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Original Article

Diagnostic accuracy and suitability of instruments that screen for obstructive sleep apnoea, insomnia and sleep quality in cardiac patients: a meta-analysis

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ABSTRACT

Background: A number of clinical guidelines recommend that all cardiac rehabilitation patients should be screened for potential sleep disorders with a validated screening instrument. There is currently no consensus on what specific tools should be used.
Objective: To identify tools that are practical to use in the clinical environment and have high diagnostic accuracy.
Methods: We systematically searched online databases to identify patient reported outcome instruments that have been used in published research studies to assess the likelihood of obstructive sleep apnoea (OSA) in cardiac patients. In studies that provided diagnostic data, these data were extracted and verified via an evidence-based diagnostic calculator. Where sufficient numbers of studies were available, a meta-analysis was conducted to determine pooled estimates of specificity, sensitivity and diagnostic odds ratios. Selected papers were qualitatively assessed using the Standards for Reporting Diagnostic accuracy studies (STARD).
Results: Of the 21 instruments identified, six detected likelihood of OSA, two assessed daytime sleepiness, five assessed insomnia and eight examined sleep quality. A meta-analysis of 14 studies that assessed diagnostic accuracy of moderate OSA, revealed moderate sensitivity for the Berlin Questionnaire, Sens = 0.49 (95% CI 0.45–0.52) and good sensitivity for the Stop-BANG, Sens = 0.93 (95% CI 0.87–0.96) but poor specificity at standard cut-off criteria.
Conclusion: There are promising practical tools available to screen patients with OSA and other sleep disorders in cardiac rehabilitation settings, but specificity could be improved. Additional assessment of sleep quality may enhance prognostic ability with both OSA and insomnia screening.

1. Introduction

Sleep-related breathing disorders such as obstructive sleep apnoea (OSA) have been associated with increased risk of developing cardiovascular disease (CVD) [1,2] and have a high prevalence in cardiac patients [3]. Similarly, it is estimated that close to 40 percent of all patients living with CVD also have insomnia [4,5], a condition which has been associated with increased comorbidity [6,7], poor diet [8], depression [9], daytime dysfunction [10] and reduced quality of life [11]. Both conditions can significantly impact sleep quality and achievement of therapeutic modifiable risk factor targets in cardiac patients [12]. There

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is also a high prevalence of comorbid insomnia and OSA (COMISA) with global estimates as high as 42% [13] With both conditions there is growing evidence that screening and treatment may assist specific aspects of rehabilitation and recovery in sub-groups of patients [14,15]. For patients with COMISA, screening for both conditions is advised since suboptimal treatment pathways may be considered if only one condition is detected [16]. Despite this growing evidence base and consensus that screening for these sleep disorders is beneficial [17], there have been very few diagnostic evaluations of relevant instruments specifically for cardiac patients.

The reference standard for identification of sleep-related breathing disorders is polysomnography (PSG) [18] and for insomnia is a structured clinical interview conducted by a trained clinician consisting of a thorough evaluation of current sleep–wake behaviour and sleep history, and additional PSG if comorbid sleep conditions such as OSA is suspected [19,20]. Both diagnostic approaches are time consuming, expensive and often impractical as a means of screening patients [21,22]. In the clinical setting such as cardiac rehabilitation, valid, convenient and effective tools that assist professionals to identify patients with potential sleep disorders are needed [17]. An ideal screening tool is one that incorporates easily-obtained information to accurately predict the probability of presence or absence of a disease in a patient [23]and therefore have high diagnostic accuracy. However, at present there is little consensus on the most appropriate non-objective instrument to use for a given sleep disorder and for a given sub-set of cardiac patients.

Better screening for cardiology patients is critical to ensure accurate and timely diagnosis and treatment of their sleep disorder in order to reduce its' impact on cardiovascular symptoms. The primary aim of this paper, therefore, is to assess the diagnostic accuracy for subjective instruments that identify two major sleep disorders in patients with CVD: obstructive sleep apnoea and insomnia. A secondary aim is to identify the most appropriate instruments that assess sleep quality with these patients.

2. Methods

The protocol for this analysis is registered in PROSPERO (CRD42020171062). In line with the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) protocol for systematic reviews of measurement properties, we defined the following:

1) Constructs of interest, ie, obstructive sleep apnoea, insomnia, sleep quality
2) Population of interest, ie, cardiac patients (acute coronary syndrome (ACS), patients who have undergone major surgical procedures such as coronary artery bypass graft surgery (CABGS), atrial fibrillation patients, heart failure patients)
3) Type of measurement instrument, ie, subjective, self-report, observer ratings
4) Measurement properties, ie, reliability, validity, interpretability, and clinical utility

2.1. Search strategy

Databases including MEDLINE (PubMed), Embase, Cochrane Database and PsycINFO (Ovid) were searched by MLG with replication by AJ, to identify patient reported outcome instruments that have been used to assess the likelihood of sleep disorders in cardiac patients published from 1 January 2010 to 25 August 2020. An example of a PubMed search strategy is provided in the supplementary material (Appendix 1). We also searched for ongoing, recently completed and unpublished clinical studies, conference proceedings and reference lists of selected studies. After screening, a total of 380 papers were assessed for eligibility (Fig. 1) with 145 included in the qualitative analysis and 19 providing validation data.

