or ODI	Setting: Home then laboratory

Study	Population	Target condition	Assessment scale	Reference standard	Comments
Canada	Age: mean 50 (SD 12.3) Male/Female ratio: 84/44 Ethnicity: not reported		portable sleep monitor, with RDI and AHI		
Sangkum 2017[480] Cross-sectional USA	N=208 recruited and analysed People with suspected obstructive sleep apnoea Age: mean 52.9 (SD 0.9) Male/Female ratio: 75/133 Ethnicity: African American (69%); white (28%); Hispanic (0.5%)	Obstructive sleep apnoea	STOP-BANG questionnaire	Laboratory polysomnography with a pre-specified OSA diagnostic AHI >5 events/hour	Setting: initial clinical evaluation site and laboratory
Vana 2013[553] Cross-sectional USA	N=60 recruited, 47 analysed People undergoing screening for obstructive sleep apnoea and sleep-disordered breathing Age: mean 46.4 (SD 13.2) Male/Female ratio: 16/31	Obstructive sleep apnoea and sleep-disordered breathing	Epworth Sleepiness Scale questionnaire; STOP-Bang questionnaire	Polysomnography with a pre-specified diagnostic AHI ≥5 for OSA and RDI ≥5 for SDB	Setting: not reported

Study	Population	Target condition	Assessment scale	Reference standard	Comments
	Ethnicity: Caucasian (76.6%); African American (10.6%); Native American/Asian/multiracial/'Mexican' (12.8%). 68.1% identified as Hispanic or Latino				
Wu 2020[579]	N = 116 recruited and analysed COPD subjects with suspected sleep apnoea Age: mean 63 (Range 57, 68) Male/female ratio: 101/15 Ethnicity: not reported	Overlap syndrome	Berlin and STOP-BANG questionnaires	Laboratory polysomnography with a prespecified diagnostic AHI ≥ 5	Setting: laboratory
Xiong 2019[582]	N = 476 recruited and N = 431 analysed Patients with COPD and suspected OSA	Overlap syndrome	ESS, Berlin and STOP-BANG questionnaires	Laboratory polysomnography with a prespecified diagnostic AHI ≥ 5	Setting: laboratory

Study	Population	Target condition	Assessment scale	Reference standard	Comments
	Age: mean 67.4 (SD 8.9) Male/female ratio: 388/43 Ethnicity: not reported				

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary for assessment scales in people with suspected OSAHS

Index Test (Threshold)	Number of studies	N	Sensitivity % (95% CI)	Quality	Specificity % (95% CI)	Quality
Berlin questionnaire	4	410	Pooled[5]: 77.52% (39.99 to 94.51)	VERY LOW[1,2,4] due to risk of bias, very serious inconsistency and very serious imprecision	Pooled[5]: 31.34% (6.1 to75.26	VERY LOW[1,2,4] due to risk of bias, serious inconsistency and serious imprecision
Epworth Sleepiness Scale	3	2067	Pooled[5]: 52.42% (18.11 to 83.16)	VERY LOW[1,2,4] due to risk of bias, serious inconsistency and serious imprecision	Pooled[5]: 50.75% (21.08 to 79.37%)	VERY LOW[1,2,4] due to risk of bias, serious inconsistency and serious imprecision
STOP BANG questionnaire	7	8129	Pooled[5]: 90.31% (83.96 to 94.67)	VERY LOW[1,2,4] due to risk of bias, serious inconsistency and serious imprecision	Pooled[5]: 40.81% (27.19 to 55.01	LOW[1,2] due to risk of bias and serious inconsistency
STOP BANG or Epworth questionnaires (positive on either)	1	47	97% (84 to 100%)	LOW[1,4] due to risk of bias, and serious imprecision	20% (4 to 48%)	MODERATE[1] due to risk of bias

(1) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(2) Inconsistency was assessed by inspection of the sensitivity and specificity plots. The evidence was downgraded by 1 increment if the individual studies varied across 2 areas [(for example, 50–90% and 90–100%)] and by 2 increments if the individual studies varied across 3 areas [(for example, 0–50%, 50–90% and 90–100%)].
(3) Subgroup analysis was conducted for BMI and coexisting conditions. Subgroup analysis by BMI did not explain heterogeneity. Subgroup analysis by coexisting conditions could not be conducted because there was no sufficient information to conduct a subgroup analysis.Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect, and downgraded by 2 increments if the majority of studies are very seriously indirect
(4) Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. Two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%).The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold, and downgraded by 2 increments when the range covered two thresholds
(5) Pooled sensitivity/specificity from diagnostic meta-analysis

Table 4: Clinical evidence summary for assessment scales in people with suspected OSAHS (patients with Down syndrome)

Index Test (Threshold)	Number of studies	N	Sensitivity % (95% CI)	Quality	Specificity % (95% CI)	Quality
STOP BANG questionnaire	1	60	100 % (93 to100%)	VERY LOW[1,3] due to very serious risk of bias, and indirectness	45% (17 to 77%)	VERY LOW[1,3,4] due to very serious risk of bias, indirectness and serious imprecision

(1) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(2) Inconsistency was assessed by inspection of the sensitivity and specificity plots. The evidence was downgraded by 1 increment if the individual studies varied across 2 areas [(for example, 50–90% and 90–100%)] and by 2 increments if the individual studies varied across 3 areas [(for example, 0–50%, 50–90% and 90–100%)].
(3) Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect, and downgraded by 2 increments if the majority of studies are very seriously indirect
(4) Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. Two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%).The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold, and downgraded by 2 increments when the range covered two thresholds

Table 5: Clinical evidence summary for assessment scales in people with suspected COPD-OSAHS overlap syndrome

Index Test (Threshold)	Number of studies	N	Sensitivity % (95% CI)	Quality	Specificity % (95% CI)	Quality
Berlin questionnaire	2	547	Pooled[5]: 69.48% (11.28 to 97.87)	VERY LOW[1,4] due to risk of bias and very serious imprecision	Pooled[5]: 68.41% (2.7 to 99.39%)	VERY LOW[1,2,4] due to risk of bias, inconsistency and very serious imprecision
Epworth Sleepiness Scale	1	431	72% (67 to 77%)	MODERATE[1] due to risk of bias	47% (37 to 57%)	MODERATE[1] due to risk of bias
STOP BANG questionnaire	2	547	Pooled[5]: 89.78% (38.95 to 99.26%)	VERY LOW[1,2,4]	Pooled[5]: 49.25% (6.6 to 92.34%)	VERY LOW[1,2,4]

Index Test (Threshold)	Number of studies	N	Sensitivity % (95% CI)	Quality	Specificity % (95% CI)	Quality
				due to risk of bias, inconsistency and very serious imprecision		due to risk of bias, inconsistency and very serious imprecision

(1) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.

(2) Inconsistency was assessed by inspection of the sensitivity and specificity plots. The evidence was downgraded by 1 increment if the individual studies varied across 2 areas [(for example, 50–90% and 90–100%)] and by 2 increments if the individual studies varied across 3 areas [(for example, 0–50%, 50–90% and 90–100%)]. Subgroup analysis by BMI and coexisting conditions could not be conducted because there was no sufficient information to conduct subgroup analysis.

(3) Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect, and downgraded by 2 increments if the majority of studies are very seriously indirect

(4) Imprecision was assessed based on inspection of the confidence region in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. Two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%).The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold, and downgraded by 2 increments when the range covered two thresholds

(5) Pooled sensitivity/specificity from diagnostic meta-analysis

1.5 Economic evidence

1.5.1 Included studies

No health economic studies were included.

1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix F.

1.5.3 Health economic modelling

Original modelling was not conducted for this question.

1.5.4 Health economic evidence statements

No evidence was found

1.6 The committee's discussion of the evidence

1.6.1 Interpreting the evidence

1.6.1.1 The diagnostic measures that matter most

Questionnaires

The committee reviewed the evidence on sensitivity and specificity of the various questionnaires and tests; sensitivity as a screening measure was considered most important.

1.6.1.2 The quality of the evidence

OSAHS

Questionnaires

There was evidence from ten diagnostic accuracy studies in people with suspected OSAHS; four studies assessed the accuracy of the Berlin questionnaire, three studies assessed the accuracy of the Epworth Sleepiness Scale, seven studies assessed the accuracy of the STOP BANG questionnaire, one study assessed the accuracy of a combination of STOP BANG and Epworth. Some studies assessed more than one questionnaire. Studies varied in size however most of the studies consisted of medium to large size populations ranging from 60 to 354 participants and two studies included large populations of 2112 and 7377 participants respectively.

There was also one diagnostic accuracy study in people with suspected OSAHS and with Down syndrome, with the diagnostic accuracy of the Stop Bang questionnaire assessed in 60 patients. This study was analysed separately because patients with Down's syndrome tend to have higher incidence of OSAHS compared to the general population.

No test and treat studies (RCTs) were identified.

The quality of the evidence varied from moderate to very low quality; the majority of evidence was downgraded due to risk of bias, imprecision and inconsistency. Risk of bias was most commonly due to selection bias. The committee also acknowledged that some uncertainty existed across the effect sizes seen within the evidence, with some confidence intervals crossing the MID thresholds or line of no effect. Inconsistency was found in majority of comparisons (Berlin questionnaire, Epworth sleepiness scale and STOP BANG questionnaires). For inconsistency the evidence was downgraded by 1 increment if the individual studies varied across 2 areas [(for example, 50–90% and 90–100%)] and by 2 increments if the individual studies varied across 3 areas [(for example, 0–50%, 50–90% and 90–100%)] . Subgroup analysis was conducted for BMI and coexisting conditions. Subgroup analysis by BMI did not explain heterogeneity. Subgroup analysis by coexisting conditions could not be conducted because there was no sufficient information to conduct a subgroup analysis

OHS

No evidence was identified for people with suspected OHS.

COPD-OSAHS overlap syndrome

Questionnaires

There was evidence from two diagnostic accuracy studies in people with suspected COPD-OSAHS overlap syndrome: one study assessed 3 questionnaires (Epworth Sleepiness scale, Berlin questionnaire and STOP-BANG questionnaire) and another study assessed 2 questionnaires (Berlin questionnaire and STOP-BANG questionnaire). The studies included 116 and 431 participants respectively.

No test and treat studies (RCTs) were identified.

The quality of the evidence varied from moderate to very low quality; the majority of evidence was downgraded due to risk of bias, imprecision and inconsistency. Risk of bias was most commonly due to selection bias. The committee also acknowledged that some uncertainty existed across the effect sizes seen within the evidence, with some confidence intervals crossing the MID thresholds or line of no effect. Inconsistency was commonly due to overlap between studies and were downgraded by one increment if the individual study values varied across 2 areas: where values of individual studies are both above and below 50%, or both above and below 90% and downgraded by 2 increments if the individual study values varied across 3 areas, where values of individual studies are above and below 50%, and also above and below 90%. Subgroup analysis by BMI and coexisting conditions could not be conducted because there was no sufficient information to conduct subgroup analysis.

1.6.1.3 Benefits and harms

Questionnaires

OSAHS

The Epworth sleepiness scale is intended to assess for sleepiness rather than to diagnose OSAHS, and the limited evidence reflected this, showing that it performed poorly both for sensitivity and specificity in diagnosing OSAHS. The committee noted that some people with OSAHS do not have excessive sleepiness and that not all healthcare professionals are aware of this. However, the committee agreed that it has a useful role in assessment and in monitoring, and noted that it is part of the information required by the DVLA from medical professionals in assessing licencing in drivers with moderate and severe OSAHS once their condition is controlled (see also evidence report L on monitoring). They therefore agreed that it should be used, but not as the sole means of assessing the presence of OSAHS or as the sole basis for referral.

The committee wanted to emphasise that the Epworth sleepiness scale should not be used as a gateway for further diagnostic assessment as it has low sensitivity and specificity. However, assessment of sleepiness is vital for determining treatment and assessing response to treatment and the Epworth sleepiness scale is the standard tool for doing so.

Limited evidence showed that the STOP-Bang questionnaire has high sensitivity and low specificity for diagnosing OSAHS in both general population and in patients with Down's syndrome. Sensitivity is a priority for questionnaires because they are used only for initial assessment., The committee had some concerns about the accuracy of STOP-Bang questionnaire in people with less common presentations and in women. The committee from their experience noted that females snore less than males and their symptoms may also be different for example more sleep disturbance and less sleepiness so conventional tools which rely on former may not be as accurate. The committee agreed that it could have a role in assessment, alongside the Epworth sleepiness scale, for preliminary understanding of the persons' symptoms and concerns. Epworth sleepiness scale is used to assess only sleepiness whereas STOP-Bang questionnaire is used to assess risk of having OSAHS and includes parameters such as: snoring, tiredness, history of high blood pressure, BMI, age, neck size and gender. With this in mind the committee recommended using the Epworth questionnaire and to consider using the STOP-Bang questionnaire.

The committee did not want to make a specific recommendation for people with Down's syndrome, as the evidence was based on one small very low-quality study.

The committee agreed that the recommended questionnaires are widely used in current practice, so the recommendations are not expected to involve a change in practice.

OHS

The committee noted the lack of evidence for assessment scales in OHS and decided to make consensus recommendations based on experience and current practice.

The committee agreed that the Epworth sleepiness scale to assess sleepiness has a useful role in monitoring and assessment of sleepiness in people with OHS. However, it was noted that not all people with OHS have excessive sleepiness and that healthcare professionals may not always be aware of this. Therefore, the committee recommended to use Epworth sleepiness scale for preliminary assessment of sleepiness and not to use it as the sole basis to determine if referral is needed because not all people with OHS have excessive sleepiness.

The committee agreed that the Epworth sleepiness scale is widely used in current practice, so the recommendations are not expected to involve a change in practice.

As the committee made a strong recommendation for Epworth sleepiness scale, they did not want to make any research recommendation for this questionnaire.

The evidence for STOP-Bang questionnaire was limited to OSAHS only and there was no validation for its use in OHS. The committee agreed that the STOP-Bang questionnaire is not used in practice for OHS and therefore the committee did not make a recommendation or a research recommendation for this.

COPD-OSAHS overlap syndrome

Evidence from one study showed that Epworth sleepiness scale had moderate sensitivity and low specificity for diagnosing COPD-OSAHS overlap syndrome. Due to limited evidence, the committee also used their experience and knowledge of current practice to make the recommendations. The committee agreed that the Epworth sleepiness scale has a useful role in monitoring and preliminary assessment of sleepiness in COPD-OSAHS overlap syndrome. However, it was noted that not all people with COPD-OSAHS overlap syndrome have excessive sleepiness and that healthcare professionals may not always be aware of this. However, the committee agreed that the it has a useful role in assessment and in monitoring, and noted that it is part of the DVLA requirements for drivers with suspected OSAHS (which will include those with COPD-OSAHS overlap syndrome) to be assessed with the Epworth sleepiness scale. With this in mind the committee recommended to use Epworth sleepiness scale for preliminary assessment of sleepiness and not to use it as the sole basis determine if referral to a sleep service is needed as not all people with COPD-OSAHS syndrome have excessive sleepiness.

Limited evidence showed that STOP-Bang questionnaire had high sensitivity and low specificity for diagnosing COPD-OSAHS overlap syndrome. Sensitivity is a priority for questionnaires used for initial assessment, however the committee had some concerns about its accuracy in people with less common presentations and in women. The committee from their experience noted that females snore less than males and their symptoms may also be different for example more sleep disturbance and less sleepiness, so conventional tools which rely on former may not be as accurate. The committee agreed that it could have a role in assessment, alongside the Epworth sleepiness scale, at referral for preliminary understanding of the persons' symptoms and concerns. Epworth questionnaire is used to assess only sleepiness whereas STOP-Bang questionnaire is used to assess risk of having OSAHS and includes parameters such as: snoring, tiredness, history of high blood pressure, BMI, age, neck size and gender. With this in mind the committee recommended using the Epworth questionnaire and to consider using the STOP-Bang questionnaire.

The committee from their experience discussed that spirometry is routinely measured in clinical practice to assess the severity of COPD and aids the understanding of the relative contribution of COPD and OSAHS to symptom load and pathophysiology. With this in mind the committee recommended offering spirometry to assess the severity of COPD in people with suspected COPD–OSAHS overlap syndrome and cross-referred to the recommendations on spirometry in the NICE guideline on Chronic obstructive pulmonary disease in over 16s: diagnosis and management.

The committee agreed that the Epworth sleepiness scale and STOP-Bang questionnaire are widely used in current practice, so the recommendations are not expected to involve a change in practice. Spirometry is routinely used in the assessment of COPD patients, so the recommendations are not expected to involve a change in practice.

As the committee made strong recommendations for Epworth sleepiness scale and STOP-Bang questionnaire, they did not want to make any research recommendations for these questionnaires.

1.6.2 Cost effectiveness and resource use

There were no economic evaluations identified for this review question.

The STOP-Bang score and Epworth Sleepiness Scale (ESS) are commonly used in the assessment of OSAHS. The committee did not feel that completing both questionnaires would result in increased resource use (staff time), as both are short in length and, in their absence, similar questions would be asked by the clinician, which would take the same length of time or longer.

As the recommended questionnaires are widely used in current practice, the committee was of the view that their recommendation would not result in increased expenditure for the NHS.

Finally, the committee made weak consensus recommendations for the OHS/COPD-OSAHS overlap syndrome population based on their clinical expertise and current practice as there was no clinical or economic evidence available to steer recommendations.

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Appendices

Appendix A: Review protocols

Table 6: Review protocol diagnosis of obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome and COPD-OSAHS overlap syndrome

Field	Content
PROSPERO registration number	Not registered
Review title	Assessment scales
Review question	What assessment scales should be used if obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome is suspected (for example, the Epworth sleepiness scale, STOP-Bang sleep apnoea questionnaire or Berlin questionnaire)?
Objective	To determine which assessment scales are most useful in identifying possible cases of obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome.
Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos 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.
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).
Population	Inclusion: People in whom OSAHS/OHS/COPD-OSAHS overlap syndrome is suspected based on symptoms or co-existing conditions Population will be stratified by: Suspicion of OSAHS vs OHS vs COPD-OSAHS overlap syndrome
Intervention/Exposure/Test	• Epworth sleepiness scale • STOP-BANG questionnaire • Berlin questionnaire

	For test and treat studies, negative test results must receive no OSAHS/OHS/overlap syndrome treatment and positive test results should receive some form of OSAHS/OHS/COPD-OSAHS overlap syndrome (including CPAP, surgery, mandibular devices – directness to be assessed against results of intervention reviews elsewhere in the guideline).
Comparator/Reference standard/Confounding factors	**Accuracy** For diagnosis of OSAHS reference standard will be AHI/RDI/ODI >5 by hospital polysomnography For diagnosis of OHS reference standard will be hypercapnia on arterial/capillary blood gases **Test and treat** Any testing strategy compared with any other including the reference standards listed above
Types of study to be included	Single gate cross-sectional study designs will be included in the accuracy review. Two gate study designs will be excluded from the accuracy review RCTs will be prioritised for test and treat comparisons, if insufficient RCTs are found, non-randomised studies will be considered if they adjust for key confounders (age, BMI, co-existing conditions).
Other exclusion criteria	None
Context	NA
Primary outcomes (critical outcomes)	**Accuracy outcomes**: • Sensitivity • Specificity • PPV • NPV **Test and treat outcomes**: • Mortality (dichotomous) • Generic or disease specific quality of life (continuous)

Secondary outcomes (important outcomes)	**Test and treat outcomes**:
	• Sleepiness scores (continuous, e.g. Epworth)
	• Apnoea-Hypopnoea index or respiratory disturbance index (continuous)
	• Oxygen desaturation index (continuous)
	• Healthcare resource use (rates/dichotomous)
	• Impact on co-existing conditions:
	  o HbA1c for diabetes (continuous)
	  o Cardiovascular events for cardiovascular disease (dichotomous)
	  o Systolic blood pressure for hypertension (continuous)

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).	
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Diagnostic test accuracy studies: QUADAS-2 • Standard RCT checklists will be used to critically appraise individual studies for the test and treat evidence. 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.	
Strategy for data synthesis	RevMan will be used for production of paired forest plots and pairwise meta-analysis of test and treat outcomes. WinBUGS will be used for meta-analysis of diagnostic accuracy studies. GRADEpro will be used to assess the quality of evidence for each test and treat outcome. **For test and treat studies** Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects.	
Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: • BMI – obese vs non-obese • Co-existing conditions vs no co-existing conditions	
Type and method of review	☐	Intervention
	☒	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)

Language	English
Country	England
Anticipated or actual start date	NA
Anticipated completion date	NA
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
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
Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
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.
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
Other registration details	NA – not registered
Reference/URL for published protocol	NA – not registered

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.
Keywords	-
Details of existing review of same topic by same authors	NA
Additional information	-
Details of final publication	www.nice.org.uk

Table 7: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[353] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded, then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.

- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'.
- Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

Sleep Apnoea search strategy 3_diagnostic tests/assessment

This literature search strategy was used for the following reviews;

- What assessment scales should be used if obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome or COPD-OSAHS overlap syndrome is suspected (for example, the Epworth sleepiness scale, STOP-Bang sleep apnoea questionnaire or Berlin questionnaire)?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[353]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 7 of 12 CENTRAL to 2020 Issue 7 of 12	None
Epistemonikos (Epistemonikos Foundation)	Inception – 29 November 2018	None

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6

8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
29.	27 not 28
30.	(Epworth or ESS or ESS-CHAD).ti,ab.
31.	(STOP-bang or stopbang or "snoring tired observed pressure").ti,ab.
32.	((sleep* or Berlin or STOP*) adj3 (questionnair* or questionair*)).ti,ab.
33.	((score* or scoring or stratif* or assess*) adj3 (system* or schem*)).ti,ab.
34.	exp Oximetry/
35.	(oxymet* or oximet*).ti,ab.
36.	Capnography/
37.	capnogra*.ti,ab.
38.	(oxi-capnogra* or oxicapnogra* or oxy-capnogra* or oxycapnogra*).ti,ab.
39.	POLYSOMNOGRAPHY/
40.	(polysomnogra* or PSG).ti,ab.
41.	(polygraph* or HRP).ti,ab.
42.	ACTIGRAPHY/
43.	actigraph.ti,ab.
44.	(venous adj3 bicarbonat*).ti,ab.
45.	or/30-44
46.	29 and 45
47.	randomized controlled trial.pt.
48.	controlled clinical trial.pt.
49.	randomi#ed.ti,ab.
50.	placebo.ab.
51.	randomly.ti,ab.