2.2. Data extraction

The main purpose of our review was to find instruments that were currently used by health professionals to identify sleep disorders in cardiac patients, therefore, extraction data was limited to the last 10 years. We collected information about study characteristics and quality using a standardized data collection form. The following characteristics were included: instrument name, cardiac diagnosis, sample size, age, proportion of females, country, study setting, study design, recruitment method and response rate. We recorded accuracy data for the various instruments according to specific cut-off scores and diagnostic levels of severity (AHI) in contingency tables (see Supplemental Table 2).

2.3. Assessment of validation studies

2.3.1. Obstructive sleep apnoea

Where available, data were extracted and verified via an online evidence-based diagnostic calculator, the NIHR DEC Newcastle tool for assessing the technical accuracy of a diagnostic test [24]. As recommended by standard guidelines for conducting reviews of diagnostic studies [25] the method involved reconstructing a diagnostic two by two table for true positive, false positive, true negative and false negative cells. The following indices were calculated: sensitivity [probability that a test result will be positive when the disease is present (true positive rate)]; specificity [probability that a test result will be negative when the disease is not present (true negative rate)]; positive predictive value (probability that the disease is present when the test is positive); negative predictive value (probability that the disease is not present when the test is negative); positive likelihood ratio [ratio between the probability of a positive test result given the presence of the disease and the probability of a positive test result given the absence of the disease, ie, = True positive rate/False positive rate = Sensitivity/(1-Specificity)]; negative likelihood ratio (ratio between the probability of a negative test result given the presence of the disease and the probability of a negative test result given the absence of the disease, ie = False negative rate/True negative rate = (1-Sensitivity)/Specificity; global accuracy: overall probability that a patient will be correctly classified). In addition, the Diagnostic Odds Ratio (DOR) was calculated, a single indicator of test accuracy that incorporates sensitivity and specificity and is not affected by the prevalence of the target disease [26].

2.3.2. Insomnia

To be considered for validation in this meta-analysis, any study must include, in addition to the instrument, some standard diagnostic criteria for insomnia. Suitable criteria for reference include the International Statistical Classification of Diseases and Related Health Problems [ICD] [27], the Diagnostic and Statistical Manual of Mental Disorders [DSM] [28], or International Classification of Sleep Disorders [ICSD] [29].

2.3.3. Quality of included studies

We based our assessment of quality on the Standards for Reporting Diagnostic accuracy studies (STARD 2015) [30,31] The STARD checklist consisted of 30 questions that were weighted equally (yes = 1, no = 0). The total score (out of 30) was calculated