52.	Clinical Trials as topic.sh.
53.	trial.ti.
54.	or/47-53
55.	Meta-Analysis/
56.	exp Meta-Analysis as Topic/
57.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
58.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
59.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
61.	(search* adj4 literature).ab.
62.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
63.	cochrane.jw.
64.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
65.	or/55-64
66.	exp "sensitivity and specificity"/
67.	(sensitivity or specificity).ti,ab.
68.	((pre test or pretest or post test) adj probability).ti,ab.
69.	(predictive value* or PPV or NPV).ti,ab.
70.	likelihood ratio*.ti,ab.
71.	likelihood function/
72.	((area under adj4 curve) or AUC).ti,ab.
73.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
74.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
75.	gold standard.ab.
76.	or/66-75
77.	Epidemiologic studies/
78.	Observational study/
79.	exp Cohort studies/
80.	(cohort adj (study or studies or analys* or data)).ti,ab.
81.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
82.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
83.	Controlled Before-After Studies/
84.	Historically Controlled Study/
85.	Interrupted Time Series Analysis/
86.	(before adj2 after adj2 (study or studies or data)).ti,ab.
87.	exp case control studies/
88.	case control*.ti,ab.
89.	Cross-sectional studies/
90.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
91.	or/77-90

92.	46 and (54 or 65 or 76 or 91)

1 **Embase (Ovid) search terms**

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	limit 24 to English language
26.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
27.	25 not 26
28.	(Epworth or ESS or ESS-CHAD).ti,ab.
29.	(STOP-bang or stopbang or "snoring tired observed pressure").ti,ab.
30.	((sleep* or Berlin or STOP*) adj3 (questionnair* or questionair*)).ti,ab.
31.	((score* or scoring or stratif* or assess*) adj3 (system* or schem*)).ti,ab.
32.	oximetry/ or transcutaneous oxygen monitoring/
33.	(oxymet* or oximet*).ti,ab.
34.	capnometry/
35.	capnogra*.ti,ab.
36.	(oxi-capnogra* or oxicapnogra* or oxy-capnogra* or oxycapnogra*).ti,ab.
37.	polysomnography/
38.	(polysomnogra* or PSG).ti,ab.
39.	(polygraph* or HRP).ti,ab.
40.	actimetry/
41.	actigraph.ti,ab.
42.	(venous adj3 bicarbonat*).ti,ab.

43.	or/28-42
44.	27 and 43
45.	random*.ti,ab.
46.	factorial*.ti,ab.
47.	(crossover* or cross over*).ti,ab.
48.	((doubl* or singl*) adj blind*).ti,ab.
49.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
50.	crossover procedure/
51.	single blind procedure/
52.	randomized controlled trial/
53.	double blind procedure/
54.	or/45-53
55.	systematic review/
56.	meta-analysis/
57.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
58.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
59.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
61.	(search* adj4 literature).ab.
62.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
63.	cochrane.jw.
64.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
65.	or/55-64
66.	exp "sensitivity and specificity"/
67.	(sensitivity or specificity).ti,ab.
68.	((pre test or pretest or post test) adj probability).ti,ab.
69.	(predictive value* or PPV or NPV).ti,ab.
70.	likelihood ratio*.ti,ab.
71.	((area under adj4 curve) or AUC).ti,ab.
72.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
73.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
74.	diagnostic accuracy/
75.	diagnostic test accuracy study/
76.	gold standard.ab.
77.	or/66-76
78.	Clinical study/
79.	Observational study/
80.	family study/
81.	longitudinal study/
82.	retrospective study/
83.	prospective study/
84.	cohort analysis/

85.	follow-up/
86.	cohort*.ti,ab.
87.	85 and 86
88.	(cohort adj (study or studies or analys* or data)).ti,ab.
89.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
90.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
91.	(before adj2 after adj2 (study or studies or data)).ti,ab.
92.	or/78-84,87-91
93.	exp case control study/
94.	case control*.ti,ab.
95.	cross-sectional study/
96.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
97.	or/92-96
98.	44 and (54 or 65 or 77 or 97)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Sleep Apnea Syndromes] explode all trees
#2.	(sleep* near/4 (apn?ea* or hypopn?ea*)):ti,ab
#3.	(sleep* near/4 disorder* near/4 breath*):ti,ab
#4.	(OSAHS or OSA or OSAS):ti,ab
#5.	(obes* near/3 hypoventil*):ti,ab
#6.	pickwick*:ti,ab
#7.	(OR #1-#6)
#8.	(Epworth or ESS or ESS-CHAD):ti,ab
#9.	(STOP-bang or stopbang or "snoring tired observed pressure"):ti,ab
#10.	((sleep* or Berlin or STOP*) near/3 (questionnair* or questionair*)):ti,ab
#11.	((score* or scoring or stratif* or assess*) near/3 (system* or schem*)):ti,ab
#12.	MeSH descriptor: [Oximetry] explode all trees
#13.	(oxymet* or oximet*):ti,ab
#14.	MeSH descriptor: [Capnography] this term only
#15.	capnogra*:ti,ab
#16.	(oxi-capnogra* or oxicapnogra* or oxy-capnogra* or oxycapnogra*):ti,ab
#17.	MeSH descriptor: [Polysomnography] this term only
#18.	(polysomnogra* or PSG):ti,ab
#19.	(polygraph* or HRP):ti,ab
#20.	MeSH descriptor: [Actigraphy] this term only
#21.	actigraph:ti,ab
#22.	(venous near/3 bicarbonat*):ti,ab
#23.	(OR #8-#22)
#24.	#7 and #23

Epistemonikos search terms

1.	((title:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*) OR

	abstract:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*)))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to sleep apnoea population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and quality of life studies.

B.2.1 Health economic studies strategy

Table 9: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 6 July 2020	Exclusions Health economics studies
Embase	2014 – 6 July 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

	exp Sleep Apnea Syndromes/
1.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
2.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
3.	(OSAHS or OSA or OSAS).ti,ab.
4.	(obes* adj3 hypoventil*).ti,ab.
5.	pickwick*.ti,ab.
6.	or/1-6
7.	limit 7 to English language
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/9-16
17.	randomized controlled trial/ or random*.ti,ab.
18.	17 not 18

19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/19-25
26.	8 not 26
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/28-43
44.	27 and 44

Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.

16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	health economics/
27.	exp economic evaluation/
28.	exp health care cost/
29.	exp fee/
30.	budget/
31.	funding/
32.	budget*.ti,ab.
33.	cost*.ti.
34.	(economic* or pharmaco?economic*).ti.
35.	(price* or pricing*).ti,ab.
36.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
37.	(financ* or fee or fees).ti,ab.
38.	(value adj2 (money or monetary)).ti,ab.
39.	or/26-38
40.	25 and 39

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL TREES
#2.	(sleep* adj4 (apn?ea* or hypopn?ea*))
#3.	(sleep* adj4 disorder* adj4 breath*)
#4.	(OSAHS or OSA or OSAS)
#5.	(obes* adj3 hypoventil*)
#6.	(pickwick*)
#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6

B.2.2 Quality of life studies strategy

Table 10: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 26 November 2019	Exclusions Quality of life studies
Embase	1974 – 26 November 2019	Exclusions Quality of life studies

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter/
10.	editorial/
11.	news/
12.	exp historical article/
13.	Anecdotes as Topic/
14.	comment/
15.	case report/
16.	(letter or comment*).ti.
17.	or/9-16
18.	randomized controlled trial/ or random*.ti,ab.
19.	17 not 18
20.	animals/ not humans/
21.	exp Animals, Laboratory/
22.	exp Animal Experimentation/
23.	exp Models, Animal/
24.	exp Rodentia/
25.	(rat or rats or mouse or mice).ti.
26.	or/19-25
27.	8 not 26
28.	quality-adjusted life years/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.
32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.
34.	(euroqol* or eq5d* or eq 5*).ti,ab.
35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.

41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/28-46
48.	27 and 47

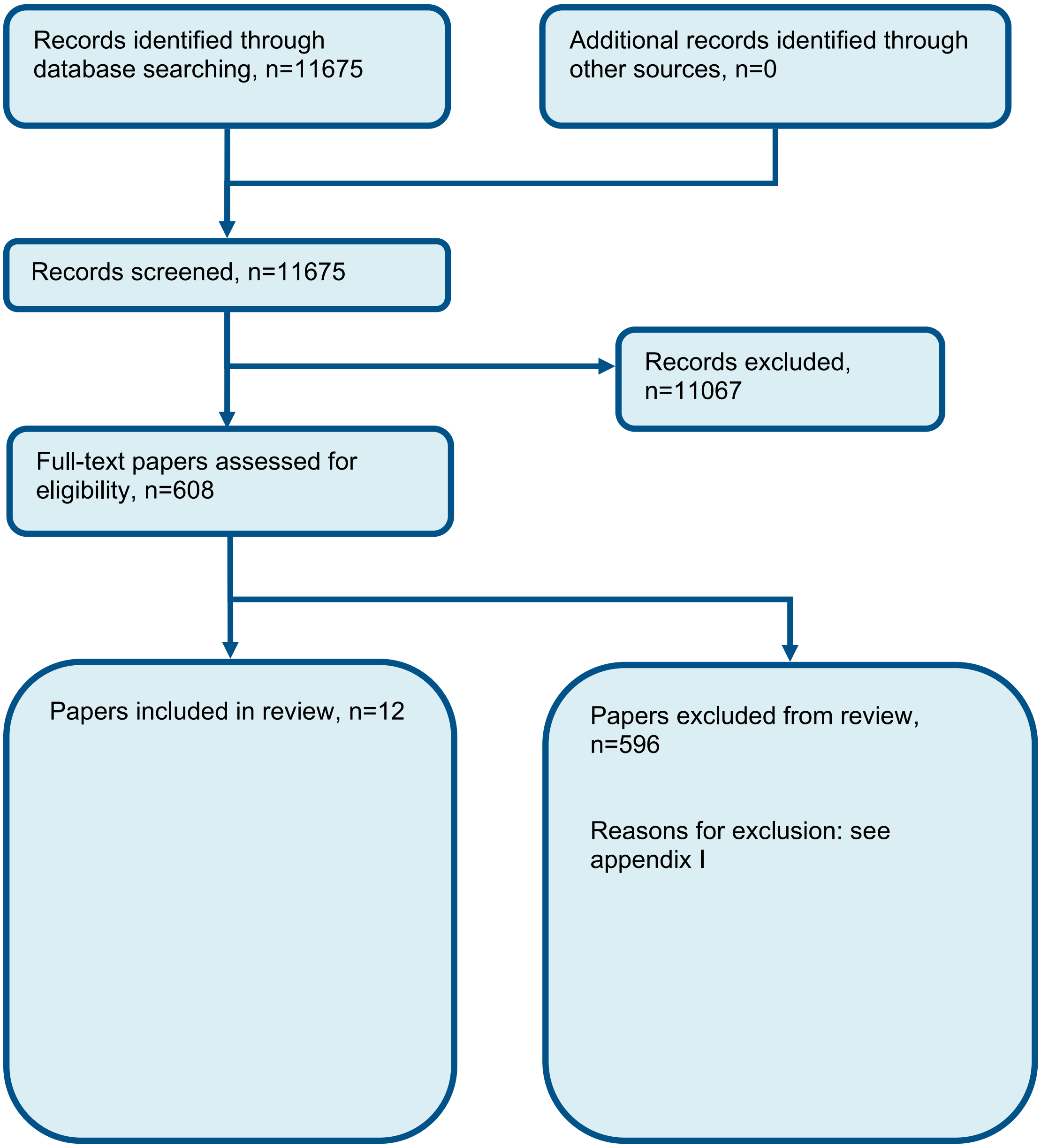
Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	quality adjusted life year/
27.	"quality of life index"/
28.	short form 12/ or short form 20/ or short form 36/ or short form 8/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.
32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.

34.	(euroqol* or eq5d* or eq 5*).ti,ab.
35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.
41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/26-46
48.	25 and 47

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of diagnosis



1 # Appendix D: Clinical evidence tables

2

Reference	**Ahmadi 2008[18]**
Study type	Retrospective chart review
Study methodology	Data source: charts identified in order from alphabetically filed charts, and the first 130 charts were selected that met study inclusion/exclusion criteria Recruitment: For the chart collection, the person collecting the data chose charts in order from the alphabetically filed charts in the clinic. Those charts that met the criteria were selected, and the process was continued until 130 qualified charts, as determined by the inclusion criteria, were collected.
Number of patients	n = 130 analysed
Patient characteristics	Age, mean (SD): male: 42.2 (SD not reported); female: 45.1 (SD not reported) Gender (male to female ratio): 70/50 Ethnicity: not reported Setting: respiratory ward or sleep laboratory Country: Canada Inclusion criteria: referral for sleepiness and/or poor sleep; recordings available from two overnight PSGs; a completed questionnaire battery including the Berlin questionnaire. Exclusion criteria: Charts of patients with incomplete or missing data for the respiratory variables. Sleep disorders included those secondary to psychiatric or neurological disorders. Charts of patients who slept less than 240 minutes on either of the two nights were excluded from the study.
Target condition(s)	Sleep apnoea/ hypopnoea syndrome
Index test(s) and reference standard	Index test The Berlin questionnaire was scored as previously reported by Netzer and colleagues. Berlin questionnaire, scoring positively on less than 2 categories were identified as being low risk of having sleep apnoea.

<table>
<tr><th>Reference</th><th>Ahmadi 2008[18]</th></tr>
<tr><td></td><td><u>Reference standard</u>
Laboratory PSG with no pre-specified diagnostic AHI, RDI or ODI: apnoeas/hypopnoeas were scored where there was a 50% or greater reduction in the baseline amplitude of respiration or at least 3% reduction in oxygen saturation, either lasting for a minimum of 10 seconds._Maximum RDI across two nights as observed by PSG, multiple cut-offs reported, RDI of 5 (as per protocol) extracted
Prevalence 56 subjects (RDI>5)

Time between measurement of index test and reference standard: not reported</td></tr>
<tr><td>2×2 table</td><td><table>
<tr><th></th><th>Reference standard +</th><th>Reference standard −</th><th>Total</th></tr>
<tr><td>Index test +</td><td>38</td><td>38</td><td>76</td></tr>
<tr><td>Index test −</td><td>18</td><td>36</td><td>54</td></tr>
<tr><td>Total</td><td>56</td><td>74</td><td>130</td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td><u>Index text: BQ (≥3% oxygen desaturation)</u>
Sensitivity: 67.8% (54 – 79)
Specificity: 48.6% (37 – 60)

Positive predictive value: not reported
Negative predictive value: not reported
Area under the curve (95% confidence interval): not reported</td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
<tr><td>Limitations</td><td>Risk of bias: Very serious. Retrospective chart review; unclear if study inclusions/exclusions appropriate as part of study criteria; test results could have been interpreted with knowledge of the other test results; time interval between the index test and reference standard not reported
Indirectness: None</td></tr>
<tr><td>Comments</td><td>Study population included people with sleep disorders secondary to psychiatric or neurological disorders; RERA not included in definition of RDI from laboratory PSG. Sensitivity and specificity calculated by excel spreadsheet by NGC.</td></tr>
</table>

Reference	**Boynton 2013[68]**
Study type	Cross-sectional
Study methodology	Data source: Adults referred for diagnostic polysomnography completed the STOP questions and answered four yes/no questions (BANG self-reported) about their body mass index (weight and height), age, neck circumference, and gender, which were also assessed by laboratory technologists (BANG-measured). Recruitment: not reported
Number of patients	n = 219 recruited and analysed
Patient characteristics	Age, mean (SD): 46.3 (SD 13.9) Gender (male to female ratio): 91/74 of those identified as being high risk for OSA Ethnicity: not reported Setting: respiratory ward or sleep laboratory Country: USA Inclusion criteria: at least 18 years old; English-speaking; referred for diagnostic, baseline polysomnography to assess for OSA. Exclusion criteria: unable to read, sign, or understand informed consent; previously diagnosed or treated for OSA
Target condition(s)	Obstructive sleep apnoea
Index test(s) and reference standard	<u>Index test</u> STOP-BANG questionnaire: patients were classified as having high risk for OSA if they had a total STOP-BANG score ≥3 points, out of a possible 8 points. As both self-reported and measured or observed values for BMI, age, neck circumference, and gender were collected, two sets of scores were calculated. One STOP-BANG score was based entirely on patient responses to STOP questions and their self-reported BANG values. The second STOP-BANG score was based on patient responses to STOP questions and the BANG values that were measured by technicians or obtained from patient health records. This version of the questionnaire was completed by the research team after the study appointment. (STOP-BANG questionnaire, self-reported, high risk if score of 3 or more out of 8) <u>Reference standard</u>

Reference	**Boynton 2013**[68]
	In centre polysomnography (PSG): the results of a single nocturnal, laboratory-based sleep study were used. The diagnosis of OSA required an AHI >5 events per hour of sleep, coupled with daytime sleepiness or symptoms of disturbed sleep. Obstructive and central apnoeas were defined as the complete absence of airflow for at least 10 seconds, in the presence or absence of continued respiratory effort respectively. Hypopneas were defined as a ≥50% decrease in airflow followed by an arousal, awakening, or ≥3% desaturation from baseline levels, consistent with American Academy of Sleep Medicine guidelines available at the time the studies were performed. Both the technologists who scored the studies and the physicians who interpreted them were masked to STOP-BANG scores. Prevalence – 169 subjects (AHI>5) (In centre PSG, multiple AHI cut-offs provided included >5 (extracted below))

2×2 table

	Reference standard +	Reference standard −	Total	Calculated by NGC
Index test +	134	25	159	
Index test −	35	25	60	
Total	169	50	219	

Statistical measures	<u>Index text: STOP-BANG (≥3% oxygen desaturation)</u> Sensitivity: 79.3% (75.6-82.8) Specificity: 50% (37.6-62.0) Positive predictive value: 84.3% Negative predictive value: 41.7% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.722 (0.645 – 0.799) Moderate-severe (AHI≥15): 0.746 (0.682 – 0.811) Severe (AHI≥30): 0.762 (0.696 - 0.827)
Source of funding	Supported by the National Institutes of Health, the University of Michigan Medical School Summer biomedical Research Program, and the University of Michigan Sleep Disorders Centre
Limitations	Risk of bias: Serious. Enrolment method unclear; index test results could have been interpreted with knowledge of the reference standard results. Indirectness: None
Comments	Incomplete reporting of the reference standard methods. Paper only provides totals and not TP, FP, FN, or TN. These have been calculated using diagnostic calculation spreadsheet using sensitivity, specificity, PPV, NPV and totals.

Reference	**Cowan 2014[93]**
Study type	Cross-sectional
Study methodology	Data source: Prospective observational study conducted during May-December 2012. Recruitment: consecutive
Number of patients	n = 129 analysed
Patient characteristics	Age, mean (SD): 49 (SD 11) Gender (male to female ratio): 82/47 Ethnicity: not reported Setting: Tertiary sleep centre Country: UK Inclusion criteria: Consecutive patients aged ≥16 years referred to the North Glasgow sleep service (a tertiary centre) for assessment of possible OSA were invited to participate Exclusion criteria: not reported
Target condition(s)	<u>Suspected obstructive sleep apnoea</u>
Index test(s) and reference standard	<u>Index tests</u> ESS – a validated measure of daytime sleepiness including eight questions, each with four possible responses, that assess the likelihood of dozing in different situations; score of ≥11/24 denotes excessive daytime somnolence. Berlin questionnaire – includes questions in three categories that relate, first, to snoring and witnessed apnoeas, second to tiredness, fatigue and sleepiness, and third, to hypertension and obesity. High risk of OSA is defined by scoring positively in ≥2 categories. STOP-BANG – includes four yes/no questions that relate to snoring, tiredness, observed apnoeas, and high blood pressure it also includes four additional questions relating to BMI, age, neck circumference and gender, and high risk OSA is defined as a score of ≥3.