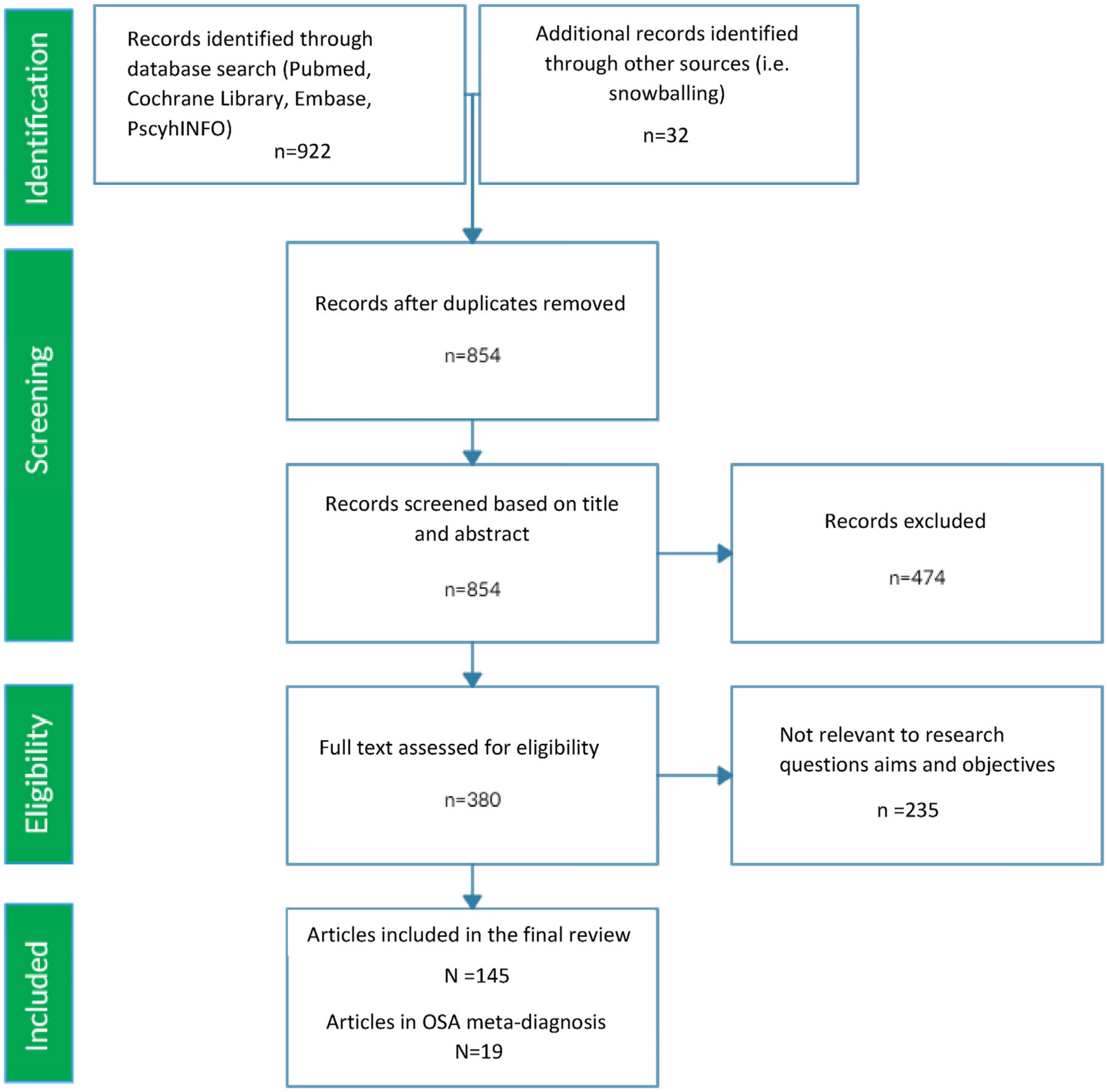

Fig. 1. Flow diagram of the reviewing process according to PRISMA.

for each study by two raters. Each article was assessed independently by two readers using a standard form. Disagreements were resolved by consensus discussion or arbitration by a third reviewer.

2.3.4. Meta-analysis

Where sufficient data were available, we performed bivariate meta-analyses using methods described by Reitsma et al. [32] to obtain pooled estimates of specificity and sensitivity. Our meta-analysis used a random effects model and summary receiver operating characteristic (SROC) curves were derived from Meta-Disc [33] version 1.4 (Hospital Ramony Cajal, Madrid, Spain). Additional parameters were calculated using the Metandi software [34] addon for Stata 16.0 (StataCorp, College station, TX, USA). The parameters from pooled data were calculated and forest plots were created for the predictive parameters using the DerSimonian and Laird random effect model [35] Diagnostic Odds Ratios (DOR) and receiver operating curve (ROC) analysis was presented to assess the diagnostic ability of each instrument. The criteria for AUC classification were 0.90–1 (excellence), 0.80 to 0.90 (good), 0.70 to 0.80 (fair), 0.60 to 0.70 (poor), and 0.50 to 0.60 (failure) [36] The extent of heterogeneity was assessed using the inconsistency index (I-squared) (I^2 >33%:heterogeneity present) [37] and the Cochrane Q test (P value < 0.05: heterogeneity present). Additionally, the Spearman correlation coefficient was calculated to verify whether heterogeneity could be explained by a threshold effect [25]. A strong positive correlation between sensitivity and specificity would suggest threshold effect and the results will present a "shoulder-arm" point distribution on the SROC curve [33]. Publication bias was assessed using Deek's funnel plot asymmetry test (P < 0.05 indicates the presence of publication bias), the preferred method for meta-analysis of diagnostic accuracy [38]. At least four studies had to have diagnostic accuracy available in order to conduct pooled estimates for a given test at specific OSA severity levels.

3. Results

3.1. Instruments identified

A total of 22 instruments were identified that have been used in research studies involving cardiac patients (five for detecting likelihood of OSA, two for assessment of daytime sleepiness, five for insomnia and eight for sleep quality (see Table 1).

3.2. Diagnostic accuracy of instruments that predict probability of OSA

There were 19 studies conducted with cardiac patients that have examined validity of subjective measures with objective measures (Table 2). The studies included a total of 3692 patients (15.9% female) with mean age ranging from 54 to 70 years. OSA prevalence in these studies varied considerably, from 36% to 87% for mild OSA and from 10% to 63% for moderate OSA. The 11 studies that were conducted with the Berlin Questionnaire (BQ) indicated better sensitivity than specificity. Moderate levels of overall accuracy were obtained with best results obtained for mild levels of OSA (AHI $\geq$5/hour). Most of the studies demonstrated poor specificity with between half to three-quarters of each sample being false positive at the standard cutoff. Validity of the STOP-Bang (9 studies) was also mixed and depends largely on the severity of OSA and the cut-off chosen. The standard cutoff $\geq$3 tended to perform poorly with overall accuracy varying between 40 and 50%. Mason et al. [39] and Nunes et al. [40] using the gold standard PSG for validation found better specificity and less chance of false positives when the cut-off value was raised to 5 or 6. With atrial fibrillation patients, Abumuamar et al. [41] conducted a fine grained validation of the STOP-Bang assessing every cutoff level from 3 to 6 at mild and moderate OSA severity levels. As observed in the studies with ACS patients, the ability to prevent false positives improved with increased cutoff values, but overall accuracy peaked at a cutoff value of 5; increasing the cutoff value also reduced sensitivity of the test. At best the global accuracy of the STOP-Bang at any combination did not exceed 66% and the ROC was of moderate predictive value at 0.74. Two studies also compared the diagnostic accuracy of level 3 portable at home sleep study devices with the gold standard, PSG [42,43]. In both studies, all subjective measures could not match the diagnostic accuracy of a level 3 portable device which obtained between 82 and 89% global accuracy at mild levels of severity, compared to between 61% and 69% global accuracy for the BQ and STOP-Bang. Overall, the STOP-Bang in cardiac patients did not perform as well as the reference group (eg, non-cardiac surgery patients) [44]. The Epworth Sleepiness Scale (ESS) performed poorly with all types of patients in all studies with global accuracy below 50% [45].