Reference	Cowan 2014[93]				
	Reference standard – Home polygraphy studies were performed using the SOMNOmedics SOMNOscreen kit (Randersacker, Germany) with channels that recorded body position, thoraco abdominal movements, oronasal airflow, heart rate, pulse oximetry and snoring. An Apnoea was defined as cessation of nasal flow for ≥10s, while a hypopnea was defined as 50% reduction in nasal flow for ≥10 s, or lesser reduction in flow associated with oxygen desaturation of ≥4%. Prevalence (ESS ≥11/24) – 92 patients had AHI ≥ 5 Prevalence (Berlin positive)– 94 patients had AHI ≥ 5 Prevalence (STOP-BANG ≥3/8) – 93 patients had AHI ≥ 5 Time between measurement of index test and reference standard: not reported				
2×2 table	ESS	Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	63	17	80	
	Index test −	29	11	40	
	Total	92	28	120	
2×2 table	Berlin	Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	87	29	116	
	Index test −	7	2	9	
	Total	94	31	125	
2×2 table	SB	Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	88	21	109	
	Index test −	5	9	14	
	Total	93	30	123	

Reference	**Cowan 2014[93]**
Statistical measures	Index text ESS Sensitivity 68.4% Specificity 39.2% Positive predictive value: not reported Negative predictive value: not reported Area under the curve (95% confidence interval) All OSA (AHI≥5): not reported Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index text Berlin Sensitivity 92.6% Specificity 6.5% Positive predictive value: 75% Negative predictive value: 22% Area under the curve (95% confidence interval) All OSA (AHI≥5): not reported Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index text SB Sensitivity 94.6% Specificity 30% Positive predictive value: 81% Negative predictive value: 64% Area under the curve (95% confidence interval) All OSA (AHI≥5): not reported Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported

Reference	Cowan 2014[93]
Source of funding	This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.
Limitations	Risk of bias: Serious. Exclusion criteria not reported Indirectness: none
Comments	Study reported number of patients positive on questionnaires (ESS, Berlin and STOP-BANG) and with AHI ≥5, sensitivity, specificity was calculated using 2x2 tables

Reference	de Carvalho 2020[96]
Study type	Cross-sectional
Study methodology	Data source: This study was carried out from October 2017 to October 2018 and included 66 adults with Down’s Syndrome (DS) attending the Down Syndrome Reference Center (CRISDOWN) of Hospital Regional da Asa Recruitment: not reported
Number of patients	n = 66 recruited, 60 analysed
Patient characteristics	Age, mean (SD): 27.7 (SD 9.1) Gender (male to female ratio): 33/27 Ethnicity: not reported Setting: sleep laboratory Country: Brazil Inclusion criteria: The inclusion criteria comprised individuals with DS treated at the service, of both genders, good overall health status, aged 18 years and older, capable to understand and accept the study and its procedures. Exclusion criteria: individuals under 18 years of age; patients undergoing treatment for sleep disorders; patients with a history of conditions that could affect brain structure or function (such as cerebrovascular accident or head trauma); those who refused to participate in the study.
Target condition(s)	Sleep apnoea/hypopnoea syndrome

Reference	**de Carvalho 2020[96]**
Index test(s) and reference standard	Index test: STOP-BANG questionnaire: due to absence of cut-off points specifically defined for the adult population with the Down's syndrome the following was used - risk for OSA in the SBQ (3 or more affirmative answers) These questionnaire was answered by the patients' proxies, in agreement with other studies in individuals with DS. Reference standard Polysomnography (PSG), with pre-specified AHI >15, In the present study, the equipment used to perform the type III PSG assessments was the ApneaLink Air (ResMed Germany Inc.), which has been previously used in other important studies. This equipment allowed monitoring with the use of nasal pressure cannula for airflow and snore detection), chest piezoelectric strap (for respiratory effort detection) and pulse oximetry (to monitor peripheral arterial oxygen saturation—SpO2 and heart rate). The total recording time was used as the denominator to calculate the respiratory event index (REI). The PSG was assembled by a specialized technician from the Sleep Laboratory of our service. The respiratory events were defined as follows: (1) hypopnea, when there was a 30% reduction in airflow for at least 10 seconds, observed through the nasal cannula, associated with a decrease in SpO2 of at least 3%; (2) obstructive apnoea, due to the absence or reduction 90% of airflow for at least 10 seconds in the presence of respiratory effort; (3) mixed apnoea, due to the absence or reduction 90% of airflow, without the presence of respiratory effort only at the beginning of the event; (4) central apnoea, due to absence or 90% reduction in airflow for at least 10 seconds associated with absence of respiratory effort throughout the event. Prevalence – 49 subjects (AHI>15) Time between measurement of index test and reference standard: not reported but the ESS, STOP-BANG and Berlin questionnaires were completed prior to polysomnography

2×2 table All OSAS (AHI ≥ 15) STOP-BANG questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	49	6	55	
	Index test −	0	5	5	
	Total	49	11	60	

Reference	de Carvalho 2020[96]
Statistical measures	Index text: STOP-BANG questionnaire, AHI>15, Sensitivity: 100% Specificity: 45% Positive predictive value: not reported Negative predictive value: not reported Area under the curve, Area under the curve, not reported
Source of funding	This study was supported by grants from the Fundac¸ão de Ensino e Pesquisa em Ciências da Sau´de (FEPECS), process number 064.000.560/2015, of Public Notice number 40 of 10/29/2015, published in DODF n. 213, of 11/06/2015, regarding the Homologation of the Final Selection Result of Research Projects. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Fundac¸ão de Ensino e Pesquisa em Ciências da Sau´de (FEPECS
Limitations	Risk of bias: Serious. Included patients with down syndrome. Indirectness: Serious. AHI ≥15
Comments	Paper only provides total number of patients diagnosed by polysomnography, number of people at risk of OSA using STOP-BANG questionnaire. Sensitivity, specificity and TP, FN, FP, TN values not provided.

Reference	Duarte 2020[108]
Study type	Cross-sectional
Study methodology	Data source: This was a cross-sectional study, comprising the period from January 2017 to June 2019, including adults which were consecutively referred for PSG evaluation due to suspected sleep disordered breathing by their attending physicians Recruitment: not reported
Number of patients	n = 8138 recruited, 7377 analysed (patients grouped into two large and independent cohorts: derivation (N=3771) and validation (N=3606)

Reference	Duarte 2020[108]
Patient characteristics	Age, mean (SD) derivation cohort: 45.9 (SD 14.6) Age, mean (SD) validation cohort: 45.9 (SD 14.6) Gender (male to female ratio) derivation cohort: 1983/1788 Gender (male to female ratio) validation cohort: 1961/1645 Ethnicity: not reported Setting: sleep laboratory Country: Brazil Inclusion criteria: of both genders, aged ≥18 years and with suspected of OSA. Exclusion criteria: previously diagnosed OSA, use of home sleep study for diagnosis, incomplete clinical data and technically inadequate PSG This was a cross-sectional study, comprising the period from January 2017 to June 2019, including adults which were consecutively referred for PSG evaluation due to suspected sleep disordered breathing by their attending physicians. Then, all subjects were grouped into two separate cohorts: derivation (from January 2017 to February 2018) and validation (from May 2018 to June 2019).
Target condition(s)	Sleep apnoea/hypopnoea syndrome
Index test(s) and reference standard	<u>Index test for both derivation and validation cohorts:</u> STOP-BANG questionnaire (final score from 0 to 8, high risk with 3 or more points) consists of 8 yes-or-no questions (1 point for each affirmative answer): loud snoring, tiredness, observed apnoea, hypertension, BMI >35 kg/m2, age >50 years, NC > 40 cm, and male gender. <u>Reference standard</u> Polysomnography (PSG), with a prespecified diagnostic AHI ≥ 5, All subjects underwent an attended, in-lab PSG (EMBLA® S7000, Embla Systems, Inc., Broomfield, Colorado, United States) consisting of continuous monitoring of electroencephalogram, electrooculogram, electromyogram (chin and legs), electrocardiogram, airflow, thoracic and abdominal impedance belts, oxygen saturation, snoring microphone and sensors for body position. Polysomnographic records were manually interpreted by two board-certified sleep physicians, according to a guideline previously published in 2012 by the American Academy of Sleep Medicine (AASM),28 which were blinded to the values of all screening instruments collected prior to PSG. Apnoeas were classified from a drop ≥90% of baseline airflow lasting at least 10 s,

Reference	Duarte 2020[108]				
	while hypopneas were classified from a ≥30% pre-event drop over ≥10 s associated with desaturation of oxygen ≥3% or an arousal.28 The AHI was calculated as the number of apnoea plus hypopnea/total sleep time (in hours). Polysomnographic diagnosis of OSA was based on apnoea/hypopnea index (AHI) ≥5.0/h and its severity was classified as follows: ≥5.0/h as any OSA (OSA≥5), ≥15.0/h as moderate/ severe OSA (OSA≥15), and ≥30.0/h as severe OSA (OSA≥30). Prevalence: derivation cohort 2984 subjects (AHI>5), validation cohort 2842 subjects (AHI>5) Time between measurement of index test and reference standard: not reported				
2×2 table Derivation cohort All OSAS (AHI ≥ 5) STOP-BANG questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	2602	389	2991	
	Index test −	382	398	780	
	Total	2984	787	3771	
2×2 table Validation cohort All OSAS (AHI ≥ 5) STOP-BANG questionnaire		Reference standard +	Reference standard −	Total	
	Index test +	2501	366	2867	
	Index test −	341	398	739	
	Total	2842	764	3606	
Statistical measures	<u>Index text derivation cohort: STOP-BANG questionnaire, AHI ≥5</u> Sensitivity: 87.2% Specificity: 50.6% Positive predictive value: 87% Negative predictive value: 51.1% Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.789(0.771-0.806) <u>Index text derivation cohort: STOP-BANG questionnaire, AHI ≥5</u> Sensitivity: 88% Specificity: 52.1% Positive predictive value: 87.2% Negative predictive value: 53.9% Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.797(0.779-0.815)				

Reference	**Duarte 2020[108]**
Source of funding	Funding not stated
Limitations	Risk of bias: None Indirectness: None
Comments	Paper only provides sensitivity specificity, positive predictive value, negative predictive value totals and not TP, FP, FN, or TN. These have been calculated using diagnostic calculation spreadsheet using sensitivity, specificity, PPV, NPV and totals.

Reference	**Felfeli 2020[126]**
Study type	Cross-sectional
Study methodology	Data source: The study was conducted at a tertiary academic centre between March 22, 2017, and April 7, 2018. Patients completed the Berlin and STOP-BANG questionnaires screening for OSA at presentation. Diagnostic test properties of the 2 questionnaires compared with polysomnography at a certified sleep laboratory centre as the gold standard for detection of OSA were calculated Recruitment: consecutive
Number of patients	n = 27 analysed
Patient characteristics	Age, mean (SD): 69.6 (SD 11.5) Gender (male to female ratio): 11/15 Ethnicity: not reported Setting: Tertiary sleep centre

Reference	**Felfeli 2020[126]**				
	Country: Canada Inclusion criteria: Consecutive adult patients (>18 years of age) with a new diagnosis of RVO confirmed with intravenous fluorescein angiography were enrolled. Exclusion criteria: Patients with a known diagnosis of OSA were excluded				
Target condition(s)	Suspected obstructive sleep apnoea				
Index test(s) and reference standard	Index tests Berlin questionnaire – cut-off not stated STOP-BANG questionnaire – cut-off not stated Reference standard – All patients were then scheduled to undergo a polysomnography at a certified University of Toronto - affiliated academic sleep laboratory centre (Sleep and Alertness Clinic, Toronto, Ont.), which has maintained standards endorsed by the Ontario Ministry of Health for over 30 years. The polysomnography was conducted using the following channels: tracheal sounds by microphone tapes to the neck, nasal flow by cannula linked to a pressure transducer, oxygen saturation by digital oximetry, heart rate through the pulse oximetry signal, thoracic and abdominal movements by piezoelectric sensors, and body position by mercury sensors and actigraphy. Patients required overnight stay at the sleep clinic for completion of the study. Apnoeic episodes were defined as complete cessation of breathing for at least 10 seconds, or hypopnea in which airflow is decreased by 50% for 10 seconds, or hypopnea in which airflow is decreased by 30% for 10 seconds with decreased oxygen saturation. Polysomnography data were analysed by both a certified technician and a physician with specialisation in sleep disorders who were masked to the patients' disease and groupings. The AHI (number of events/hour) was assigned to each patient's polysomnography. Severity of OSA was classified as mild (AHI 5-15), moderate (AHI 16-30), and severe (AHI >30). An AHI <5 was considered a normal test and thus negative for OSA. The other parameters recorded from polysomnography were the AHI during rapid eye movement (REM) sleep (AHI-REM, commonly measured owing to the expected decrease in muscle tone in REM sleep), the percentage of lowest saturation of peripheral oxygen (SPO2- min), and the cumulative time of SPO2 below 90% (CT90%). Prevalence 21 subjects (AHI>15) Time between measurement of index test and reference standard: not reported				
2×2 table	Berlin	Reference standard +	Reference standard −	Total	

Reference	**Felfeli 2020[126]**				
Berlin	Index test +	9	2	11	
	Index test −	12	4	16	
	Total	21	6	27	
2×2 table Stop-Bang	SB	Reference standard +	Reference standard −	Total	
	Index test +	18	3	21	
	Index test −	3	3	6	
	Total	21	6	27	
Statistical measures	<u>Index text Berlin</u> Sensitivity 42.6% Specificity 66.7% Positive predictive value: 81.8% Negative predictive value: 25% Area under the curve, not reported <u>Index text SB</u> Sensitivity 85.7% Specificity 50% Positive predictive value: 81% Negative predictive value: 64% Area under the curve, not reported				
Source of funding	Not stated				
Limitations	Risk of bias: Serious. Indirectness: serious AHI>15 for reference standard				
Comments	Paper only provides sensitivity specificity, positive predictive value, negative predictive value totals and not TP, FP, FN, or TN. These have been calculated using diagnostic calculation spreadsheet using sensitivity, specificity, PPV, NPV and totals.				

Reference	**Hesselbacher 2012[164]**
Study type	Cross-sectional

Reference	Hesselbacher 2012[164]
Study methodology	Data source: patients referred for polysomnographic diagnosis of OSA completed questionnaires, including demographic data and ESS. OSA was determined based on a respiratory disturbance index (RDI) 15 by polysomnography. Recruitment: consecutive
Number of patients	n = 2112 studied, 1900 analysed
Patient characteristics	Age, mean (SD): 54 (15) Gender (male to female ratio): Ethnicity: Caucasian (males 53%, females 50%), Hispanic (males 43%, 48%), Other (males 3%, females 2 %) Setting: sleep centre Country: USA Inclusion criteria: not reported Exclusion criteria: not reported All study participants were aged ≥12 years prior to a diagnosis of OSA.
Target condition(s)	Obstructive sleep apnoea
Index test(s) and reference standard	Index test: ESS Cut-off not stated Reference standard PSG RDI >/=15 Prevalence – study did not report prevalence, however it did report % of people without OSA – 17% (~323 subjects), prevalence was calculated using sensitivity, specificity and number of people without OSA.

2×2 table

	Reference standard +	Reference standard −	Total
Index test +	852	139	991
Index test −	725	184	909
Total	1577	323	1900

Reference	Hesselbacher 2012[164]
Statistical measures	Index text ESS (cut-off not stated) Sensitivity: 54% Specificity: 57% Positive predictive value: 64% Negative predictive value: 47% Area under the curve (95% confidence interval): not reported
Source of funding	Funding not stated
Limitations	Risk of bias: serious. Inclusion and exclusion criteria not reported Indirectness: serious RDI ≥15 for reference standard
Comments	This study included adults and children (aged ≥12 years), paper provided sensitivity, specificity and number of people with no OSA. TP, FP, FN and TN values were calculated using 2x2 tables. Positive predictive value and negative predictive value reported in the paper seems to be inaccurate.

Reference	Pereira 2013[416]
Study type	Cross-sectional
Study methodology	Data source: Consecutive patients referred to the Sleep Disorders Clinic completed 3 testing components: (1) 3 questionnaires (Berlin, STOP-Bang, and Sleep Apnea Clinical Score [SACS]); (2) Level III at-home PM (MediByte) study; and (3) Level I in-laboratory PSG. The utility of individual questionnaires, the Level III device alone, and the combination of questionnaires and the Level III device were compared with the PSG. Recruitment: consecutive
Number of patients	n = 128 recruited and analysed
Patient characteristics	Age, mean (SD): 50 (12.3)

Reference	Pereira 2013[416]
	Gender (male to female ratio): 84/44 Ethnicity: not reported Setting: Home then laboratory Country: Canada Inclusion criteria: the ability to apply the Level III monitoring equipment without supervision (after brief initial training) and a primary residence within 100 miles of the sleep clinic (for returning the portable monitor equipment) Exclusion criteria: known COPD; congestive heart failure; uncontrolled asthma
Target condition(s)	Obstructive sleep apnoea
Index test(s) and reference standard	Index tests Berlin questionnaire: details not reported; completed prior to portable sleep monitoring and PSG Sleep Apnoea Clinical Score questionnaire: details not reported; completed prior to portable sleep monitoring and PSG Stop Bang questionnaire: details not reported; completed prior to portable sleep monitoring and PSG Portable sleep monitor (MediByte; Braebon Medical Corporation, Ottawa, ON): this was a level III device, worn on two consecutive nights at home. The first night of recording was used in the analysis, with the second night as a back-up if recording from the first night did not provide sufficient data. The device consists of two inductance bands for thoracic and abdomen measurement, a nasal cannula pressure transducer airflow signal, finger pulse oximetry, and a body position sensor. Patients were given the option to either manually turn on the device before switching off the lights at night and turn off the device once awake in the morning, or to have the device start and stop automatically at predetermined times. RDI was the outcome measure for data from the monitor, defined as the number of apnoeas and hypopnoeas per hour of recording time. Reference standard Laboratory polysomnography (PSG) with no pre-specified diagnostic AHI, RDI or ODI: full, overnight PSG recordings were conducted using Sandman Elite SD32+ digital sleep recording system (Natus [Embla]; Otawa, ON) and included 4 EEG channels, 2 EOG channels, submental EMG, intercostal (diaphragmatic surface) EMG, bilateral anterior tibialis EMG, ECG, respiratory piezo bands (chest and abdomen), finger pulse oximetry, a vibration snore sensor, nasal pressure airflow, and oronasal thermocouple. PSG recordings were conducted as either a diagnostic study or, in the event of severe OSA, a split-night study. For split-night studies, the initial diagnostic period was followed by the introduction of treatment during the night, and only the diagnostic part of the recording was used for comparison.

Reference	Pereira 2013[416]				
	Data from the questionnaires and portable monitoring were manually scored by an experienced scorer who was blinded to the results of the in-lab PSG. The PSGs were manually scored using standard criteria by registered polysomnographic technologists, who in turn were blinded to results of the questionnaires and the portable monitoring device. Sixty-four percent of the scored portable monitoring device data were reviewed by an experienced technologist (with concordance between the two scorers of 99.2%), and all PSG studies were reviewed by a sleep specialist. For both the index test and PSG data, apnoeas were scored as a cessation of airflow ≥50% for ≥10 seconds, and hypopnoeas were scored as a reduction in pressure-derived airflow of 50% to 90% from baseline for ≥10 seconds followed by ≥3% oxygen desaturation. For the PSG, the definition of hypopnoea also included ≥50% reduction in pressure-derived airflow amplitude associated with arousal, in the absence of a desaturation ≥3% (alternative criteria). The agreement of each of the four screening tools was assessed, compared with PSG, at different AHI thresholds Prevalence – 116 subjects (AHI ≥ 5) Time between measurement of index test and reference standard: PSG completed following portable sleep monitoring at home, time point not reported				
2×2 table Berlin questionnaire		Reference standard +	Reference standard −	Total	
	Index test 1 +	100	9	109	
	Index test 1 −	16	3	19	
	Total	116	12	128	
2×2 table Sleep Apnea clinical score questionnaire		Reference standard +	Reference standard −	Total	
	Index test 1 +	38	2	40	
	Index test 1 −	78	10	88	
	Total	116	12	128	
2×2 table Stop Bang questionnaire		Reference standard +	Reference standard −	Total	
	Index test 1 +	104	7	111	
	Index test 1 −	12	5	17	
	Total	116	12	128	

Reference	Pereira 2013[416]
Statistical measures	<u>Index text 1, Berlin questionnaire</u> Sensitivity 86% Specificity 25% Positive predictive value: 91.7% Negative predictive value: 15.8% Area under the curve (95% confidence interval) at PSG cut-off AHI≥10 All OSA (AHI≥10): 0.565 (CI not reported) Moderate-severe (AHI≥15): Severe (AHI≥30): <u>Index text 2, Sleep Apnoea Clinical Score questionnaire</u> Sensitivity 33% Specificity 83% Positive predictive value: 95% Negative predictive value: 11.4% Area under the curve (95% confidence interval) at PSG cut-off AHI≥10 All OSA (AHI≥10): 0.540 (CI not reported) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported <u>Index text 3, Stop Bang questionnaire</u> Sensitivity 90% Specificity 42% Positive predictive value: 93.7% Negative predictive value: 29.4% Area under the curve (95% confidence interval) at PSG cut-off AHI≥10 All OSA (AHI≥10): 0.575 (CI not reported) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported

Reference	**Pereira 2013[416]**
Source of funding	Innovation Fund, the Ontario Ministry of Health and the William M. Spear Foundation from the Queen's University
Limitations	Risk of bias: Serious. Unclear if all study exclusions appropriate as part of study exclusion criteria and unclear time between index testing and measurement of the reference standard. Indirectness: None
Comments	

Reference	**Sangkum 2017[480]**
Study type	Cross-sectional
Study methodology	Data source: Two hundred and eight subjects who were referred for an evaluation of possible OSA at Tulane Comprehensive Sleep Center Recruitment: not reported
Number of patients	n = 208 recruited and analysed
Patient characteristics	Age, mean (SD): 52.9 (0.9) Gender (male to female ratio): 75/133 Ethnicity: African American (69%); white (28%); Hispanic (0.5%) Setting: initial clinical evaluation site and laboratory Country: USA

Reference	Sangkum 2017[480]
	Inclusion criteria: not reported Exclusion criteria: age <18 years old; incomplete or absent questionnaire; incomplete body type identification; PSG refusal; pregnant women Participants undergoing OSA evaluation with polysomnography were recruited
Target condition(s)	Obstructive sleep apnoea
Index test(s) and reference standard	<u>Index tests</u> STOP-BANG questionnaire: administered during the initial clinical evaluation, a score greater than or equal to 3 was determined as ‘high risk’ for OSA STOP-BANG-Apple questionnaire: as above but with additional data included on fat distribution type (apple, pear or indeterminate); apple and pear body type is defined as excess upper body fat and lower body fat respectively. Indeterminate body type refers to fat distribution that cannot categorise as apple or pear such as a patient with low body fat or generalised distribution of excess body fat. Fat distribution type was determined by subjective visual inspection (i.e. eyeball test). STOP questionnaire: not pre-specified in methods but results reported (cut-off score=2) STOP-Apple questionnaire: not pre-specified in methods but results reported (cut-off score=2) <u>Reference standard</u> Laboratory polysomnography with a pre-specified AHI >5 events per hour diagnostic of OSA: overnight PSG included sleep staging, monitored using electroencephalogram, bilateral electro-oculogram, and a surface submental electromyogram. Respiratory parameters were monitored using pulse oximetry, snoring microphone, nasal thermistors and pressure transducer, and thoracic and abdominal inductance plethysmograms. The heart rate was continuously monitored using an electrocardiogram. Bilateral tibialis EMG leads were placed to detect periodic limb movements. A registered PSG technologist under the supervision of the sleep physician visually scored all studies. The technologist was blinded to clinical information and the results of STOP-BANG-apple scores. Using the 2012 American Academy of Sleep Medicine for Scoring of Sleep and Associated Events, apnoea was defined as cessation of the airflow ≥90% detected through the nasal thermistor sensor for at least 10 seconds. Hypopnoea was defined by a peak airflow signal excursion of ≥30% using nasal pressure, with ≥3% oxygen desaturation or associated arousal. Prevalence – 165 subjects (AHI>5) Time between measurement of index test and reference standard: not reported