Meta-analysis of diagnostic accuracy was conducted for the BQ and Stop-Bang (cut-off $\geq$3) at mild (AHI $\geq$5) and moderate OSA levels (AHI $\geq$15). There were insufficient studies available to assess pooled data for severe OSA (AHI $\geq$30), or for other instruments apart from the BQ and Stop-BANG. Diagnostic accuracy forest plots and ROC are presented in Fig. 2 (BQ) and 3 (Stop-Bang). The pooled diagnostic accuracy calculations (Table 3) confirmed only fair sensitivity for the BQ (0.49) and good sensitivity (0.93) for the Stop-BANG for predicting probability of patients with moderate OSA. However, with specificity, the test's ability to correctly reject healthy patients without OSA, the BQ performed slightly better (0.66) and the Stop-BANG performed poorly (0.15). Overall global accuracy as determined by the AUC was marginally better for the Stop-Bang. A similar pattern of results was observed for mild OSA levels (AHI $\geq$5) with relatively better sensitivity in the Stop-Bang compared to the BQ and poor to moderate specificity in both instruments. At both levels of OSA severity the Stop-Bang exhibited higher diagnostic odds ratios and AUROC than the BQ indicating better overall accuracy in prediction.

The I^2 calculations indicated that high heterogeneity existed among eligible studies particularly for the Stop-Bang. To verify whether this heterogeneity could be explained by a threshold effect, the Spearman approach was applied. A value of0.100 (p = 0.873) for the BQ and 0.200 (p = 0.800) for the Stop-Bang indicated the absence of the threshold effect in our meta-analysis. Hence, heterogeneity should be explained by other factors such as different clinical or sociodemographic characteristics and differences in the study design. We conducted a meta-regression analysis to assess whether covariates such as affected the relative diagnostic odds ratio (RDOR). There were no significant effects of all covariates on the RDOR: impact of diagnostic category (ACS versus patients with Atrial Fibrillation) (coef = 0.47, p = 0.127, RDOR 1.60 95% CI 0.87–2.97); percentage female in each study (coef = 0.03, p = 0.164, RDOR = 1.03 95% CI = 0.98–1.07); reference (PSG or portable monitor) (coef = 0.47,p = 0.127, RDOR = 1.60 95% CI 0.87–2.97) and quality of study (coef = −0.048, p = 0.135, RDOR = 0.95 95% CI 0.89; 1.02).

Inter-rater agreement on quality of included studies was substantial (Kappa = 0.64, 72% agreement, SE = 0.10) Publication bias as assessed by Deek's funnel plot asymmetry test revealed no bias for the BQ (p = 0.11) or Stop-Bang (p = 0.85).

3.2.1. Other studies that have assessed probability of OSA in cardiac patients

A total of 24 studies, including the 19 that provided diagnostic accuracy details, were identified that assessed OSA in cardiac patients (Supplemental Table 4).

3.3. Insomnia

A total of 23 studies were identifies that measured insomnia in studies with cardiac patients. Insomnia has been assessed in cardiac patients initially in the hospital/coronary care setting but more recently in cardiac rehabilitation programs and ehealth settings (Supplemental Table 5). There were no studies identified that specifically provided diagnostic accuracy information with cardiac patients. As shown in Supplemental Table 5, one tool, the Insomnia Severity Index (ISI), was most frequently used in this domain (over 80% of studies assessing insomnia) and has proven suitable for adaptation in a variety of settings. Importantly, this measure has been shown to be responsive to change following cognitive based interventions for insomnia [46–49] and has been widely used in a variety of settings with patients presenting a wide range of cardiovascular conditions.

Other instruments that have been used to assess insomnia symptoms with cardiac patients include the Pittsburgh Sleep Quality Index, Bergen Insomnia Scale, Dysfunctional Beliefs and Attitudes about Sleep (DBAS) and Insomnia Symptoms from the Sleep Habits Questionnaire.

3.4. Sleep quality

Over 90% of studies that assessed sleep quality in cardiac patients (Supplemental Table 6) used the Pittsburgh Sleep Quality Index. Sleep quality has been utilised in a variety of settings and has been associated with factors such as demographics [49–54], severity of cardiac condition [49,53–56], further adverse cardiac events [57], medication usage [58], cognitive impairment [59], anxiety and depression [54,60,61], quality of life [62–64], Type D personality [65], post-traumatic stress [66], exercise tolerance [67,68], cardiac rehabilitation attendance [69,70] and has been used in a variety of interventions as either a primary or secondary outcome [49,71–75].

Table 1
Characteristics of identified instruments that have been used in research with cardiac patients.

Domain/Tool name	Components	No. items	Range of scores	Standard cutoff score	Time to complete	Mode	Recall period
Obstructive Sleep Apnoea							
Berlin Questionnaire [109]	Snoring Daytime somnolence Hypertension & BMI	10	0–10	2 or more categories positive	5–10 min	Self	Lifetime
STOP [44]	OSA	4	0–4		1 min	Self	Lifetime
STOP-BANG [44,104]	OSA	8	0–8	≥3	1–3 min	2 items staff/6 items self	Lifetime
NoSAS Score [110]	OSA	5	0–17	≥8		Staff	
Mallampati score [111]	OSA	1	1–4	class 3 or 4	2 min	Clinician	Present
Sleep Apnea Scale of Sleep Disorders Questionnaire [112]	Sleep disturbances due to sleep apnoea and sleep apnoea risk factors	8	0–60	In sleep clinic patients 36 for men 32 for women	8 min	Self	Lifetime
Daytime Sleepiness							
Epworth Sleepiness Scale [113]	Sleep propensity in daily situations	8	0–24	≥10	8 min	Self	1–4 weeks
Stanford Sleepiness Scale [114]	current state of sleepiness	1	1–7	No cutoff	1 min	Self	At current time
Insomnia							
Insomnia Severity Index [115]	Insomnia	7	0–28	15–21 = Clinical insomnia	5 min	Self	Last 2 weeks
Athens Insomnia Scale [88]	Insomnia	8	0–24	≥6	5 min	Self	Last month
Jenkins Sleep Scale [116]	Insomnia	4	0–5	2	2 min	Self	Last month
Vicious cycles of sleeplessness scale [117]	Insomnia	8	0–32		5–7 min	Self	
Bergen Insomnia Scale [118]	Insomnia	6	0–42	Scoring 3 or above on at least one of the first four items and scoring 3 or above on at least one of the last two items	3 min	Self	Last month
Sleep quality							
Functional Outcomes of Sleep Questionnaire	Activity level, vigilance, intimacy and sexual relationships, general productivity, social outcome	30	0–100	≥18 = normal sleep	10–15 min	Self	At current time
Functional [119] Outcomes of Sleep Questionnaire (FOSQ-10) [78]	Activity level, vigilance, intimacy and sexual relationships, general productivity, social outcome	10	5–20	≥18 = normal sleep	2–5 min	Self	At current time
Pittsburgh Sleep Quality Index [120]	Sleep quality, latency, duration, habitual sleep efficiency, sleep disturbances, medications, daytime dysfunction	19	0–19	>5 "bad sleepers"	10 min	Self	Previous month
Verran and Snyder-Halpern Visual Analogue Sleep Scale [121]	Disturbance (sleep fragmentation and latency), Effectiveness (Alteration in sleep pattern, Dissatisfaction with sleep, Feeling unrested), and Supplementation (Difficulty in daily functioning, Difficulty initiating sleep)	16	0–700 Disturbance. 0–600 Effectiveness, 0–400 Supplementation	Scores of the three subscales were categorized into three levels	5–10 min	Self 15 Visual analogue items, 1 item computed by staff	Previous night
Richards-Campbell Sleep Questionnaire [122]	Sleep depth, sleep latency, number of awakenings, efficiency, and sleep quality		0–100	Scores over 50 indicative of sleep problems	2–5 min	Self but items read aloud by staff recommended, 5 Visual analogue items	Previous night
Uppsala Sleep Inventory [123]		80					
Uppsala Sleep Inventory-Chronic Heart Failure [124]	Sleep complaints, physical and emotional arousals, daytime symptoms, sleep need, and sleep disruption	26					
Jenkins Sleep Scale [116]	Sleep latency, frequent awakenings, trouble remaining asleep, and subjective feelings of fatigue and sleepiness	4	0–20	Higher scores indicative of sleep problems	2–5 min	Self	Past month

Abbreviations: OSA: obstructive sleep apnoea; BMI: body mass index.

Table 2
Validation of tool to assess probability of obstructive sleep apnoea in patients who have cardiac illness.