Reference	**Sangkum 2017[480]**				
2×2 table STOP-BANG questionnaire (cut-off of 3)	STOP-BANG questionnaire (cut-off of 3)	Reference standard +	Reference standard −	Total	
	Index test 1 +	156	37	193	
	Index test 1 −	6	9	15	
	Total	162	46	208	
2×2 table STOP-BANG-Apple questionnaire (cut-off of 4)	STOP-BANG-Apple questionnaire (cut-off of 4)	Reference standard +	Reference standard −	Total	
	Index test 2 +	146	28	174	
	Index test 2 −	16	18	34	
	Total	162	46	208	
2×2 table STOP questionnaire (cut-off score of 2)	STOP questionnaire (cut-off score of 2)	Reference standard +	Reference standard −	Total	
	Index test 3 +	157	41	198	
	Index test 3 −	5	5	10	
	Total	162	46	208	
Index text 24 STOP-Apple questionnaire (cut-off score of 3)	Index text 24 STOP-Apple questionnaire (cut-off score of 3)	Reference standard +	Reference standard −	Total	
	Index test 4 +	143	28	171	
	Index test 4 −	19	18	37	
	Total	162	46	208	

Reference	Sangkum 2017[480]
Statistical measures	Index text 1, STOP-BANG questionnaire (cut-off of 3) Sensitivity 96.3% Specificity 19.6% Positive predictive value: 81% Negative predictive value: 60% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.7760 (CI not reported) Moderate-severe (AHI≥15): Severe (AHI≥30): Index text 2 STOP-BANG-Apple questionnaire (cut-off of 4) Sensitivity 90.1% Specificity 39.1% Positive predictive value: 84% Negative predictive value: 53% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.7982 (CI not reported) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index text 3, STOP questionnaire (cut-off score of 2) Sensitivity 96.9% Specificity 10.9% Positive predictive value: 79.3% Negative predictive value: 50% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.6262 (CI not reported) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index text 4 STOP-Apple questionnaire (cut-off score of 3)

Reference	Sangkum 2017[480]
	Sensitivity 88.3% Specificity 39.1% Positive predictive value: 83.6% Negative predictive value: 48.6% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.6789 (CI not reported) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported
Source of funding	National Institute of General Medical Sciences of the National Institutes of Health
Limitations	Risk of bias: Serious. Enrollment method unclear; unclear if all study exclusions appropriate, and test results could have been interpreted with knowledge of the other test results. Indirectness: None
Comments	

Reference	Vana 2013[553]
Study type	Cross sectional
Study methodology	Data source: This study compared the predictive abilities of the STOP-Bang and Epworth Sleepiness Scale (ESS) for screening sleep clinic patients for obstructive sleep apnoea (OSA) and sleep-disordered breathing (SDB). Recruitment: 'a convenience sample', consecutive
Number of patients	n = 60 recruited, 47 analysed

Reference	Vana 2013[553]
Patient characteristics	Age, mean (SD): 46.4 (13.2) Gender (male to female ratio): 16/31 Ethnicity: Caucasian (76.6%); Native American/Asian/multiracial/'Mexican' (12.8%); African American (10.6%). 68.1% identified as Hispanic or Latino Setting: not reported Country: USA Inclusion criteria: over 18 years old; no previous diagnosis of OSA Exclusion criteria: health conditions that could affect electroencephalogram tracings and sleep staging in PSG, such as dementia or daily forgetfulness, severe brain injuries, developmental delays, or stimulant use. Study participants all spoke English or Spanish
Target condition(s)	Obstructive sleep apnoea and sleep- disordered breathing
Index test(s) and reference standard	<u>Index tests</u> Epworth Sleepiness Scale questionnaire: a validated questionnaire (8 items; scale 0-24 where 0=unlikely to fall asleep in any situation and 24=high chance of falling asleep in all eight situations) that measures subjective sleepiness. The ESS final scores were dichotomised into ≤10 (low risk for sleepiness) and >10 (high risk). STOP-Bang questionnaire (SB35 and SB 30): this questionnaire evaluated eight risk factors for OSA (snoring, tiredness, observed apnoeas, blood pressure, body mass index >35 or >30kg/m^2, age >50 years, neck circumference, and male gender). Each participant had two STOP-Bang total scores: one total score calculated with the >30kg/m^2 cut point and one total score calculated with the >35kg/m^2 cut point. High risk for SDB was defined as three or more affirmative answers to the eight STOP-Bang items. Low risk was defined as two or fewer affirmative answers. <u>Reference standard</u> Polysomnography (PSG) with a pre-specified diagnostic AHI ≥5 for OSA and RDI ≥5 for SDB: a one-night diagnostic or split PSG was completed on participants who agreed to undergo PSG. The following leads were used: central and occipital electroencephalograms; bilateral electro-oculograms; submental electromyelograms; continuous pulse oximetry; nasal and oral thermistors; nasal pressure transducer; snoring microphone; thoracic and abdominal piezo electrodes; electrocardiogram; bilateral tibialis electromyelographic leads. Acceptable polysomnograms had at least 120 minutes of total sleep time, were based on 4% oxyhaemoglobin desaturations,

Reference	Vana 2013[553]				
	were completed within 3 months of screenings, and met established polysomnographic standards for evaluating OSA. All tracings were visually scored by sleep technologists using updated American Academy of sleep Medicine scoring criteria (1999) and were reviewed and interpreted by a board-certified sleep physician. Apnoea was defined as a complete cessation of airflow >10 seconds. Hypopnoeas were defined as decreased nasal pressure transducer amplitudes of 30% or more lasting >10 seconds and accompanied by 4% oxyhaemoglobin desaturations or arousals. Respiratory effort related arousals were defined as respiratory events that demonstrated increased respiratory efforts, clear drops in airflow, and arousals, but did not meet the criteria for apnoeas or hypopnoeas. The AHI was calculated by summing the number of apnoeas and hypopnoeas during sleep and dividing by the number of hours of sleep. Similarly, the RDI was calculated by summing the number of apnoeas, hypopnoeas, and respiratory effort related arousals and dividing by the number of hours of sleep. <u>Prevalence – 32 subjects</u> Time between measurement of index test and reference standard: not reported				
2×2 table	ESS	Reference standard +	Reference standard −	Total	
	Index test 1 +	10	7	17	
	Index test 1 −	22	8	30	
	Total	32	15	47	
2×2 table	STOP-Bang questionnaire, SB30	Reference standard +	Reference standard −	Total	
	Index test 2 +	31	10	41	
	Index test 2 −	1	5	6	
	Total	32	15	47	
2×2 table	STOP-Bang questionnaire, SB35	Reference standard +	Reference standard −	Total	
	Index test 3 +	30	10	40	
	Index test 3 −	2	5	7	
	Total	32	15	47	
2×2 table	STOP-Bang questionnaire, SB35 OR ESS	Reference standard +	Reference standard −	Total	
	Index test 4 +	31	12	43	

Reference	**Vana 2013[553]**				
	Index test 4 −	1	3	4	
	Total	32	15	47	
Statistical measures	Index test 1, Epworth Sleepiness Scale questionnaire Sensitivity 31.3% Specificity 53.3% Positive predictive value: 58.8% Negative predictive value: 26.7% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.423 (0.269 – 0.577) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index test 2, STOP-Bang questionnaire, SB30 Sensitivity 96.9% Specificity 33.3% Positive predictive value: 75.6% Negative predictive value: 33.3% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.651(0.524 – 0.778) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported Index test 3, STOP-Bang questionnaire, SB35 Sensitivity 93.8% Specificity 33.3% Positive predictive value: 75% Negative predictive value: 71.4% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.635 (0.505 – 0.766) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported				

Reference	Vana 2013[553]
	<u>Index test 4, STOP-Bang questionnaire, SB35 OR ESS</u> Sensitivity 96.9% Specificity 20% Positive predictive value: 72.1% Negative predictive value: 75% Area under the curve (95% confidence interval) All OSA (AHI≥5): 0.584 (0.475 – 0.694) Moderate-severe (AHI≥15): not reported Severe (AHI≥30): not reported
Source of funding	Not reported
Limitations	Risk of bias: Serious. Unclear if all study exclusions appropriate, and test results could have been interpreted with knowledge of the other test results. Thirteen of 60 (22%) did not undergo PSG and were excluded from analysis Indirectness: None
Comments	

Reference	Wu 2020[579]
Study type	Cross-sectional
Study methodology	Data source: Patients from the Pneumology Department of Zhongshan hospital were invited, screened, and enrolled into this study from September 2015 to October 2019. Recruitment: not reported
Number of patients	n = 328 recruited, 116 analysed
Patient characteristics	Age, mean (SD): 63 (range 57, 68) Gender (male to female ratio): 101/5 Ethnicity: not reported Setting: sleep laboratory

Reference	Wu 2020[579]
	Country: China Inclusion criteria: Age ≥40 years, ≤80; Diagnosis of COPD by GOLD guidelines. Exclusion criteria: Sleep less than 4 hours tested by PSG; Patients on home oxygen therapy or mechanical ventilation; Acute exacerbation of COPD in the preceding month; Other lung diseases; Sleep disorders other than OSA; Active or unstable cardiovascular diseases; Non-controlled arterial hypertension; Severe dementia; Severe untreated psychiatric conditions; Neuromuscular disease; Unwilling or undisciplined patient.
Target condition(s)	Overlap syndrome
Index test(s) and reference standard	Index test 1: Berlin questionnaire - comprises three categories including 10 questions. Part (category) 1 of BQ includes information on snoring and apnea, part 2 reflects daytime sleepiness or fatigue, and part 3 combines information about obesity and hypertension. BMI cut-off point was adjusted from 30.0 to 25.0 in MBQ compare to BQ. High risk of OSA is defined as ≥2 positive results of the three categories of BQ or MBQ. Index test 2: STOP-BANG questionnaire is a tool involving 3 subjective items (snoring, tiredness, and observed apnoea) and 5 objective items (hypertension, age, sex, body mass index (BMI), and neck circumference), a score ≥ 3 is regarded as having a moderate to severe risk of OSA. Reference standard PSG was tested in Sleep Center of Zhongshan Hospital by a PSG recorder (Respironics, Alice-5 Respironics, Pittsburgh, Pennsylvania, USA) within 1 week after pulmonary function examination, including electromyogram, electrocardiogram, electrooculogram, oronasal flow, thoracoabdominal movements, arterial oxygen saturation, body position, and snoring sounds. Breathing was recorded with nasal pressure transducer. PSG reports were analysed by two skilled specialists followed by guideline.21 Apnoea was defined as a decrease of at least 90% of airflow from baseline, lasting 10 s or longer, and hypopnea was defined as ≥30% decrease of airflow Lasting at least 10 s, associated with either an arousal or a ≥3% O2 saturation according to American Academy of Sleep Medicine criteria.22 The mean number of apnoeas and hypopneas per hour of sleep (Apnoea–Hypopnea Index [AHI]) was calculated, and OSA was diagnosed if the Apnoea–Hypopnea Index (AHI) was ≥5 events per hour. Prevalence – 62 subjects

Reference	**Wu 2020[579]**				
	Time between measurement of index test and reference standard: not reported but polysomnography was performed after the questionnaires were completed.				
2×2 table All OSAS (AHI ≥ 5) Berlin questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	33	66	39	
	Index test −	29	48	77	
	Total	62	54	116	
2×2 table All OSAS (AHI ≥ 5) STOP-BANG questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	52	22	74	
	Index test −	10	32	42	
	Total	62	54	116	
Statistical measures	<u>Index text: Berlin questionnaire, AHI ≥5</u> Sensitivity: 53% Specificity: 89% Positive predictive value: 85% Negative predictive value: 62% Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.71 (0.64-0.79) <u>Index text: STOP-BANG questionnaire, AHI ≥5</u> Sensitivity: 84% Specificity: 59% Positive predictive value: 70% Negative predictive value: 76% Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.72 (0.64 – 0.80)				
Source of funding	This work was supported by grants from the National Key Research and Development Program of China (NO. 2018YFC1313600) and the National Natural Science Foundation of China (No. 81570081, 81770083).				
Limitations	Risk of bias: None. Indirectness: None				

Reference	**Wu 2020[579]**
Comments	Paper only provides totals and not TP, FP, FN, or TN. These have been calculated using diagnostic calculation spreadsheet using sensitivity, specificity, PPV, NPV and totals.

1

Reference	**Xiong 2019[582]**
Study type	Cross-sectional
Study methodology	Data source: From Dec 2016 to Dec 2018, a total of 476 consecutive patients with suspected COPD were enrolled as the study candidates, those who met the inclusion criteria and exclusion criteria were enrolled as study participants. The inclusion criteria were: subjects aged at least 40 years old with a diagnosis of COPD conforming to GOLD guideline. Recruitment: not reported
Number of patients	n = 476 recruited, 431 analysed
Patient characteristics	Age, mean (SD): 67.4 (SD 8.9) Gender (male to female ratio): 388/43 Ethnicity: not reported Setting: sleep laboratory Country: China Inclusion criteria: subjects aged at least 40 years old with a diagnosis of COPD conforming to GOLD guideline Exclusion criteria: those were less than 40 years old or pregnant; patients with evidence of bronchial asthma, bronchiectasis, pulmonary fibrosis, intratracheal neoplasms, destructive sequelae of tuberculosis, etc; 3) patients with combined other diseases affecting survival, such as neoplastic diseases, renal insufficiency, or acute myocardial infarction; those with history of stroke, heart failure, neuromuscular, cognitive impairment or other mental and psychological diseases that would prevent completion of pulmonary function test, questionnaire or PSG; and 5) those who had other sleep disorders such as obesity hypoventilation syndrome.
Target condition(s)	COPD-OSAHS Overlap syndrome

Reference	Xiong 2019[582]				
Index test(s) and reference standard	Index test 1: ESS questionnaire - Epworth sleepiness scale (ESS) is used to measure drowsiness of subjects in different situations during the day. In China, a subject with a score of ≥9 is considered at high risk of excessive daytime sleepiness. Index test 2: Berlin questionnaire - (BQ) comprises three categories including 10 questions, high risk of OSA is defined as ≥ two positive results of the three categories. Index test 3: STOP-BANG - (SBQ) is a tool involving 4 dichotomous items and 4 clinical parameter items, a score≥ 3 is regarded as having a moderate to severe risk of OSA. Reference standard Polysomnography (PSG), all subjects with confirmed COPD underwent assessment of sleep events with a multichannel sleep diagnostic system (SOMNOscreen Plus Tele PSG, SOMNOmedics GmbH, Germany) in the sleep laboratory for no less than 7 hrs monitoring at night. All tracings were manually scored according to the American Academy of Sleep Medicine criteria.20 Subjects who experienced AHI ≥5 events/hour during sleep were considered to have OSA. Depending on the AHI, OSA severity is divided into mild (5–14.9), moderate (15–29.9), or severe (≥30). Prevalence – 335 subjects Time between measurement of index test and reference standard: not reported				
2×2 table All OSAS (AHI ≥ 5) ESS questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	242	51	293	
	Index test −	93	45	138	
	Total	335	96	431	
2×2 table All OSAS (AHI ≥ 5) Berlin questionnaire		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	272	58	330	
	Index test −	63	38	101	
	Total	335	96	431	
2×2 table All OSAS (AHI ≥ 5)		Reference standard +	Reference standard −	Total	Calculated by NGC
	Index test +	311	57	368	

Reference	**Xiong 2019[582]**			
STOP-BANG questionnaire	Index test −	24	39	63
	Total	335	96	431
Statistical measures	Index text: ESS questionnaire, AHI ≥5 (≥3% oxygen desaturation) Sensitivity: 72.2% Specificity: 46.9% Positive predictive value: not reported Negative predictive value: not reported Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.609(0.561 – 0.655) Index text: Berlin questionnaire, AHI ≥5 (≥3% oxygen desaturation) Sensitivity: 81.2% Specificity: 39.6% Positive predictive value: not reported Negative predictive value: not reported Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.634(0.578 – 0.680) Index text: Stop-Bang questionnaire, AHI ≥5 (≥3% oxygen desaturation) Sensitivity: 92.8% Specificity: 40.6% Positive predictive value: not reported Negative predictive value: not reported Area under the curve, manually scored, (95% confidence interval) All OSA (AHI≥5): 0.723 (0.723 (0.678 – 0.764)			
Source of funding	This work was supported by the National Key Research and Development Program of China (project number: 2016YFC1304403). The sponsor had no role in the design or conduct of this research.			
Limitations	Risk of bias: Serious. Enrolment method unclear and inclusion/exclusion criteria not reported Indirectness: Serious. AHI ≥10			
Comments	Paper only provides totals and not TP, FP, FN, or TN. These have been calculated using diagnostic calculation spreadsheet using sensitivity, specificity and totals.			

Reference	**Xiong 2019[582]**

Appendix E: Coupled sensitivity and specificity forest plots and sROC curves

E.1 Coupled sensitivity and specificity forest plots-OSAHS

Figure 2: Berlin questionnaire (reference standard: AHI/RDI/ODI >5 by hospital polysomnography)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmadi 2008	38	38	18	36	0.68 [0.54, 0.80]	0.49 [0.37, 0.61]
Cowan 2014	87	29	7	2	0.93 [0.85, 0.97]	0.06 [0.01, 0.21]
Felfeli 2020	9	2	12	4	0.43 [0.22, 0.66]	0.67 [0.22, 0.96]
Pereira 2013	100	9	16	3	0.86 [0.79, 0.92]	0.25 [0.05, 0.57]

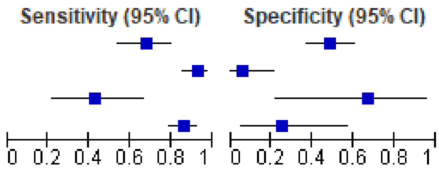


Figure 3: Epworth Sleepiness scale (reference standard: AHI/RDI/ODI >5 by hospital polysomnography)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cowan 2014	63	17	29	11	0.68 [0.58, 0.78]	0.39 [0.22, 0.59]
Hesselbacher 2012	852	139	725	184	0.54 [0.52, 0.57]	0.57 [0.51, 0.62]
Vana 2013	10	7	22	8	0.31 [0.16, 0.50]	0.53 [0.27, 0.79]

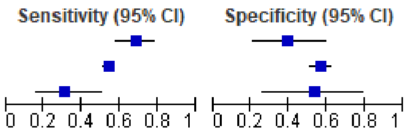


Figure 4: STOP BANG (reference standard: AHI/RDI/ODI >5 by hospital polysomnography)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Boynton 2013	134	25	35	25	0.79 [0.72, 0.85]	0.50 [0.36, 0.64]
Cowan 2014	88	21	5	9	0.95 [0.88, 0.98]	0.30 [0.15, 0.49]
Duarte 2020 Derivation cohort	2602	389	382	398	0.87 [0.86, 0.88]	0.51 [0.47, 0.54]
Duarte 2020 Validation Cohort	2501	366	341	398	0.88 [0.87, 0.89]	0.52 [0.48, 0.56]
Felfeli 2020	18	3	3	3	0.86 [0.64, 0.97]	0.50 [0.12, 0.88]
Pereira 2013	104	7	12	5	0.90 [0.83, 0.95]	0.42 [0.15, 0.72]
Sangkum 2017	156	37	6	9	0.96 [0.92, 0.99]	0.20 [0.09, 0.34]
Vana 2013	30	10	2	5	0.94 [0.79, 0.99]	0.33 [0.12, 0.62]

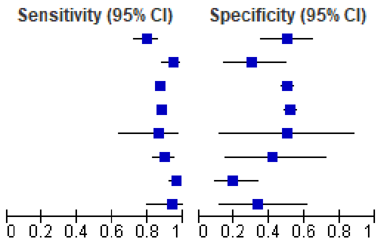
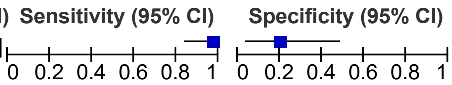