Study	Diagnosis	OSA prevalence	Validation method	Diagnostic AHI	Instrument cutoff	Sensitivity	Specificity	PPV	NPV	Overall accuracy % (95% CI)
Shapira-Daniels et al. (2020) [97]	Afib	82% mild 45% moderate	Type III portable monitoring	AHI ≥ 5	SB ≥ 3	81	42	87	33	74 (67–80)
Mohammadieh et al. (2019) [43]	Afib	68% mild 34% moderate 15% severe	PSG	AHI ≥ 10	Mallampati ≥3	67	56	60	64	61 (53–69)
					BQ	61	69	67	64	65 (57–73)
					SB ≥ 5	44	94	89	63	69 (61–77)
					ESS ≥10	17	81	46	49	49 (40–57)
					Type 3 mon	81	83	83	81	82 (75–88)
Calcaianu et al. (2019) [125]	ACS	68% mild	PSG	AHI ≥15	BQ	46	93	95	38	59 (44–72)
Kadhim et al. (2019) [126]	Afib	66% mild	PSG	AHI ≥ 5	ESS ≥6	45	62	70	37	48 (43–53)
					ESS ≥10	16	87	70	35	40 (36–45)
		34% moderate		AHI ≥15	ESS ≥6	49	61	39	70	57 (43–53)
					ESS ≥10	21	87	45	68	65 (60–69)
Mason et al. (2018) [39]	CABGS	47% mild	Nocturnal oximetry oxygen	ODI ≥5/hr	SB ≥ 3	95	5	47	50	47 (38–56)
					SB ≥ 6	32	75	53	56	54 (48–61)
		10% moderate	desaturation index (ODI)	ODI ≥15/hr	SB ≥ 3	100	6	48	100	55 (46–64)
					SB ≥ 6	75	77	27	97	76 (70–81)
Reuter et al. (2018) [127]	CVD	38% mild	Type III portable monitoring	AHI ≥15	BQ	73	42	43	72	54 (42–65)
					SB ≥ 3	97	12	40	88	45 (34–56)
Abumuamar et al. (2018) [41]	Afib	85% mild	Type II portable monitoring	AHI ≥5	SB ≥ 3	89	36	86	5	39 (29–49)
					SB ≥ 6	16	100	100	0	29 (20–39)
		60% moderate		AHI ≥15	SB ≥ 3	100	19	65	100	67 (60–77)
					SB ≥ 6	14	86	62	40	43 (33–54)
Cho et al. (2017) [128]	ACS	37% moderate	PSG	AHI ≥15	BQ	58	66	50	73	63 (49–76)
					SB ≥ 3	53	50	37	64	50 (36–64)
Jonasson et al. (2017) [129]	Afib	85% mild 49% moderate	Type III portable monitoring	AHI ≥ 10	SB ≥ 3					68 (59–76)
					NoSAS					69 (61–77)
					Acoustic pharyngometry					51 (41–60)
Nunes et al. (2015) [40]	CABGS	52% moderate	PSG	AHI ≥15	BQ	67	26	50	42	47 (31–63)
					STOP	100	5	50	33	49 (34–66)
					SB ≥ 3	90	5	51	33	51 (35–67)
					SB ≥ 4	86	26	56	63	55 (44–66)
					SB ≥ 5	52	47	50	50	50 (39–61)
					SB ≥ 6	29	74	55	48	53 (41–64)
					SB ≥ 7	5	95	50	47	50 (39–61)
Szymanski et al. (2015) [130]	ACS	63% mod moderate	Type III portable monitoring	AHI ≥15	OSACS score					AUC 0.87
Zhao et al. (2015) [131]	CABGS	79% mild	Portable monitoring wristworn	AHI ≥ 5	BQ	48	66	84	25	51 (43–59)
Lee et al. (2016) [132]	PCI	45% mild	Type III portable monitoring	AHI ≥15	BQ	43	72	56	61	59 (56–62)
Pittman et al. (2014) [133]	Afib	36% mild	Nocturnal oximetry	ODI ≥5/hr	SB ≥ 3	97	43	49	97	63 (52–72)
Martinez et al. (2012) [134]	Angina	44% moderate	Type III portable monitoring	AHI ≥15	BQ	72	50	53	70	60 (46–73)
Danzi-Soares et al. (2012) [42]	CABGS	87% mild 54% moderate	PSG	AHI ≥ 5 AHI ≥15	BQ	72	44	90	19	69 (56–79)
					ESS ≥10	27	89	88	20	34 (23–47)
					Type 3 mon	92	67	95	55	89 (79–95)
					BQ	74	34	57	52	56 (43–68)
					ESS ≥10	21	71	49	39	44 (33–57)
					Type 3 mon	66	78	78	66	71 (59–82)
Laporta et al. (2012) [135]	CVD	75% mild 44% moderate	PSG	AHI ≥5 AHI ≥10	BQ	81	39	80	41	70 (60–80)
					CDSS	99	87	96	95	96 (89–99)
					BQ	85	37	52	76	58 (48–69)
					CDSS	98	82	81	98	89 (81–95)
Sert Kuniyoshi et al. (2011) [129]	MI	73% mild	PSG	AHI ≥5	BQ	68	46	77	34	62 (51–71)
		46% moderate		AHI ≥15		65	36	47	54	49 (39–60)
		21% severe		AHI ≥30		71	37	23	83	44 (34–55)
Capodanno et al. (2011) [45]	Angina	85% mild	Type III portable monitoring	AHI ≥15	ESS >8	42	66	87	17	46 (40–51)

Abbreviations: OSA severity: mild AHI ≥5 mod (moderate) AHI ≥15 severe AHI ≥30; Afib = atrial fibrillation; CABGS = coronary artery bypass surgery; MI = myocardial infarction; PCI = percutaneous coronary intervention; CVD = cardiovascular disease; AHI: apnoea-hypopnoea index; ODI = oxygen desaturation index; PSG = polysomnography; BQ = Berlin Questionnaire; ESS = Epworth Sleepiness Scale; NoSAS = SB = Stop-Bang; CDSS= Clinical Decision-Support System; PPV = positive predictive value; NPV = negative predictive value; AUC = area under curve.

4. Discussion

This review examined three major categories of instruments relevant to screening sleep disorders in cardiac patients: OSA, insomnia and sleep quality. With the absence of published diagnostic accuracy tests for insomnia and sleep quality in cardiac patients, meta-analysis of diagnostic accuracy tests for this population was only possible for moderate OSA. For OSA screening, a