Figure 5: STOP BANG or ESS (reference standard: AHI/RDI/ODI >5 by hospital polysomnography)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Vana 2013	31	12	1	3	0.97 [0.84, 1.00]	0.20 [0.04, 0.48]



sROC curves

Figure 6: **Berlin questionnaire**

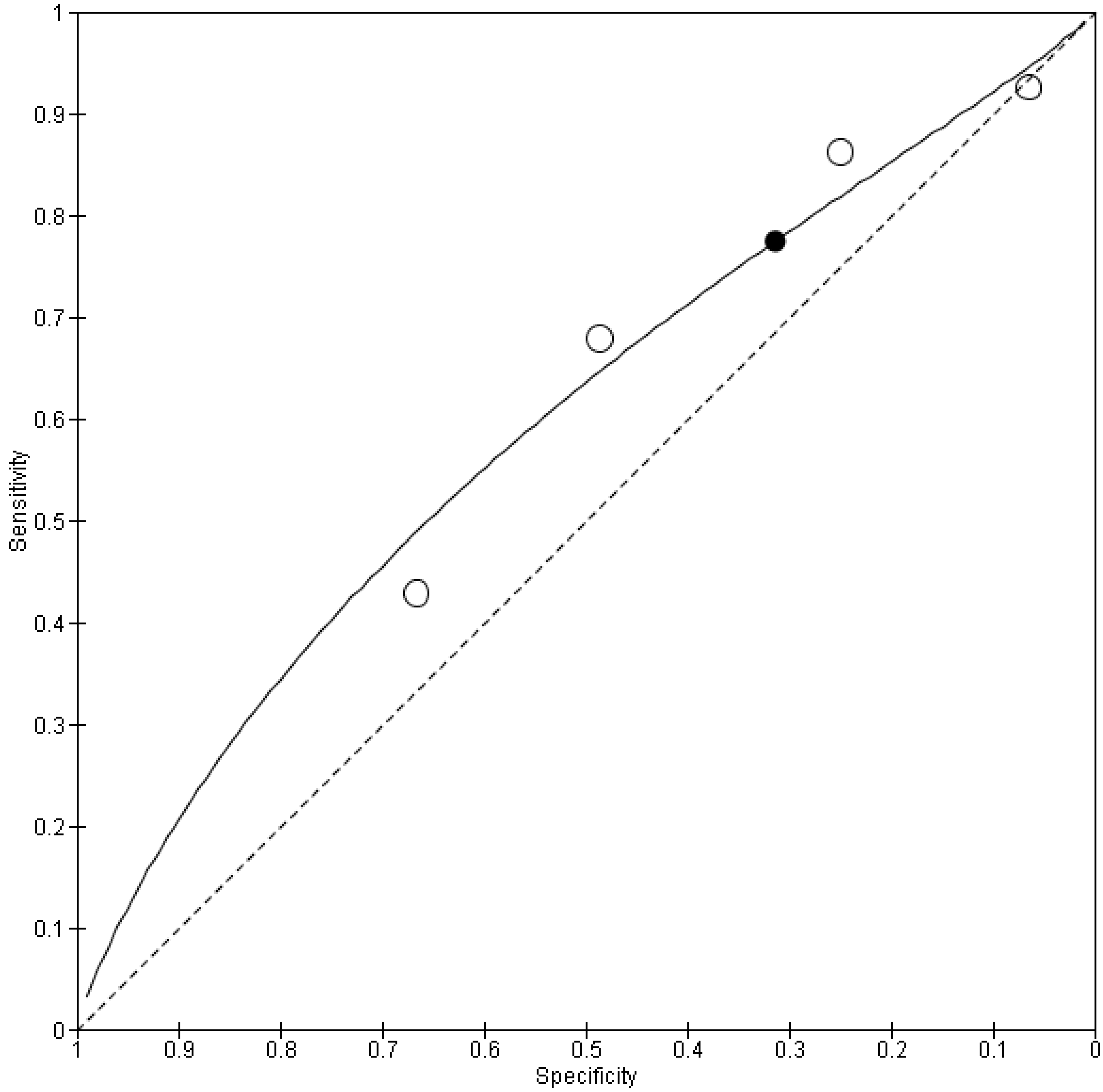


Figure 7: Epworth Sleepiness scale

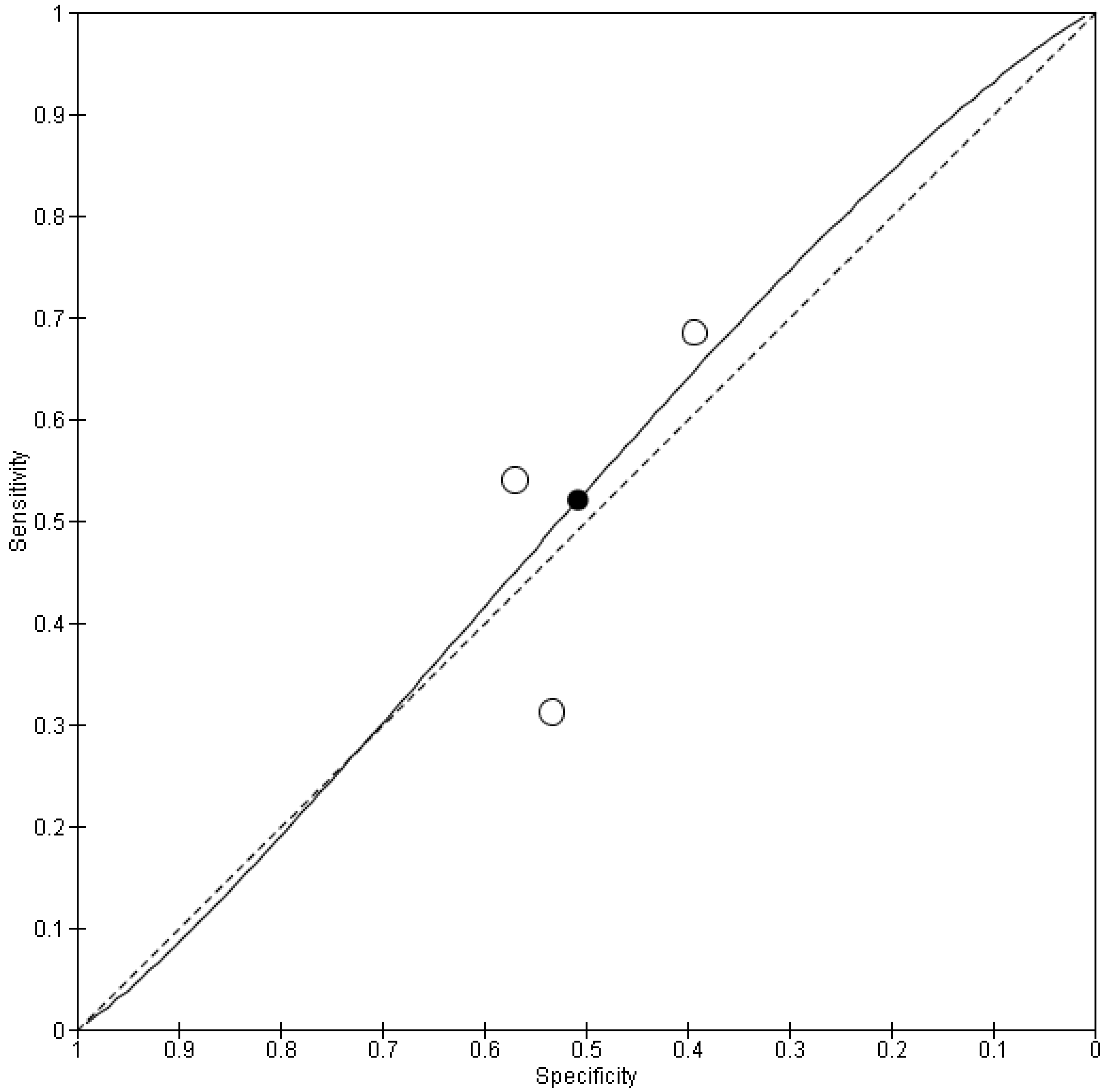


Figure 8: STOP BANG

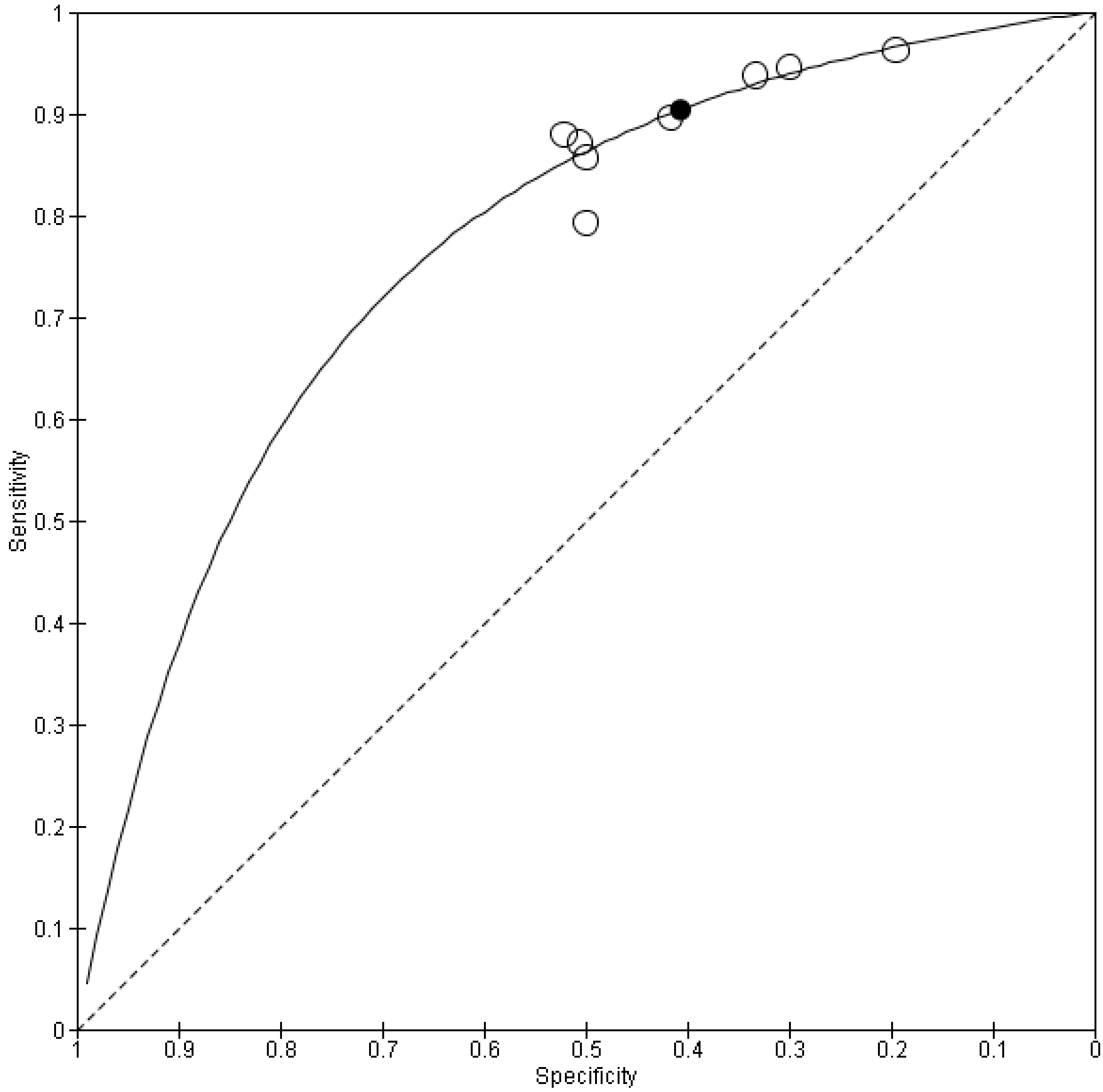
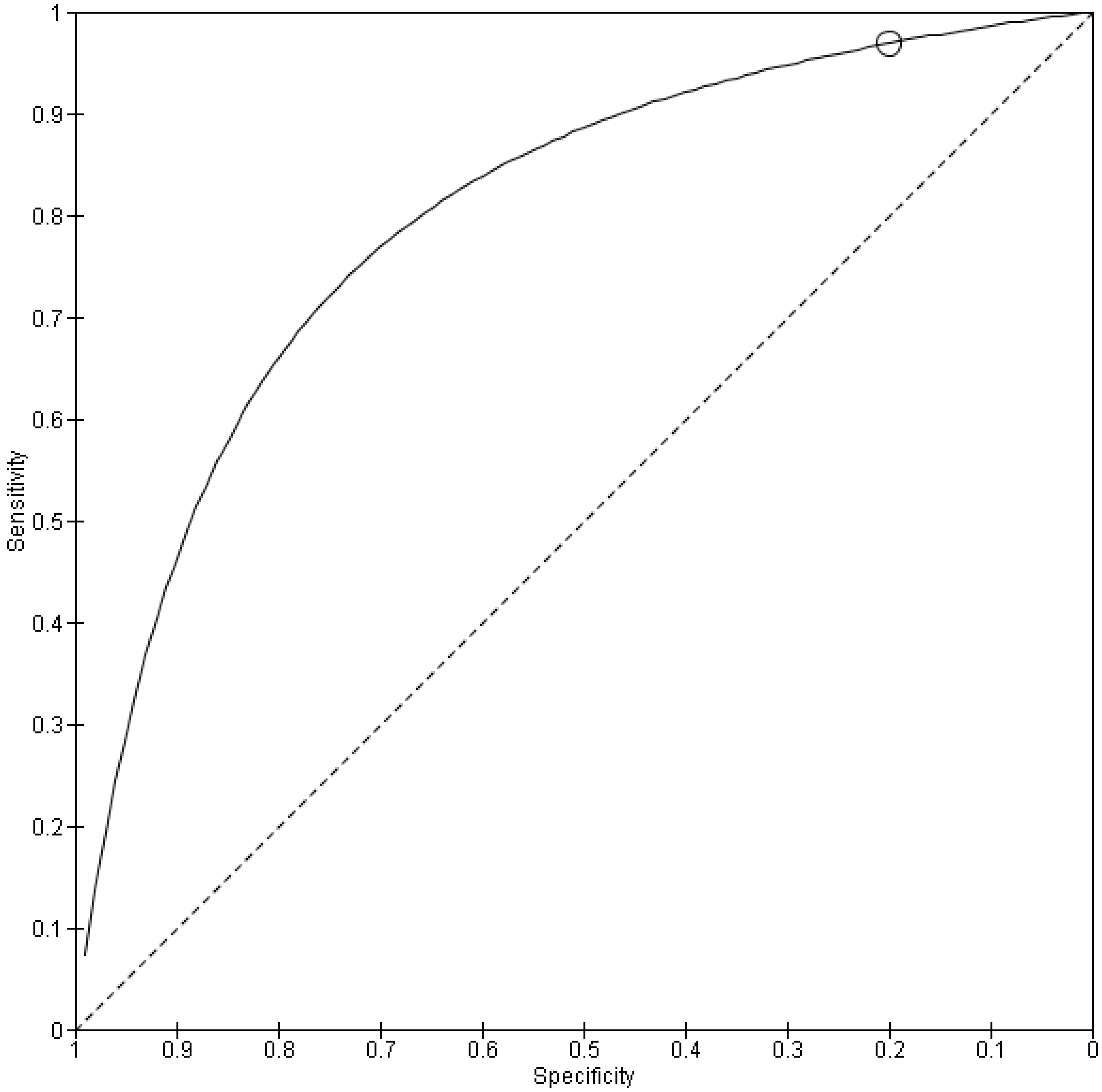


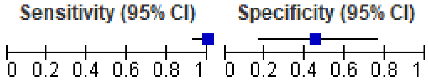
Figure 9: STOP BANG or ESS



E.2 Coupled sensitivity and specificity forest plots-OSAHS (patients with Down syndrome)

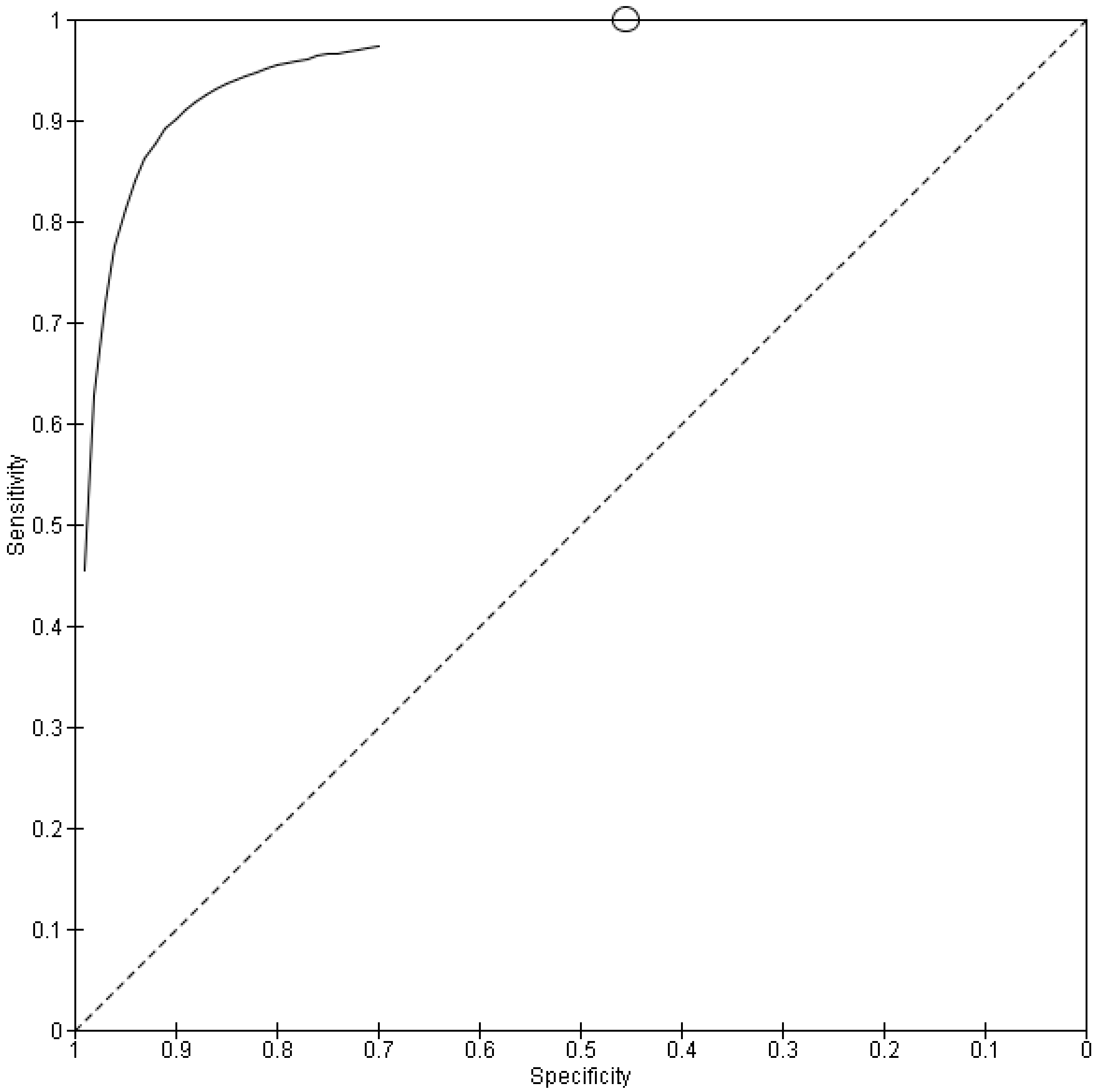
Figure 10: STOP-BANG

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
de Carvalho, 2020	49	6	0	5	1.00 [0.93, 1.00]	0.45 [0.17, 0.77]



sROC curves

Figure 11: STOP-BANG



E.3 Coupled sensitivity and specificity forest plots-COPD-OSAHS overlap syndrome

Figure 12: Berlin

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
WU 2020	33	6	29	48	0.53 [0.40, 0.66]	0.89 [0.77, 0.96]
Xiong 2020	272	58	63	38	0.81 [0.77, 0.85]	0.40 [0.30, 0.50]

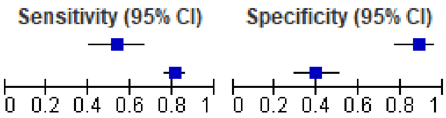


Figure 13: Epworth Sleepiness scale

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Xiong 2020	242	51	93	45	0.72 [0.67, 0.77]	0.47 [0.37, 0.57]

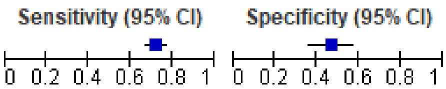
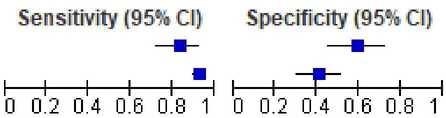


Figure 14: Stop-Bang

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
WU 2020	52	22	10	32	0.84 [0.72, 0.92]	0.59 [0.45, 0.72]
Xiong 2020	311	57	24	39	0.93 [0.90, 0.95]	0.41 [0.31, 0.51]