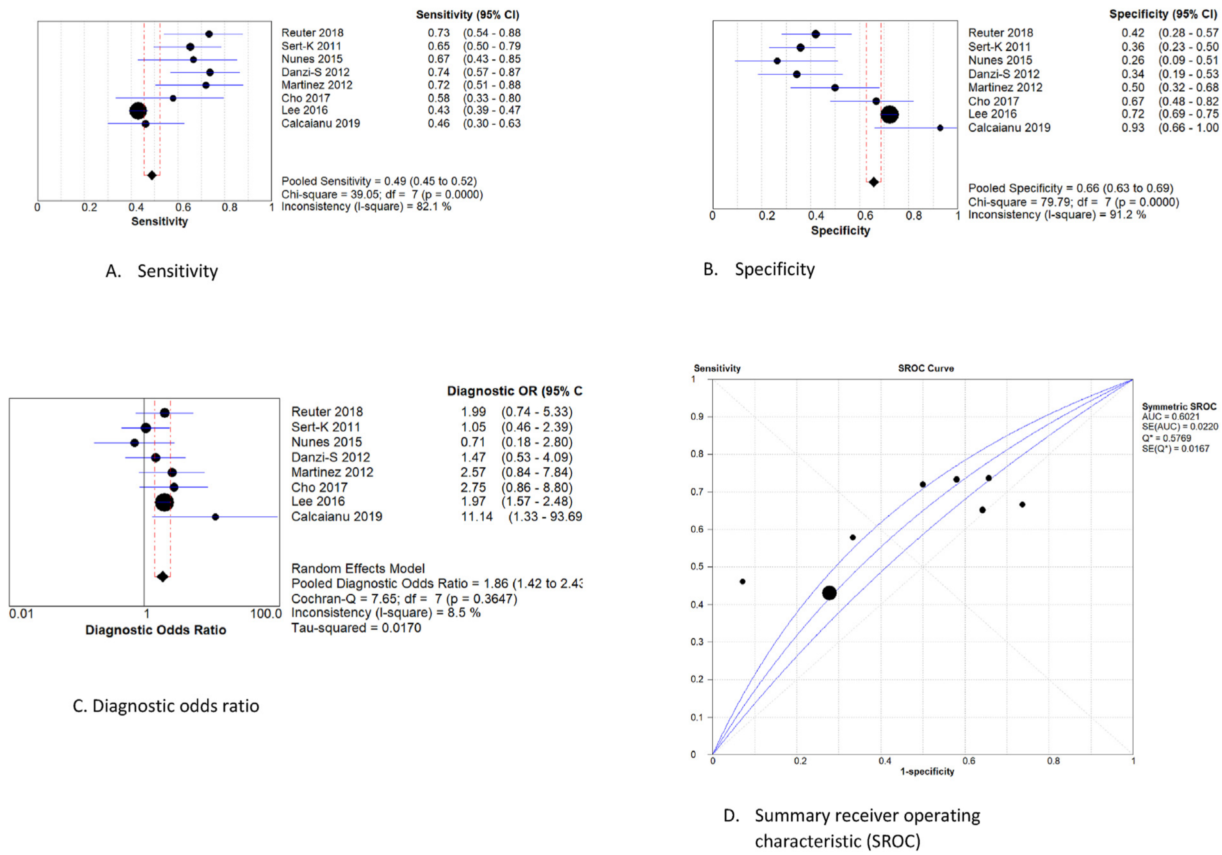

Fig. 2. Diagnostic accuracy forest plots and receiver operating characteristics for the Berlin Questionnaire at moderate OSA severity (AHI ≥15).

comparison of the BQ and the Stop-Bang, revealed acceptable sensitivity for the BQ and good sensitivity for the Stop-Bang, but poor specificity for both instruments. An ideal diagnostic test in a population such as cardiac patients with a high prevalence and therefore high pre-test probability of disease, should have higher sensitivity while maintaining high specificity [76]. The high sensitivity of the STOP-Bang instrument, and to a lesser extent, the BQ, can assist health professionals identify patients with high risk of moderate-to-severe OSA, but the low specificity, evident in both instruments, means that there is also a high probability that many patients will be unnecessarily referred to PSG testing.

An obvious solution to increase the specificity of the Stop-Bang is to increase the cut-off value from the standard score of ≥3. Perhaps the best demonstration of this is the study by Nune et al. [40] where a cut-off of 3–7 was used for a cohort of CABGS patients. As the STOP-Bang cut-off was increased, the sensitivity decreased and specificity increased. Similarly, using cut-off scores of 5 or 6 for patients with atrial fibrillation, resulted in good specificity but poor sensitivity [41,43]. Another possible solution is to use a combination of tests to increase accuracy. An example of this has been demonstrated in primary care settings [77], where a combination of ESS (cut-off ≥8) and Stop-Bang scores improved specificity or sensitivity, over and above the Stop-Bang alone. Alternatively, it has been argued that the poor diagnostic accuracy of the ESS shows that this method is not clinically appropriate and it would be preferable to add low cost (portable Type III) diagnostic testing to increase specificity [18]. Further, there is evidence that OSA is a heterogenous condition with a variety of clinical and pathophysiologic characteristics and the asymptomatic (non-sleepy) phenotype is commonly seen among cardiac patients, meaning that ESS scores will therefore be largely irrelevant in many of these patients. Perhaps a combination of brief tools such as the Stop-Bang and a brief measure of functional outcomes (eg. the FOSQ-10 [78]) and routinely collected clinical scores (eg, Mallampati score) may maximise predictive ability while keeping assessment practical. Research with combinations of tools such as these is still at a preliminary stage [79].

To date, insomnia assessment, has not been validated in cardiac patients against the gold standard diagnostic interview. The most frequently used instrument, the ISI, has been well validated in non-cardiac populations such as those with chronic and primary insomnia [80,81], primary care outpatients [82], cancer patients [83], and patients with back pain [84] and is recommended by The American Academy of Sleep Medicine (AASM) as an important quality and satisfaction outcome measure [85]. A meta-analysis of validation studies for the ISI in other patient groups have demonstrated good pooled sensitivity (0.88: 0.79 to 0.93) and specificity (0.85:0.68 to 0.94) indicating high diagnostic ability with a high diagnostic odds ratio [86]. These diagnostic properties, combined with its practicality (eg, brief and easy to administer and score, suitable for online administration [87]) establishes it as the dominant instrument in this category. An alternative choice to assess insomnia is the PSQI However, like the ISI, it has not been specifically validated with cardiac patients despite its widespread use. In comparison to the ISI, however, the PSQI has lower pooled specificity [0.75 (0.64–0.84)] [86], and is 12 items longer than the ISI as it also measures other areas of sleep disturbance. Another respected instrument is the Athens Insomnia Scale [88] which is brief and comparable to the ISI in diagnostic accuracy [86,89] but has been included in very few published research papers.