sROC curves

Figure 15: Berlin

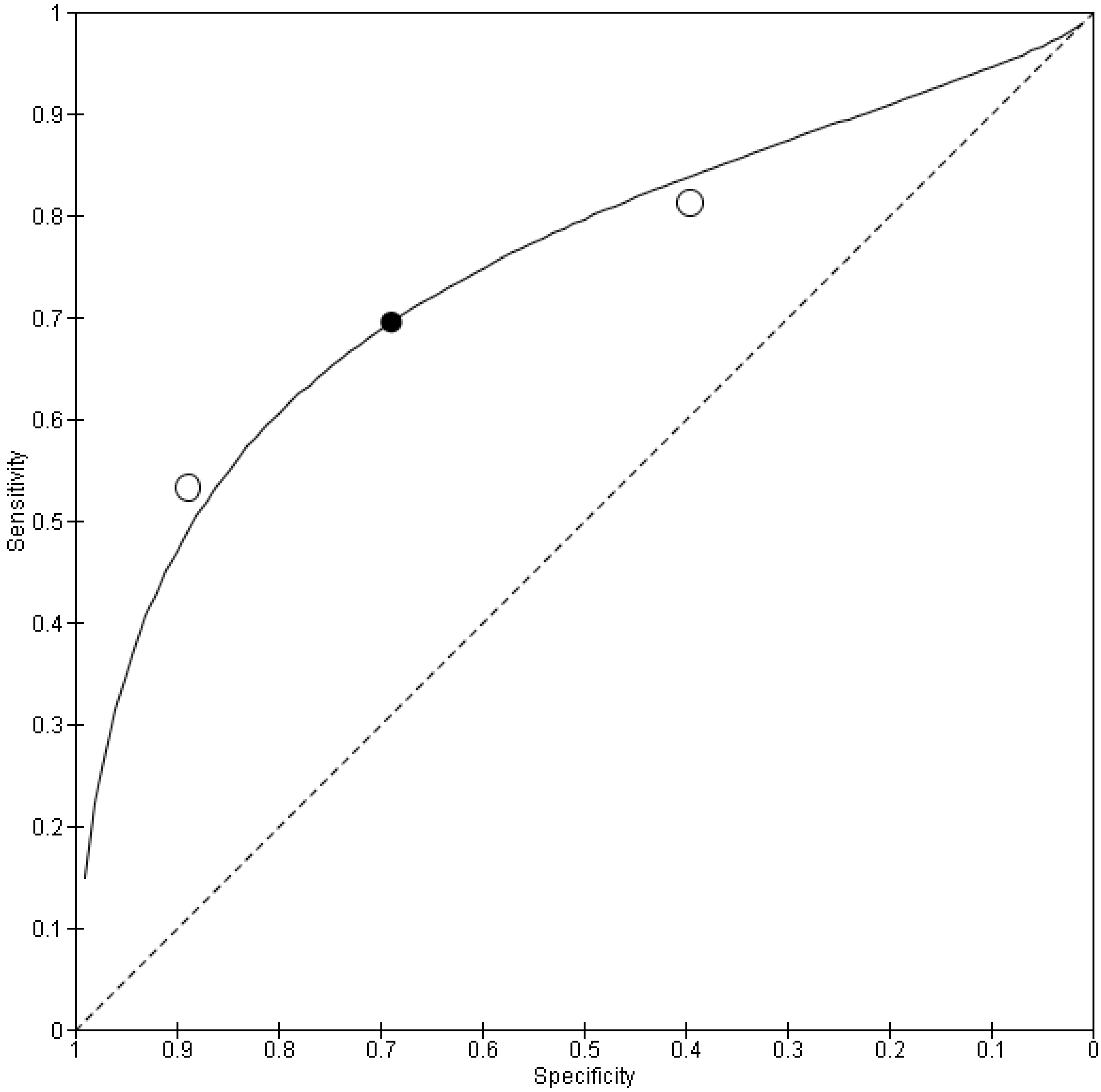


Figure 16: Epworth sleepiness scale

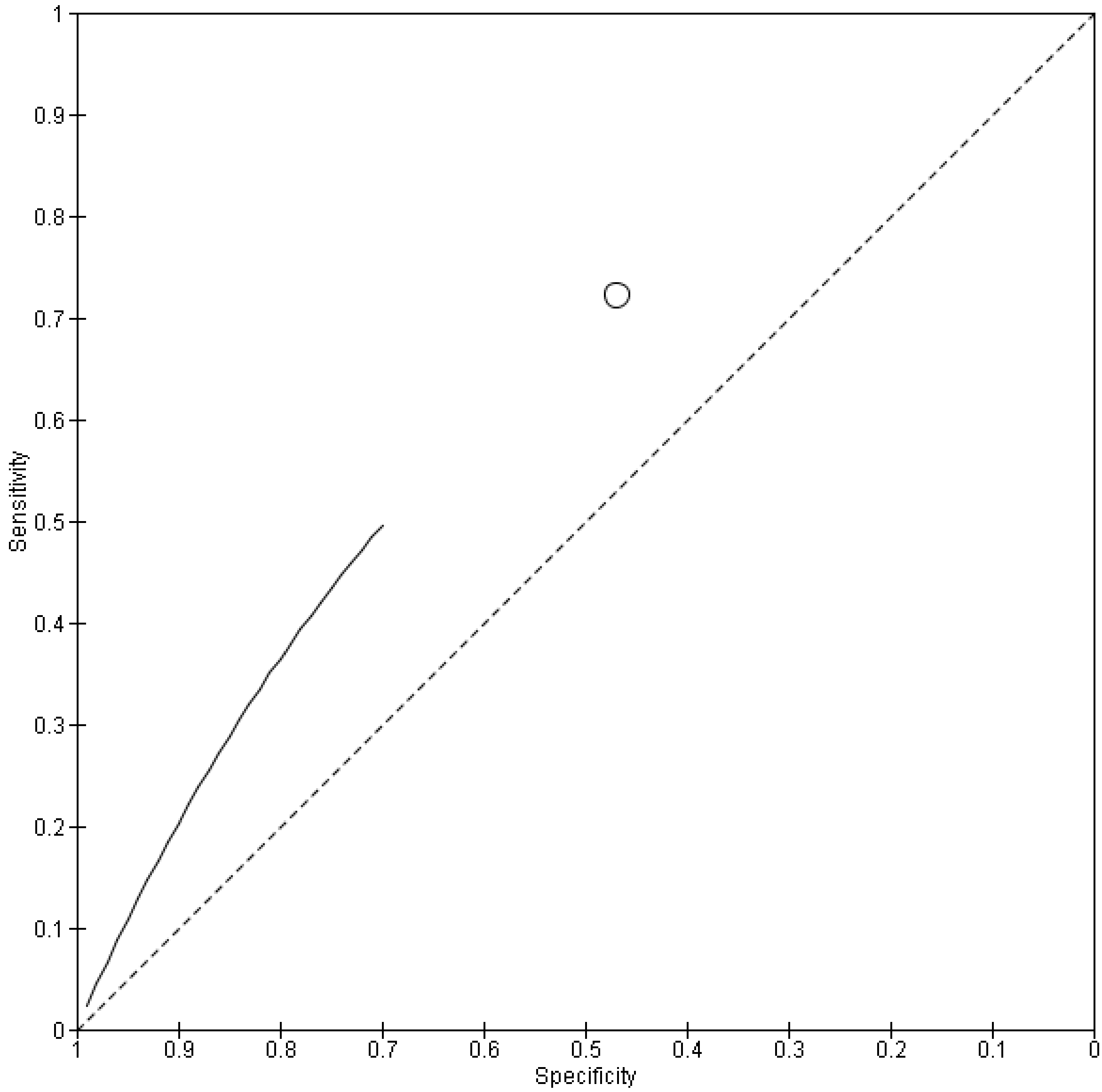
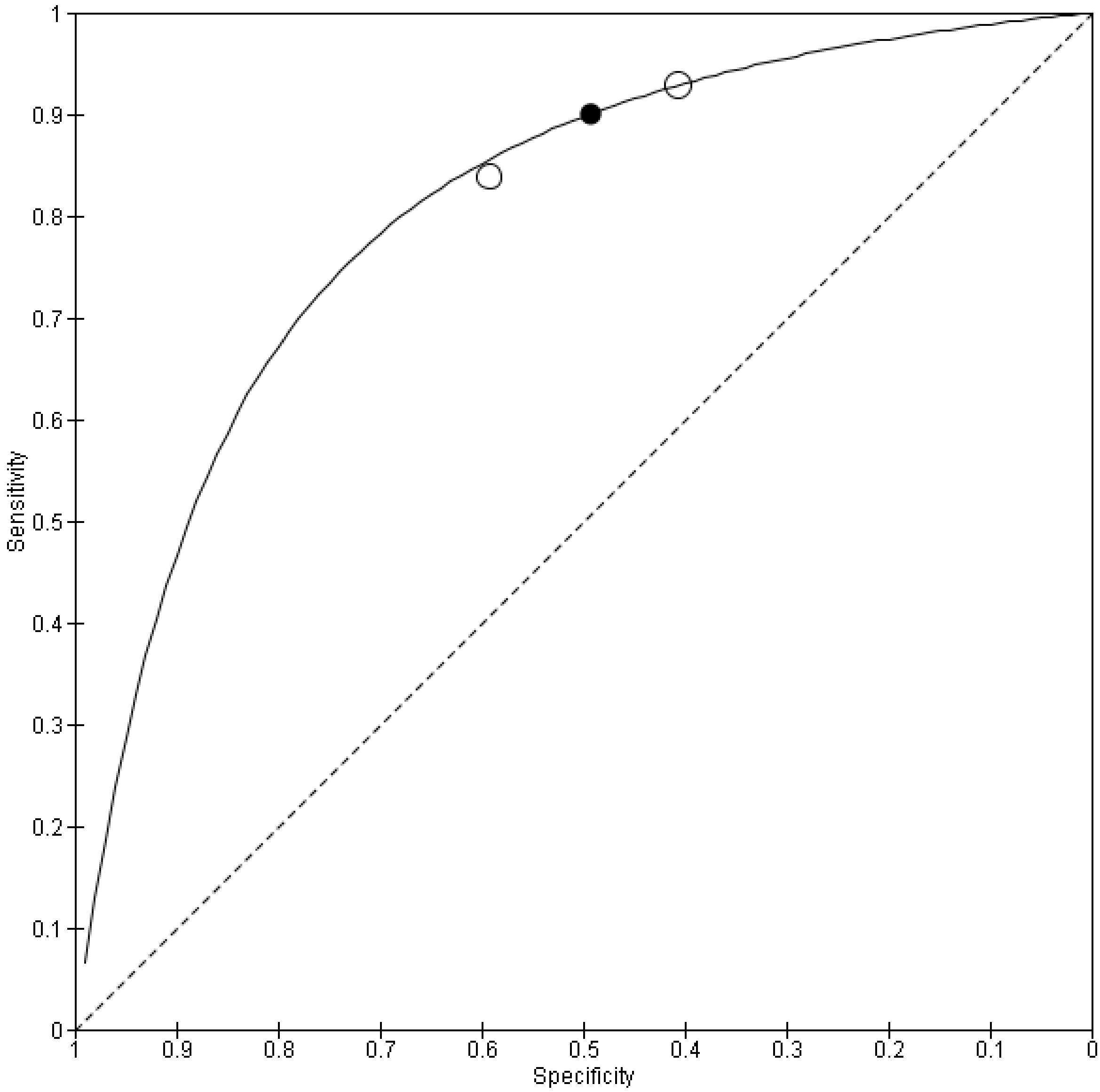
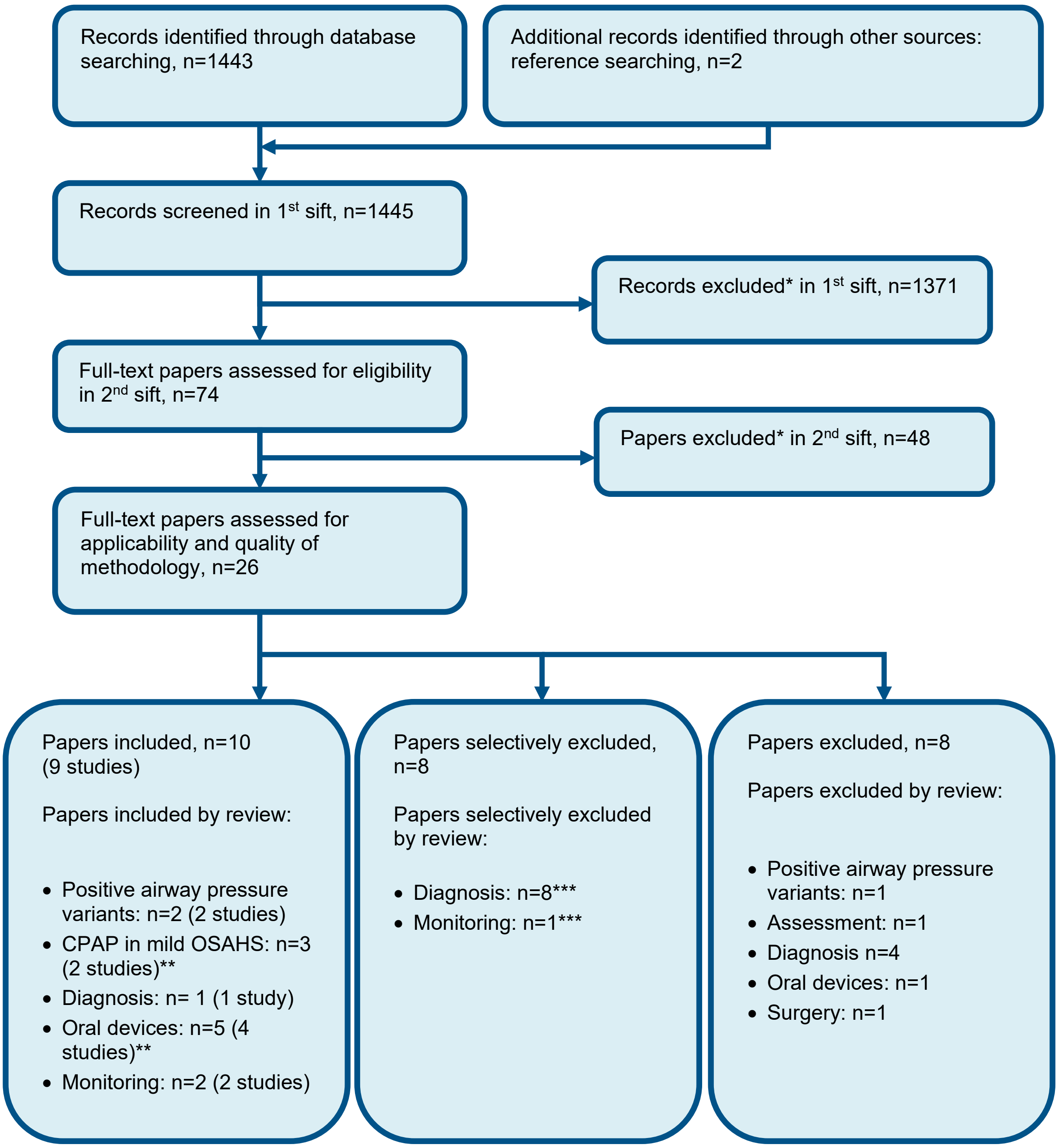


Figure 17: Stop-Bang



Appendix F: Health economic evidence selection

Figure 18: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language
** Two studies (in three papers) were included for two different questions
*** One study was considered for two different questions

Appendix G: Health economic evidence tables

None

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 11: Studies excluded from the clinical review

Reference	Exclusion Reason
Aaronson 2012[2]	Not an assessment scale – hospital oximetry, ODI recorded using polygraph Inappropriate population -stroke patients
Aaronson 2014[1]	Inappropriate assessment scale - SAS questionnaire Inappropriate reference standard -hospital oximetry Inappropriate population –stroke patients
Abad 2016[3]	Not an assessment scale – SleepWise nonintrusive video system
Abdelghani 2004[4]	Inappropriate reference standard – PSG at home or in hospital
Abdeyrim 2015[7]	No usable outcomes – no diagnostic accuracy data
Abdeyrim 2016[5]	Inappropriate study design – case control study/ no diagnostic accuracy study
Abdeyrim 2016[6]	Not an assessment scale - impulse oscillometry
Abdullah 2018[8]	Inappropriate assessment scale - The Bahasa Malaysia version of the STOP-BANG questionnaire
Abeyratne 2005[10]	Not an assessment scale - novel feature termed the 'intra-snore-pitch-jump' (ISPJ) to diagnose OSA.
Abeyratne 2013[9]	Inappropriate assessment scale - snore based multi-feature class OSA screening tool
Abraham 2006[11]	Inappropriate population - class III systolic heart failure patients with suspected sleep disordered breathing Not an assessment scale - cardiorespiratory testing system (ClearPath).
Abrahamyan 2018[12]	Systematic review - references checked
Abrishami 2010[13]	Systematic review - references checked
Abumuamar 2018[14]	Inappropriate population - patients with atrial fibrillation, recruited from arrhythmia clinics. Not general population
Acharya 2011[15]	Not an assessment scale – electrocardiogram signals
Adachi 2003[16]	Not an assessment scale – pulse rate rise
Adams 2016[17]	Inappropriate reference standard – home unattended polysomnography
Akhter 2018[19]	Not an assessment scale – snoring sound

Reference	Exclusion Reason
Alakuijala 2016[20]	Not an assessment scale – snoring sound
Alchakaki 2016[21]	Not an assessment scale – snoring sound
Alhouqani 2015[22]	Inappropriate assessment scale – Arabic version of stop bang questionnaire
Almazaydeh 2012[23]	Not an assessment scale – ECG data
Alshaer 2013[24]	Not an assessment scale – acoustic analysis of breathing sounds
Alshaer 2016[25]	Not an assessment scale - cordless acoustic portable device (BresoDx™)
Alvarez 2006[28]	Not an assessment scale – hospital oximetry
Alvarez 2006[31]	Not an assessment scale - nocturnal oximetry using Cross Approximate Entropy (Cross-ApEn).
Alvarez 2007[30]	Not an assessment scale – hospital oximetry
Alvarez 2009[29]	Not an assessment scale – hospital oximetry
Alvarez 2010[27]	Not an assessment scale – oxygen desaturation derived from PSG
Alvarez 2020[26]	Inappropriate reference standard - home polysomnography
Amra 2013[33]	Not an assessment scale - pulmonary function tests Inappropriate population – patients with sleep disordered breathing
Amra 2018[34]	Systematic review - references checked
Amra 2018[32]	Inappropriate assessment scale – Persian questionnaires
Andres-Blanco 2017[35]	Not an assessment scale – laboratory oximetry
Andreu 2012[36]	Inappropriate study design – RCT patients with negative tests were also followed up
Araujo 2018[37]	Not an assessment scale – Apnea link Tm single channel device
Arrazola-Cortes 2017[38]	Inappropriate study design – all patients underwent polysomnography only
Arunsurat 2016[39]	Inappropriate study design – not a diagnostic accuracy study, patients got Berlin questionnaire, no reference standard
Assefa 2016[40]	Not an assessment scale – ApneaStrip device
Aurora 2018[41]	Inappropriate population – Patients with heart failure scored for obstructive and central disordered breathing (ApneaLink Plus) Inappropriate index test - The nasal pressure transducers for polysomnography and respiratory polygraphy units were

Reference	Exclusion Reason
	connected to one nasal cannula through a three-way valve for contemporaneous nasal airflow measurement. The two recording systems were synchronized such that the both tests had equivalent total recording time
Avincsal 2017[42]	Inappropriate assessment scale – modified Stop Bang questionnaire, using modified modified Mallampi score
Ayappa 2008[43]	Inappropriate population – patients with suspected sleep disordered breathing Not an assessment scale - The ARES™ consists of the Unicorder device, a self-administered questionnaire, and off-line analysis software.
Ayas 2003[44]	Inappropriate population – patients without suspected OSA
Babaeizadeh 2011[45]	Not an assessment scale - electrocardiogram derived respiration Inappropriate population –sleep disordered breathing
Bagnato 2000[46]	Not an assessment scale – AutoSet^{tm} (AS) system
BaHammam 2015[47]	Inappropriate assessment scale – Arabic version of Stop Bang questionnaire
BaHammam 2011[48]	Not an assessment scale - ApneaLink™ (AL) is a single-channel type-4 device
Ballester 2000[49]	Not an assessment scale – portable respiratory recordings device Inappropriate population – general population, not people with suspected OSAHS
Baltzan 2000[50]	Not an assessment scale - oximetry, but not oximetry alone - OxiFlow (OF) device which combines oximetry with recording of thermistor airflow.
Banhiran 2014[51]	Not an assessment scale – home polysomnography
Banhiran 2014[52]	Inappropriate assessment scale – Thai version of Stop-Bang questionnaire
Barak-Shinar 2013[53]	Inappropriate population – Sleep disordered breathing
Barreiro 2003[54]	Inappropriate study design/inappropriate comparison – polysomnography automatic reading was compared to polysomnography manual reading
Bausmer 2010[55]	No relevant outcomes – no diagnostic accuracy data
Bauters 2020[56]	Inappropriate reference standard – home polygraphy

Reference	Exclusion Reason
Beattie 2013[57]	Not an assessment scale – LC system consists of pressure sensors (i.e. LCs) that are placed under the supports of a bed. The LCs detect movement on the bed as fluctuations in the forces supported by each of the bed legs.
Behar 2015[58]	Not assessment scale – Machine learning, screening application for smartphones was analysed
Behar 2020[59]	Not an assessment scale - OxyDOSA, a published machine learning model, was trained to distinguish between non-OSA and OSA individuals using the ODI computed while including versus excluding overnight desaturations overlapping with a wake period, thus mimicking portable and PSG oximetry analyses, respectively
Ben-Israel 2012[60]	Not an assessment scale - Snore sounds were recorded using a directional condenser microphone placed 1 m above the bed.
Berry 2008[61]	Inappropriate study design – RCT patients randomised to PM-APAP and polysomnography, no diagnostic accuracy data
Best 2013[62]	Inappropriate population – patients with treatment resistant depression. Not general population.
Bille 2015[63]	Inappropriate reference standard - cardiorespiratory monitoring
Bingol 2016[64]	Inappropriate assessment scale – Stop – Bang questionnaire was used to predict OHS syndrome
Bohning 2011[65]	Not an assessment scale – hospital oximetry
Borsini 2015[67]	Inappropriate reference standard – respiratory polygraphy
Borsini 2019[66]	Inappropriate reference standard - respiratory polygraphy
Bradley 1995[69]	Not an assessment scale - Autoset Inappropriate population – unclear what population was included
Braganza 2020[70]	Inappropriate study design - non diagnostic accuracy study, study looked at threshold values for excluding CPAP failure
Bravata 2018[71]	Not assessment scale - patients were randomised to enhanced intervention, standard intervention and control group.
Brown 2014[72]	Inappropriate population – patients within 45 days of stroke onset, patients with predominantly central sleep apnoea were not excluded.

Reference	Exclusion Reason
	Not an assessment scale – ApneaLink Plus – 3 channels
Bsoul 2011[73]	Not an assessment scale - Real-time sleep apnea monitor using single-lead ECG
Cai 2013[74]	Not an assessment scale – Chinese version of ESS questionnaire
Calleja 2002[75]	Not assessment scale: /diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Carter 2004[76]	Not an assessment scale – LifeShirt (LS, VivoMetrics, Inc; Ventura CA)
Chai-Coetzer 2017[77]	Not an assessment scale–patients randomised full PSG and home RP all participants including those with negative tests were followed up
Chen 2011[78]	Inappropriate assessment scale - Chinese ESS/ Inappropriate population - sleep disordered breathing
Chiner 1999[79]	Not an assessment scale – hospital oximetry
Chiu 2017[80]	Systematic review - references checked
Christensson 2018[81]	Inappropriate reference standard- hospital polygraphy
Chu 2020[82]	Inappropriate study design - patients were randomised to high flux haemodialysis (HF-HD) followed by 2 month haemodiafiltration or vice-versa with 1 month washout via HF-HD
Chung 2007[85]	Inappropriate population – sleep disordered breathing
Chung 2008[88]	Inappropriate population – surgical patients, tertiary care
Chung 2012[83]	Inappropriate reference standard – sleep disordered breathing
Chung 2012[84]	Inappropriate population – preoperative patients, tertiary care
Chung 2013[87]	Inappropriate population – preoperative patients
Chung 2014[86]	Inappropriate population – preoperative patients, tertiary care
Claman 2001[89]	Inappropriate study design - not questionnaire/diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Clark 2009[90]	Inappropriate reference standard – Embletta polygraphy
Cooper 1991[91]	Not an assessment scale - Biox IIA ear oximeter with the output signal connected to a Rikadenki three channel chart recorder.

Reference	Exclusion Reason
Corral 2017[92]	–Not assessment scale: : home oximetry, hospital and home RP
Crowley 2013[94]	Inappropriate population – sleep disordered breathing
Damiani 2013[95]	No relevant outcomes
de Oliveira 2009[97]	Not assessment scale: home oximetry, hospital and home RP
de Silva 2011[98]	Not an assessment scale – snoring sounds
de Vries 2015[100]	Inappropriate population patients with heart failure/2 channel sleep screening tool
de Vries 2018[99]	Inappropriate population – bariatric surgery patients
Deflandre 2017[101]	Inappropriate population – surgical patients, tertiary care
Deflandre 2018[102]	Inappropriate comparison – questionnaires compared with each other
del Campo 2006[103]	Not an assessment scale – hospital oximetry
Dette 2016[104]	Inappropriate population – sleep disordered breathing
Donovan 2020[105]	Inappropriate study design - not a diagnostic accuracy study, study looked at agreement between sleep specialists and registered nurses
Doshi 2015[106]	Inappropriate reference standard – portable monitoring
Douglas 1992[107]	Not an assessment scale - polysomnography
Duarte 2017[109]	Not appropriate assessment scale – Portuguese Stop-bang questionnaire Inappropriate study design – accuracy of conditional probabilities was analysed
Dzieciolowska-Baran 2020[110]	Book chapter
Ebben 2016[111]	Not an assessment scale – hospital oximetry
Ehsan 2020[112]	Not assessment scale - accuracy of combined home and hospital oximetry in infants was analysed
El Shayeb 2014[113]	Systematic review - references checked
Ellingsen 2020[114]	Not assessment scale- accuracy of combined home and hospital oximetry in infants was analysed
Emsellem 1990[115]	Not an assessment scale - diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Epstein 1998[116]	Not an assessment scale - hospital oximetry
Eris Gulbay 2014[117]	Inappropriate study design – not diagnostic accuracy study

Reference	Exclusion Reason
Erman 2007[118]	Not an assessment scale - single channel ApneaLink
Ernst 2015[119]	Inappropriate population - snoring, sleep apnea, or diurnal somnolence
Esnaola 1996[120]	No relevant outcomes/inappropriate comparison - selected cut-off points corresponding to the specificity closest to 0.97
Fabius 2019[121]	Inappropriate reference standard - portable monitoring
Faria 2015[122]	Inappropriate assessment scale – Portuguese version Berlin and ESS questionnaires
Farney 1986[123]	Not an assessment scale – hospital oximetry
Fasbender 2019[124]	Not an assessment scale - photoplethysmography
Fawale 2016[125]	No relevant outcomes – no diagnostic accuracy data
Firat 2012[127]	Inappropriate population - all heavy-vehicle driver's license applicants
Fletcher 2000[128]	Inappropriate reference standard – no polysomnography
Forni Ogna 2015[129]	Inappropriate population – hemodialysis patients
Frangopoulos 2019[130]	Inappropriate reference standard -no polysomnography
Fry 1998[131]	No relevant outcomes – no diagnostic accuracy data
Fuller 2014[132]	Inappropriate comparison – patients randomised to risk assessment only vs risk assessment+ nasal flow group
Gabryelska 2020[133]	inappropriate assessment scale - BOAH scale
Gagnadoux 2002[134]	Not an assessment scale – home polysomnography
Gantner 2010[135]	Inappropriate reference standard – home polysomnography
Garg 2014[136]	Not an assessment scale - diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Gasa 2013[137]	Inappropriate population- bariatric patients Inappropriate study design – predictive models using anthropometric and clinical predictors were analysed
Geessinck 2018[138]	Inappropriate study design – Markov model
Gergely 2009[139]	Not an assessment scale – sleep strip
Giampa 2018[140]	Inappropriate assessment scale – NoSAS questionnaire

Reference	Exclusion Reason
Gjerve 2011[141]	Not assessment scale: home oximetry, hospital and home RP
Glantz 2013[142]	Inappropriate population – coronary artery disease patients No relevant outcomes – no diagnostic accuracy data
Glazer 2018[143]	Inappropriate population- patients undergoing bariatric surgery, tertiary care
Goldstein 2018[144]	Not an assessment scale – HSAT, no diagnostic accuracy data
Golpe 1999[146]	No relevant outcomes – validity indices of oximetry parameters were calculated
Golpe 2002[145]	Inappropriate study design - not questionnaire/diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Goodrich 2009[147]	Not assessment scale: home oximetry, hospital and home RP
Graco 2018[148]	Inappropriate population - chronic tetraplegia Inappropriate assessment scale – tetraplegia specific questionnaire
Gros 2015[149]	Inappropriate population – Parkinson's disease Not an assessment scale – Embletta gold Natus, three channels
Grover 2008[151]	Inappropriate population – sleep disordered breathing
Grover 2018[150]	No relevant outcomes – no diagnostic accuracy data
Gu 2020[152]	Not an assessment scale - Belun ring platform, which captures oxygen saturation, photophlethysmography accelerometers signals
Gugger 1997[153]	Not an assessment scale – Resmed AutoSet
Guimaraes 2012[154]	Not in English
Gumb 2018[155]	Inappropriate population – patients recruited without regard to OSA symptoms
Gunduz 2018[156]	No relevant outcomes – no diagnostic accuracy data
Gupta 2016[157]	Inappropriate assessment scale - Hindi Berlin questionnaire
Gyulay 1993[158]	Inappropriate study design/ Not an assessment scale - diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Ha 2014[159]	Inappropriate assessment scale – Chinese questionnaires
Hara 2006[160]	Not an assessment scale – voice program

Reference	Exclusion Reason
Hashizaki 2014[161]	Not an assessment scale - contactless biomotion sensor
Heneghan 2008[162]	Not an assessment scale - Electrocardiogram recording
Herer 2002[163]	Inappropriate population – Sleep disordered breathing
Hilmisson 2019[165]	Not an assessment scale - ECG analysis
Holmedahl 2019[166]	Not assessment scale- patients were randomised to beetroot juice containing nitrate or placebo
Hong 2018[167]	Inappropriate population – sleep disordered breathing
Horvath 2018[168]	Inappropriate population – bariatric surgery patients, tertiary care Inappropriate reference standard – hospital polygraphy
Hui 2017[169]	Not assessment scale- ambulatory approach versus the hospital-based approach
Hussain 2003[170]	Not assessment scale- patients with normal oximetry results were recruited
Iber 2004[171]	Not an assessment scale – home polysomnography
Ibrahim 2007[172]	No relevant outcomes – nodiagnostic accuracy data
Ioachimescu 2020[173]	Not assessment scale- non diagnostic accuracy study, study analysed performance of peripheral arterial tonometry
Isaac 2017[174]	Inappropriate population – patients admitted for any medical reason
Jen 2020[175]	Not assessment scale: home oximetry, hospital and home RP
Jobin 2007[176]	Systematic review - references checked
Kahal 2020[177]	Inappropriate comparison - respiratory poligraphy manual scoring compared to respiratory polygraphy automatic scoring
Kaminska 2010[178]	Systematic review - references checked
Karakoc 2014[179]	Inappropriate reference standard – no polysomnography
Karaloglu 2017[180]	Inappropriate comparison – polysomnography vs polysomnography
Katzan 2016[181]	Inappropriate population – cerebrovascular patients (ischemic stroke, intracerebral haemorrhage and carotid occlusion
Khandoker 2009[182]	Not an assessment scale - short-term electrocardiogram recordings
Kicinski 2016[183]	Inappropriate population – sleep disordered breathing
Kiely 1996[184]	Not an assessment scale -ResCare Autoset

Reference	Exclusion Reason
Kim 2015[185]	Inappropriate assessment scale – Korean questionnaires
Kim 2015[186]	Inappropriate study design - economic analysis
Korvel-Hanquist 2018[187]	Inappropriate assessment scale– Danish Stop Bang questionnaire
Kristiansen 2020[188]	Inappropriate comparison - manual respiratory polygraphy compared to automatic respiratory polygraphy
Kukwa 2020[189]	Inappropriate study design - study comparing in-laboratory PSG and HSAT using a peripheral arterial tone (PAT) technology device. No diagnostic accuracy data
Kum 2015[191]	Inappropriate assessment scale – Turkish ESS questionnaire
Kum 2018[190]	Not an assessment scale – oximetry from polysomnography
Kuna 2011[192]	Not assessment scale– analysis under 3 conditions 1. traditional PSG, 2. modified PSG + Lifeshirt, 3. Lifeshirt at home. Lifeshirt – 3 channels
Lachapelle 2019[193]	Inappropriate population– patients with inconclusive home study results were included in the analysis
Lado 2011[194]	Not assessment scale– assessment of ECG databases
Lajoie 2020[195]	Not assessment scale- aim of the study was to determine the accuracy of home oximetry to distinguish between nocturnal oximetry desaturation relapsed to COPD alone or to sleep apnoea in patients with moderate to severe COPD who have significant nocturnal hypoxemia with clinical changes in saturation/ no relevant outcomes - no sensitivity or specificity data
Lam 2010[196]	Inappropriate population – patients screened from Diabetes mellitus database No relevant outcomes
Laohasiriwong 2013[197]	No relevant outcomes – no diagnostic accuracy data
Laporta 2012[198]	Inappropriate population – Ischemic heart disease patients. Patients recruited from cardiology clinic. Not general population
Laranjeira 2018[199]	Inappropriate study design – not a diagnostic accuracy study
Lauritzen 2018[200]	Inappropriate assessment scale – Danish Berlin questionnaire
Lazaro 2020[201]	Not in English

Reference	Exclusion Reason
Le 2016[202]	Inappropriate study design – not diagnostic accuracy study
Leclerc 2014[203]	No relevant outcomes - No diagnostic accuracy data
Lee 2008[204]	Not an assessment scale – multisensory manometry No relevant outcomes – no diagnostic accuracy data
Lee 2011[208]	Inappropriate population – patients with diagnosed OSA
Lee 2012[212]	Inappropriate population – patients with diagnosed OSA
Lee 2013[207]	Not assessment scale- snoring detection method based on hidden Markov models
Lee 2015[206]	Not assessment scale- Nasal pressure recordings for automatic snoring detection
Lee 2015[210]	Inappropriate population – patients with diagnosed OSA
Lee 2015[211]	Inappropriate population – patients with diagnosed OSA
Lee 2016[205]	Inappropriate population – patients with diagnosed OSA
Lee 2016[209]	Inappropriate population – patients with diagnosed OSA
Leitzen 2014[213]	No relevant outcomes – no diagnostic accuracy data
Lentini 2006[214]	Not an assessment scale – serum creatine phosphokinase
Leppanen 2016[215]	Not assessment scale– study analysed RemLogic™ plug-in
Levartovsky 2016[216]	Not an assessment scale – breathing and snoring sounds recorded by polysomnography
Levendowski 2009[217]	Inappropriate population – untreated OSA patients
Levendowski 2015[219]	Not an assessment scale - neck device measuring loud snoring
Levendowski 2018[218]	No usable outcomes – no diagnostic accuracy data
Levy 1996[220]	Not an assessment scale – hospital oximetry
Li 2014[223]	Inappropriate population – confirmed OSA
Li 2017[222]	Not an assessment scale - photoplethysmograph
Li 2018[221]	Not an assessment scale - single-lead ECG signal
Liam 1996[224]	Not an assessment scale – Edentrace II
Liesching 2004[225]	Not assessment scaleSNAP technology sleep sonography

Reference	Exclusion Reason
Lim 2008[227]	Not an assessment scale – polysomnography data was analysed
Lim 2018[226]	Not an assessment scale – Soft palate length with velum obstruction
Lin 2009[228]	Inappropriate population – patients with diagnosed OSA
Ling 2012[229]	Not an assessment scale – hospital oximetry
Linz 2018[230]	Not an assessment scale - hospital oximetry
Lipatov 2018[231]	Inappropriate population – patients with negative polysomnography
Littner 2005[232]	Inappropriate study design – Literature review
Liu 2012[233]	No relevant outcomes – no diagnostic accuracy data
Liu 2017[234]	Not assessment scale– support vector machine was used to predict model for severity of OSA
Lloberes 2001[235]	Not assessment scale: home oximetry, hospital and home RP
Logar 2013[236]	Not assessment scale- modern machine learning method, the support vector machine to establish a predicting model for the severity of OSA
Lopes 2008[237]	Inappropriate study design – not a diagnostic accuracy study
Lopez-Acevedo 2009[239]	Inappropriate study design – not a diagnostic accuracy study
Lopez-Acevedo 2009[238]	Inappropriate study design – not a diagnostic accuracy study
Lu 2017[240]	Inappropriate population – asthma patients
Lucey 2016[241]	Not an assessment scale – single channel EEG
Luo 2014[242]	Inappropriate assessment scale – Chinese questionnaires
Luo 2014[243]	Inappropriate assessment scale – Chinese questionnaires
Luo 2015[244]	Not an assessment scale - nomogram
Macavei 2013[245]	Inappropriate reference standard – partial pressure of carbon dioxide (pCO2)
MacGregor 2013[246]	Not an assessment scale - tracheal breath sounds
MacGregor 2014[247]	Inappropriate study design – conference proceedings
Mador 2005[248]	Inappropriate study design – not a diagnostic accuracy study
Maeder 2015[249]	Inappropriate study design – not a diagnostic accuracy study
Maestri 2011[250]	Inappropriate study design – not a diagnostic accuracy study

Reference	Exclusion Reason
Magalang 2003[251]	Not an assessment scale – hospital oximetry
Magnusdottir 2018[252]	Not an assessment scale - single-lead electrocardiogram signal
Mahakit 2012[253]	Not an assessment scale – daytime polysomnography
Maier 2006[254]	Not an assessment scale - electrocardiogram
Maier 2011[256]	Not an assessment scale - electrocardiogram
Maier 2014[255]	Not an assessment scale - electrocardiogram
Maimon 2010[257]	Not an assessment scale - snoring
Maislin 1995[258]	Inappropriate study design – not diagnostic accuracy study
Makarie Rofail 2008[259]	Not an assessment scale – nasal flow
Malbois 2010[260]	Inappropriate comparison – oximetry compared to polygraphy
Man 1995[261]	Inappropriate population - SDB
Mandal 2014[262]	Inappropriate population – sleep disordered breathing
Manoochehri 2018[263]	Not an assessment scale – models LRM and C5.0
Manoochehri 2018[264]	Not an assessment scale – support vector machine based algorithm
Manser 2001[265]	Inappropriate study design – different scoring methods analysed, not diagnostic accuracy study
Manuel 2015[266]	Inappropriate study design – not a diagnostic accuracy study
Maranate 2015[267]	Not an assessment scale – not a diagnostic accuracy study
Marcos 2007[270]	Inappropriate study design – conference proceedings
Marcos 2008[271]	Inappropriate population – patients with atrial fibrilation
Marcos 2008[274]	Not an assessment scale – not a diagnostic accuracy study
Marcos 2009[273]	Inappropriate study design – not a diagnostic accuracy study
Marcos 2009[272]	Inappropriate study design – not a diagnostic accuracy study
Marcos 2010[269]	Inappropriate study design – not a diagnostic accuracy study
Marcos 2010[275]	Inappropriate study design – not a diagnostic accuracy study
Marcos 2011[276]	Inappropriate study design – not a diagnostic accuracy study
Marcos 2012[268]	Inappropriate study design – not a diagnostic accuracy study

Reference	Exclusion Reason
Marcos 2016[277]	Inappropriate study design – not a diagnostic accuracy study
Margallo 2014[278]	Inappropriate population- patients with resistant hypertension. Patients recruited from hypertension outpatient clinic (tertiary care University Hospital)
Marrone 2001[279]	Not assessment scale: home oximetry, hospital and home RP
Martinez 2005[285]	Not an assessment scale – hospital oximetry
Martinez 2009[284]	Inappropriate study design – not a diagnostic accuracy study
Martinez 2011[282]	Inappropriate population – sleep disordered breathing
Martinez 2012[283]	Inappropriate population – coronary artery disease/angina complaints Inappropriate reference standard – home polysomnography
Martinez-Garcia 2018[281]	Inappropriate population – patients with resistant hypertension No relevant outcomes – no diagnostic accuracy data
Martinot 2017[286]	Not an assessment scale – Mandibular position and movements
Martinot 2017[287]	Inappropriate population – sleep disordered breathing
Martins 2020[288]	no relevant outcomes -sensitivity and specificity not reported
Martinot 2017[287]	Inappropriate population – sleep disordered breathing
Marti-Soler 2016[280]	Inappropriate population – sleep disordered breathing
Masa 2011[292]	Inappropriate study design – patients randomised to home RP vs hospital PSG, no relevant outcomes
Masa 2013[289]	Inappropriate study design – RCT, no relevant outcomes
Masa 2014[294]	Not an assessment scale - single channel (ApneaLink; Resmed)
Masa 2011[291]	Inappropriate study design - RCT, no relevant outcomes
Masa 2013[290]	Inappropriate study design - RCT, no relevant outcomes
Masa 2013[293]	Inappropriate study design - RCT, no relevant outcomes
Massie 2018[295]	Not an assessment scale – hospital NightOWL
Maury 2013[296]	Not an assessment scale – oximetry + nasal flow
Maury 2014[297]	Inappropriate population – sleep disordered breathing

Reference	Exclusion Reason
Mayer 1998[299]	Inappropriate population – snoring or suspected OSAHS
Mayer 2019[298]	Not assessment scale- different heart rate accelaration and pulse transit time cut-offs calculated with total sleep time, all patients underwent polysomnography
Maziere 2014[300]	Inappropriate reference standard – hospital pulse oximetry
Mazza 2017[301]	Inappropriate population – atrial fibrillation patients who received dual-chamber pacemaker No relevant outcomes – no diagnostic accuracy data
McArdle 2000[302]	Inappropriate study design – long term outcomes were assessed in people from CPAP trial
McArdle 2020[303]	No relevant outcomes - no diagnostic accuracy data
McCall 2009[304]	Inappropriate population – depressed patients with insomnia No usable outcomes – no diagnostic accuracy data
McCarter 2014[305]	Not assessment scale– study analysed RSWA phasic burst durations
McIsaac 2015[306]	Not assessment scale- accuracy of case-ascertainment algorithms for identifying patients with OSA
McMahon 2017[307]	Inappropriate population – Sleep disordered breathing patients
McMillan 2015[308]	Inappropriate study design – health technology assessment
Medarov 2020[309]	Inappropriate reference standard - home polysomnography vs hospinal polysomnography
Mehra 2008[310]	Not an assessment scale - wrist actigraphy Inappropriate population – sleep disordered breathing
Meissner 2014[311]	Not assessment scale– multiple system atrophy/ home RP (oximetry, nasal flow, abdominal movements) polysomnography performed after 4 weeks.
Mendelson 1994[312]	Inappropriate study design – not a diagnostic accuracy study
Mendez 2010[313]	Not an assessment scale - ECG based on empirical mode decomposition and wavelet analysis
Meng 2016[314]	Not an assessment scale - micromovement sensitive mattress
Mergen 2019[315]	No relevant outcomes - specificity was not reported

Reference	Exclusion Reason
Mesquita 2012[316]	Not an assessment scale – respiratory sounds
Methipisit 2016[317]	Not assessment scale– linguistic validation of THAI version ESS questionnaire
Meurgey 2018[318]	Inappropriate population – sleep disordered breathing in bariatric patients
Michaelson 2006[319]	Not an assessment scale – SNAP testing
Mihaicuta 2017[320]	Inappropriate study design – not diagnostic accuracy study, patient network analysis
Miller 2018[321]	Inappropriate analysis – unclear calculations
Miller 2018[322]	Systematic review - references checked
Minic 2014[323]	Inappropriate population - Sleep disordered breathing in group 1 pulmonary arterial hypertension
Miyata 2020[324]	Not an assessment scale - sheet like device called SD 102 with SPO2 monitoring
Mokhlesi 2007[325]	Inappropriate study design – prevalence in OHS was measured in the population with confirmed OSA
Morales 2012[326]	Not an assessment scale – single channel ResCare AutoSet
Morales Divo 2009[327]	Not an assessment scale - ApneaGraph
Morgan 2010[328]	Inappropriate population- Sleep-disordered Breathing
Morgenstern 2010[330]	Not assessment scalestudy assessed automatic differentiation of central hypopnea
Morgenstern 2013[329]	Not an assessment scale – nasal airflow
Morillo 2009[332]	Not assessment scale- Poincare analysis of an overnight arterial oxygen saturation
Morillo 2013[331]	Not assessment scale- Probabilistic neural network approach for the detection
Moro 2016[333]	Not an assessment scale – economical study
Morrell 2012[334]	Inappropriate population – sleep disordered breathing
Morris 2005[335]	Not an assessment scale - acoustic rhinometry
Morris 2008[336]	Not an assessment scale – snoring severity score
Mou 2019[337]	Inappropriate study design – validation of STOP-Bang among clinically referred patients and tested alternative scoring designs on tool performance, with a focus on gender differences in OSA.
Mueller 2006[338]	Not an assessment scale - transthoracic impedance recording integrated into a Holter ECG system
Mulgrew 2007[339]	Not assessment scale- compared

Reference	Exclusion Reason
	standard PSG with ambulatory CPAP titration in high-risk patients identified by a diagnostic algorithm.
Munoz-Ferrer 2020[340]	Not assessment scaledesign - the study aimed to evaluate the degree of measurement agreement between stepwise, in laboratory attended polysomnography and a home, no sleep apnea test diagnostic accuracy data
Musman 2011[341]	Economic model with no new clinical evidence
Mutlu 2020[342]	No relevant outcomes- no diagnostic accuracy data
Nagappa 2015[343]	Systematic review - references checked
Nagubadi 2016[344]	Inappropriate population – sleep disordered breathing
Nahapetian 2016[345]	Inappropriate study design – prevalence in OHS was measured in the population with confirmed OSA
Nakano 2004[347]	Not an assessment scale - Tracheal Sound Analysis
Nakano 2004[349]	Inappropriate comparison – BMI compared to ODI
Nakano 2007[350]	Not an assessment scale – single channel airflow signal
Nakano 2008[346]	Not an assessment scale – snoring intensity/ no diagnostic accuracy data
Nakano 2008[351]	Not assessment scale- Somnie (1 channel)
Nakano 2014[348]	Not an assessment scale – snoring sound recorded via smartphone
Narayan 2019[352]	Not an assessment scale - smartphone-recorded sounds validated by polysomnography
Netzer 1999[354]	Inappropriate reference standard – home respiratory polygraphy
Ng 2007[358]	Not an assessment scale – snore signals
Ng 2008[356]	Not an assessment scale - frequencies of snore signals
Ng 2009[355]	Not an assessment scale – snore signals
Ng 2009[357]	Inappropriate study design - acoustical and perceptual impacts of changing the cross-sectional areas (CSA) of the pharynx and oral cavity on the production of snores
Ng 2017[362]	Not an assessment scale - Apnea link-ox (3 channels)
Ng 2019[361]	Not assessment scale– study investigated acoustical and perceptual impacts of changing the cross sectional areas (CSA) of the pharynx and oral cavity on the production of snores

Reference	Exclusion Reason
Ng 2009[359]	Not an assessment scale - Apnea link-ox (3 channels)
Ng 2010[360]	Inappropriate study design - not questionnaire/diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Nicholl 2012[364]	Inappropriate study design – not a diagnostic accuracy study
Nicholl 2013[363]	Inappropriate population patients with CKD and end-stage renal disease Inappropriate reference standard –home cardiopulmonary study
Nigro 2009[365]	Not an assessment scale – hospital oximetry
Nigro 2011[372]	Not an assessment scale - ApneaLink (1 channel)
Nigro 2012[369]	Not an assessment scale - ApneaLink (1 channel)
Nigro 2012[371]	Not an assessment scale – hospital oximetry
Nigro 2015[373]	Not an assessment scale - diagnostic accuracy of autoscoring from auto-CPAP using different cut-off points
Nigro 2016[368]	Inappropriate study design – accuracy of clinical criteria to diagnose OSA and prescribe CPAP
Nigro 2011[367]	Not an assessment scale - Apnea link single channel
Nigro 2013[370]	Not an assessment scale - Apnea link-ox (3 channels)
Nigro 2012[374]	Inappropriate study design- skilled observer compared to observer with no experience
Nigro 2010[375]	Not an assessment scale –ApneaLink 1 channel
Nigro 2019[366]	Not an assessment scale - pulse oximetry recorded from hospital polysomnography
Niijima 2007[376]	Inappropriate population/inappropriate study design – workers in transport, construction, retail and security companies/no diagnostic accuracy study
Nilius 2017[377]	Inappropriate study design – not diagnostic accuracy study, study assessed diagnostic agreement between PSG vs PDX
Nishiyama 2014[378]	Not an assessment scale – polysomnography recordings
Norman 2017[379]	Not assessment scale– Polysomnography at home vs polysomnography in hospital
Novkovic 2019[380]	no relevant outcomes - no diagnostic accuracy data
O'Brien 2007[381]	Inappropriate study design – conference paper on ECG derived respiratory signals

Reference	Exclusion Reason
O'Driscoll 2013[382]	No relevant outcomes - accuracy data for determination of sleep and wake between SenseWear and PSG
Oeverland 2002[383]	Inappropriate population – Sleep disordered breathing
Oktay 2011[384]	Not an assessment scale - ApneaLink-ox (1 channel)
Oliveira 2012[385]	Not an assessment scale – Stardust, 3 channel portable recorder
Oliveira 2015[386]	Not an assessment scale – Stardust II 3 channel recorder
Olson 1999[387]	Inappropriate study design – diagnostic accuracy of cumulative percentage time at SaO2 < 90% (CT90) and a saturation variability index
Onder 2012[388]	No relevant outcomes – no diagnostic accuracy data
Onen 2008[389]	Not an assessment scale - Observation-based Nocturnal Sleep Inventory
Ong 2010[390]	Not an assessment scale – simplified Stop-Bang questionnaire
Ortiz-Tudela 2014[391]	Not an assessment scale - wrist Temperature, motor Activity and body Position (TAP
Ozegowski 2007[392]	Not an assessment scale - ambulatory ECG
Ozmen 2011[393]	Not an assessment scale – sleep strip, 3 channels
Pallin 2014[394]	Not an assessment scale – SleepMinderTM biomotion sensor
Pamidi 2011[395]	No usable outcomes – no diagnostic accuracy data
Panchasara 2017[396]	Inappropriate study design – not diagnostic accuracy study
Pang 2006[397]	Not an assessment scale - SleepStrip
Pang 2007[398]	No usable outcomes – prevalence not reported
Park 2015[399]	Not an assessment scale – polysomnography automated vs polysomnography manual methods
Park 2015[400]	Inappropriate population – sleep disordered breathing
Parra 1997[401]	No usable outcomes – diagnostic accuracy presented on a ROC curve only
Passali 2011[402]	No usable outcomes – no diagnostic accuracy data
Pataka 2014[403]	Inappropriate assessment scale – Greek questionnaires
Pataka 2019[404]	Inappropriate assessment scale – Greek questionnaires

Reference	Exclusion Reason
Pataka 2016[406]	Inappropriate analysis - unclear calculation methods used, sensitivity and specificity was calculated including symptoms however it is unclear from the paper how thos symptoms were used
Pataka 2020[405]	Inappropriate reference standard - Embla Embletta® GOLD Portable respiratory polygraphy REI>15
Patout 2020[407]	Inappropriate study design - patients randomised to automised expiratory positive airway pressure (AVAPS-AE) or pressure support ventilation (ST)
Peker 2018[408]	No usable outcomes - no diagnostic accuracy data
Pelletier-Fleury 2001[409]	Not an assessment scale – home polysomnography
Penacoba 2020[410]	Inappropriate study design - non diagnostic accuracy study, diagnostic agreement between primary and specialized care was measured
Peng 2018[411]	Inappropriate population – suspected sleep disordered breathing
Penzel 2002[412]	Inappropriate population - patients with obstructive sleep apnea and arterial hypertension
Penzel 2004[413]	No relevant outcomes – no diagnostic accuracy data
Penzel 2004[414]	Inappropriate study design – conference paper
Pepin 2009[415]	Not an assessment scale - ECG Holter device including a nasal pressure
Peto 2017[417]	Not an assessment scale – Brussels questionnaire
Phua 2020[418]	Not assessment scale- Study investigated if WatchPat reduces time to diagnosis and treatment, no diagnostic accuracy study
Pichel 2006[419]	No usable outcomes – No diagnostic accuracy data
Pietzsch 2011[420]	Economic model with no new clinical evidence
Pihtili 2017[421]	Inappropriate study design – not a diagnostic accuracy study, study investigated frequency of predictors of OHS in obese patients
Pillar 1994[422]	No usable outcomes – diagnostic accuracy of OSA predictions made from questionnaires, clinical interviews and physical examinations
Pinna 2014[423]	Inappropriate population – sleep disordered breathing in heart failure patients
Pinto 2015[424]	Not an assessment scale – peripheral arterial tonometry

Reference	Exclusion Reason
Pissulin 2018[425]	Inappropriate assessment scale – Portuguese questionnaire
Pittman 2004[426]	Not an assessment scale – home and hospital watchPAT 100
Pittman 2004[427]	Not an assessment scale - Polysomnography
Planes 2010[428]	Not assessment scale– automatic polysomnography scoring compared to manual scoring polysomnography at home
Polese 2013[429]	Not assessment scale: home oximetry, hospital and home RP
Popovic 2009[430]	Not an assessment scale– ARES™ Unicorder, Advanced Brain Monitoring/no diagnostic accuracy data
Poupard 2012[432]	Not an assessment scale inappropriate population - ECG Holter monitor/sleep disordered breathing
Poupard 2012[433]	Not an assessment scale – hospital oximetry
Pouliot 1997[431]	Incorrect cut-off was used for reference standard AI<20
Pradhan 1996[434]	Not an assessment scale – Pittsburgh sleep quality index
Prasad 2017[435]	Inappropriate assessment scale – Modified Berlin questionnaire
Prikladnicki 2018[436]	Not an assessment scale - Orofacial Myofunctional Evaluation with Scores
Quaranta 2016[437]	Inappropriate reference standard - Somnea, polygraphy
Quintana-Gallego 2004[438]	Inappropriate population – sleep disordered breathing in heart failure
Rajeswari 2020[439]	Inappropriate study design - not a diagnostic accuracy study, different questionnaires were compared, no polysomnography
Randerath 2013[440]	Not an assessment scale - oesophageal manometry
Rashid 2020[441]	systematic review references checked
Rathnayake 2010[442]	Not an assessment scale – single channel airflow measurement. /Inappropriate population sleep disordered breathing
Rauhala 2009[443]	Not an assessment scale - Periodic limb movement screening
Rauscher 1993[444]	Not an assessment scale – hospital oximetry
Ravelo-Garcia 2014[445]	Not an assessment scale - electrocardiogram
Raymond 2003[446]	Not an assessment scale - Combined index of heart rate variability and oximetry, hospital setting

Reference	Exclusion Reason
Rebelo-Marques 2018[447]	Inappropriate assessment scale – Portuguese version of Stop Bang questionnaire
Reda 2001[448]	Not an assessment scale - pharyngo-eosophageal manometry.
Rees 1998[449]	No relevant outcomes – no diagnostic accuracy data
Reichert 2003[450]	Not assessment scale: home oximetry, hospital and home RP
Reis 2015[451]	Not an assessment scale - Portuguese version of the STOP-Bang questionnaire
Reisch 2000[452]	Not assessment scale– forced oscillation techniques compared to three standard polysomnographic signals
Reuven 2001[453]	No relevant outcomes - economic analysis with no diagnostic accuracy data
Roche 1999[456]	Not an assessment scale - heart rate variability
Roche 2002[455]	Not an assessment scale - ECG Holter monitoring
Roche 2002[458]	Not an assessment scale – hospital oximetry
Roche 2004[457]	Not an assessment scale - electrocardiogram Holter monitoring
Roche 2007[454]	Not an assessment scale - electrocardiogram Holter monitoring
Rodrigues Filho 2020[459]	Not an assessment scale - oximetry of all PSG performed by the LabSono
Rodsutti 2004[460]	Inappropriate study design – not diagnostic accuracy study
Rofail 2010[461]	Not assessment scale: home oximetry, hospital and home RP
Rofail 2010[462]	Not an assessment scale - single channel nasal airflow
Rolon 2017[463]	Inappropriate study design – polysomnography using only oximetry signals
Romano 2011[464]	Not an assessment scale - diurnal negative expiratory pressure test
Romem 2014[465]	Not an assessment scale – hospital oximetry
Romero-Lopez 2011[466]	Inappropriate assessment scale – Spanish language questionnaire
Rosen 2012[467]	Not an assessment scale – patients were randomised to hospital polysomnography and portable monitoring, patients with ahi>15 started CPAP therapy
Rosen 2018[468]	Inappropriate study design - literature review

Reference	Exclusion Reason
Rosenthal 2008[469]	Unclear analysis – prevalence not reported
Rosenwein 2015[470]	Not an assessment scale - non-contact audio recordings
Ross 1998[472]	Systematic review - references checked
Ross 2000[473]	Systematic review - references checked
Ross 2000[471]	Abstract only
Roth 2002[474]	Inappropriate assessment scale - Global Sleep Assessment Questionnaire
Rowley 2000[475]	inappropriate assessment scale – SACS questionnaire
Ryan 1995[476]	Not assessment scale: home oximetry, hospital and home RP
Saarelainen 2003[477]	Not an assessment scale - whole-body impedance cardiography
Saha 2020[478]	Not an assessment scale - patch wearable device used to record respiratory sounds and neck position and movement
Saleh 2011[479]	Inappropriate assessment scale - Arabic version of Berlin questionnaire
Santaolalla Montoya 2007[481]	Not an assessment scale – clinical prediction algorithm using various epidemiological parameters
Saricam 2020[482]	Inappropriate reference standard/ - Berlin questionnaire
Savage 2016[483]	Inappropriate population – sleep disordered breathing in patients with heart failure
Scarlata 2013[484]	Inappropriate reference standard - 35 patients polysomnography and 219 cardiorespiratory monitoring
Schafer 1997[485]	Not an assessment scale – oximetry measured with a four channel MESAM 4 device
Scharf 2004[486]	Not an assessment scale – cardiac pacemaker
Senaratna 2017[487]	Systematic review - references checked
Senn 2006[488]	Not assessment scale– patients randomised to CPAP vs polysomnography
Sergi 1998[489]	Inappropriate comparison – daytime polysomnography was compared to daytime polysomnography
Series 1991[490]	Not an assessment – daytime polysomnography was compared to daytime polysomnography
Sériès 1993[492]	Not an assessment scale - oximetry
Series 1999[491]	Not an assessment scale – nasal pressure tracing
Serrano 2018[493]	Not assessment scale – clinical prediction rules were analysed

Reference	Exclusion Reason
Sert Kuniyoshi 2011[494]	Inappropriate population – sleep disordered breathing in patients with a recent myocardial infarction
Sforza 2007[495]	Not assessment scale - heart-rate variability (HRV) measures on the degree of sleep fragmentation.
Shalaby 2006[496]	Not an assessment scale - The pacemaker trans-thoracic impedance signal
Shams 2012[497]	Not assessment scale - tracheal breath sounds
Shi 2018[498]	Inappropriate study design – conference paper, algorithm analysis
Shin 2010[499]	Inappropriate study design – algorithm analysis
Shochat 2002[500]	Not an assessment scale - SleepStrip
Shokrollahi 2016[501]	Inappropriate study design – conference paper, snoring sound analysis
Siegel 2000[502]	Not an assessment scale – ultrasonic imaging
Silva 2011[503]	Inappropriate population – sleep disordered breathing
Sivam 2018[504]	Not an assessment scale – oximetry and transcutaneous CO2 measured during polysomnography in OHS population
Skiba 2015[505]	Not assessment scale– retrospective review of Polysomnography results
Skomro 2007[506]	Not assessment scale - retrospective study of all patients who had been offered empirical CPAP therapy for suspected OSA was conducted.
Smith 2020[507]	Not an assessment scale - 2 channel apnealink tm, oximetry and nasal flow
Sola-Soler 2007[510]	Inappropriate study design – conference paper
Sola-Soler 2012[508]	Not an assessment scale - snoring analysis
Sola-Soler 2014[509]	Not an assessment scale - tracheal breath sound analysis
Sommermeyer 2012[511]	Not appropriate assessment scale– cardiorespiratory polygraphy
Song 2016[512]	Inappropriate study design - Markov model from ECG Signals
Stein 2003[513]	Not an assessment scale test- Holter recordings
Stelmach-Mardas 2017[514]	Inappropriate assessment scale – Polish Berlin questionnaire
Stendardo 2018[515]	Inappropriate study design – not diagnostic accuracy study
Stoohs 1990[516]	Not an assessment scale – MESAM device
Stoohs 1992[517]	Not an assessment scale – MESAM device

Reference	Exclusion Reason
Su 2004[519]	Not an assessment scale – SNAP digital recorder
Su 2012[518]	No usable outcomes – no diagnostic accuracy data
Subramanian 2011[520]	Not an assessment scale – NAMES assessment
Suksakorn 2014[521]	Inappropriate assessment scale – Thai version of Berlin questionnaire in patients with sleep disordered breathing
Sun 2011[522]	Inappropriate study design – artificial intelligence method to screen OSA
Sun 2019[523]	inappropriate study design - patients completed, home portable monitoring and echocardiography
Takama 2010[524]	Inappropriate population – sleep disordered breathing in patients with cardiovascular disease
Takeda 2006[525]	Not an assessment scale – Apnomonitor III test, not oximetry alone
Tanaka 2009[526]	No usable outcomes – no diagnostic accuracy data
Tauman 2006[527]	No usable outcomes no diagnostic accuracy data
Teferra 2014[528]	Inappropriate study design – analysis of artificial neural network sleep apnea tool for sleep studies
Teklu 2020[529]	Inappropriate study design/inappropriate comparison- no diagnostic accuracy data
Teramoto 2002[530]	Not an assessment scale – hospital oximetry
Terjung 2016[532]	Inappropriate population - mixed OSA and PLM population
Terjung 2018[531]	Not an assessment scale – VitaLog, no diagnostic accuracy data
Thong 2008[533]	No relevant outcomes – no diagnostic accuracy data
Thornton 2012[534]	Not an assessment scale - previously scored polysomnography was reviewed
Tian 2005[535]	Inappropriate study design conference paper
Tiihonen 2009[536]	Inappropriate reference standard – hospital polygraphy
Ting 2014[537]	Inappropriate study design – validation of prediction system to diagnose OSA
To 2009[539]	Not an assessment scale – ARES (apnea risk evaluation system)
To 2012[538]	Not assessment scale – CPAP compared with portable sleep monitoring
Tong 2014[540]	Not an assessment scale - ECG derived respiration

Reference	Exclusion Reason
Topor 2020[541]	Not an assessment scale - MATRx plus(ZephyrSleep Technologies) - level 3 device cosists of microphone and accelerometer
Traxdorf 2017[542]	Not an assessment scale – Erlangen questionnaire
Tsai 2003[543]	Not an assessment scale – decision rule(cricomental space, pharyngeal grade)
Tsukahara 2014[544]	Not an assessment scale – sheet type portable monitor SD-101
Ugon 2016[545]	No relevant outcomes – no diagnostic accuracy study
Ulasli 2014[546]	Inappropriate assessment scale – Turkish version of Berlin and ESS questionnaires
Unal 2002[547]	Not an assessment scale – polysomnography recordings were analysed
Ustun 2016[548]	Not an assessment scale – SLIM and 7 state of the art classification methods
Valipour 2007[549]	No relevant outcomes – no diagnostic accuracy data
Van Brunt 1997[550]	Not an assessment scale – snoring sounds
Van Meerhaeghe 2004[551]	Not an assessment scale – NEP (negative pressure) procedure
Van Surell 1995[552]	Not an assessment scale – CID 102 device
Varady 2002[554]	Not assessment scale – artificial neural networks for the recognition of three different patterns in the respiration signals were analysed
Vaughan 2016[555]	No relevant outcomes – no diagnostic accuracy data
Vaz 2011[556]	Not in English
Vazquez 2000[557]	Not an assessment scale – hospital oximetry
Ventura 2007[558]	Not an assessment scale - hospital oximetry
Victor Marcos 2008[559]	Inappropriate study design – oxygen saturation recordings were used. The performance of two different ensemble classifiers was analysed.
Virkkula 2002[561]	No usable outcomes – no diagnostic accuracy data
Virkkula 2005[560]	No usable outcomes – no diagnostic accuracy data
Wang 2014[562]	No usable outcomes – no diagnostic accuracy data
Ward 2009[563]	Abstract only
Ward 2012[565]	Not an assessment scale - Hospital oximetry
Ward 2015[564]	Inappropriate test - ApneaLink (3 channels)

Reference	Exclusion Reason
Weinreich 2008[566]	Inappropriate population – 11 patients with OSA, 10 with hypopnea, 11 with Cheyne-Strokes respiration and 5 with normal breathing
Weinreich 2014[568]	Not an assessment scale – SleepMinder
Weinreich 2018[567]	Not an assessment scale - non-contact device emits a very weak electromagnetic radiation and detects body movement by measuring the Doppler effect
Westerlund 2014[569]	Not an assessment scale - Karolinska Sleep Questionnaire
White 1994[571]	Not an assessment scale - sound recording and oxygen saturation
White 1995[570]	Not an assessment scale - Healthdyne NightWatch (NW) System
Whitelaw 2005[572]	Not assessment scale – patients were randomised to polysomnography or home monitoring all patients used CPAP for 4 weeks
Wieczorek 2018[573]	Not an assessment scale – PADSS (Paris Arousal Disorder Severity Scale)
Williams 1991[574]	Not an assessment scale – hospital oximetry + clinical score
Williams 2017[575]	No usable outcomes – no diagnostic accuracy data
Wiltshire 2001[576]	Not an assessment scale - diagnostic accuracy study of diagnostic tests: home oximetry, hospital and home RP
Wong 2008[577]	Not an assessment scale – nasal flow monitor
Wu 2017[578]	Not an assessment scale – fuzzy evaluation system (NFES)
Xie 2012[580]	Not an assessment scale – ECG and Peripheral SpO2 from polysomnography
Xie 2020[581]	Not assessment scale - Data were collected using Brief ICF-Sleep Disorders and Obesity Core Set Polysomnography was performed and basic characteristics of the patients were recorded.
Xu 2017[583]	Not assessment scale: home oximetry, hospital and home RP
Yaddanapudi 2018[584]	Inappropriate population/ stroke patients who underwent HRPO,. No diagnostic accuracy data
Yagi 2009[585]	No usable outcomes – Only sensitivity and positive predictive values presented in the paper
Yalamanchali 2013[586]	Systematic review - references checked
Yamaguchi 2007[587]	Not an assessment scale - SleepStrip
Yamashiro 1995[588]	Inappropriate population – Sleep disordered breathing

Reference	Exclusion Reason
Yang 2011[589]	Not an assessment scale - plethysmography
Yang 2013[590]	Inappropriate study design – literature review
Yin 2005[592]	No relevant outcomes – no diagnostic accuracy data
Yin 2006[591]	No usable outcomes – study reported only sensitivity and positive predictive value, prevalence unclear
Yuceege 2014[593]	Not an assessment scale - neck/thyromental distance
Yuceege 2015[594]	Inappropriate assessment scale – Turkish version Berlin questionnaire + gender
Yunus 2013[595]	Inappropriate assessment scale – Malay version of Berlin questionnaire
Zaffaroni 2009[596]	Not an assessment scale – SleepMinder
Zaffaroni 2013[597]	Not an assessment scale – SleepMinder
Zamarron 1999[601]	Not an assessment scale – hospital oximetry
Zamarron 2001[600]	Not an assessment scale – hospital oximetry
Zamarron 2003[598]	Not an assessment scale – hospital oximetry
Zamarron 2006[599]	Not an assessment scale – hospital oximetry
Zarei 2018[602]	Not an assessment scale - Single-Lead ECG Signal.
Zhang 2011[603]	Inappropriate population– sleep disordered breathing/no diagnostic accuracy data
Zhang 2018[604]	Not in English
Zou 2013[605]	Inappropriate assessment scale – Chinese ESS questionnaire
Zou 2015[606]	Not an assessment scale - The SleepView device is a 2-channel diagnostic tool designed for screening of sleep-disordered breathing
Zucconi 1996[607]	Not an assessment scale - unattended recording device (MicroDigitrapper-S) (M-S).
Zywietz 2004[608]	Not an assessment scale - single channel ECG

H.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below:

Table 12: Studies excluded from the health economic review

Reference	Reason for exclusion
Geessinck 2018[138]	Since there was no evidence for DiagnOSAS tool that could be included in the clinical review, this economic model evaluating the tool was considered to be not applicable.