It should be noted that insomnia assessment may be particularly important for heart failure patients because of the high prevalence

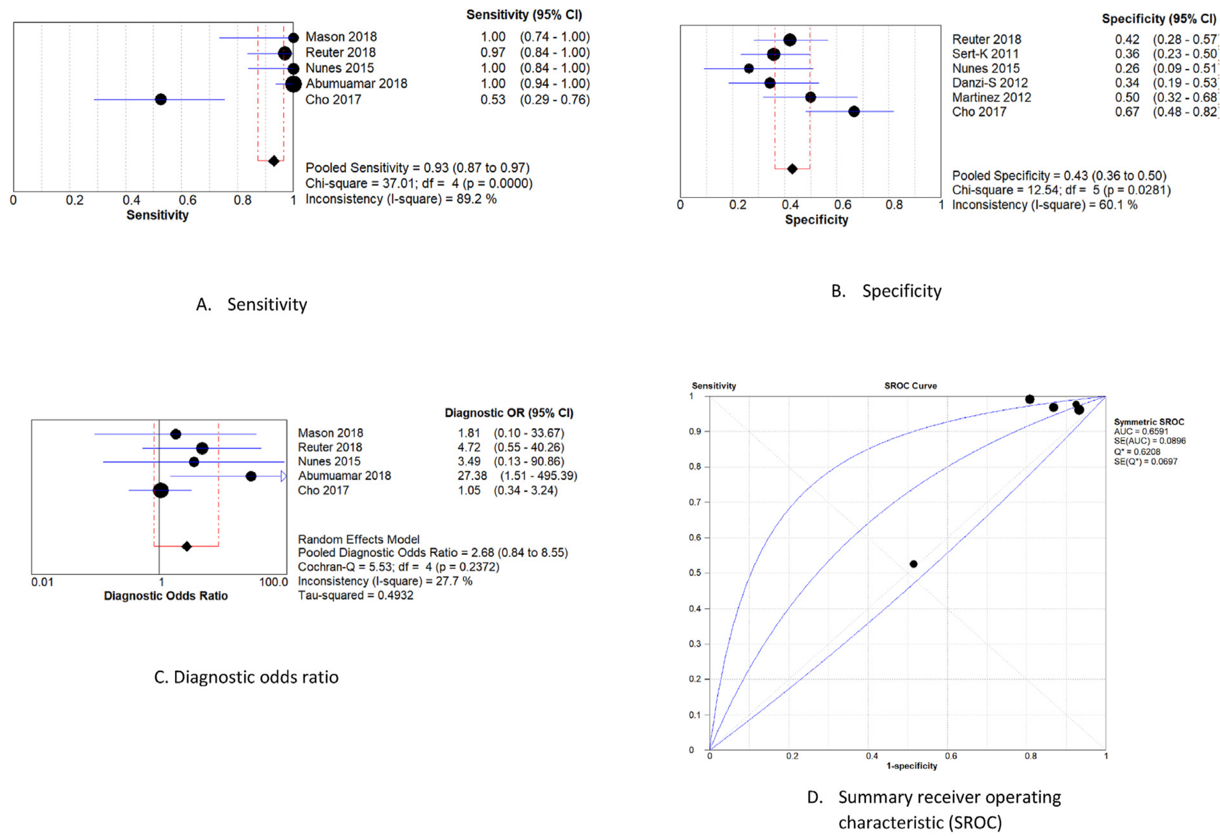

Fig. 3. Diagnostic accuracy forest plots and receiver operating characteristics for the Stop-Bang instrument using standard cutoff of ≥3 and moderate OSA severity (AHI ≥15).

Table 3
Pooled estimates of predictive values for diagnosing mild and moderate sleep apnoea in patients with acute coronary syndrome and atrial fibrillation.

Instrument	No of studies	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)	DOR Inconsistency (I-square)	AUROC (SE)
Mild OSA								
Berlin Questionnaire	4	0.64 (0.58–0.69)	0.42 (0.34–0.51)	1.16 (0.97–1.38)	0.77 (061–0.98)	1.61 (1.01–2.56)	0.10 (p = 0.54)	0.58 (0.04)
Stop-BANG ≥3	4	0.88 (0.83–0.91)	0.29 (0.22–0.37)	1.34 (0.85–2.12)	0.34 (0.14–0.82)	4.17 (1.38–12.59)	58.3 (p = 0.07)	0.72 (0.08)
Moderate OSA								
Berlin Questionnaire	8	0.49 (0.45–0.52)	0.66 (0.63–0.69)	1.27 (1.04–1.55)	0.77 (0.71–0.83)	1.86 (1.42–2.43)	0.10 (p = 0.55)	0.60 (0.02)
Stop-BANG ≥3	5	0.93 (0.87–0.96)	0.15 (0.11–0.20)	1.09 (1.03–1.17)	0.38 (0.10–1.41)	2.68 (0.84–8.55)	13.0 (p = 0.33)	0.66 (0.09)

Abbreviations: OSA = Obstructive sleep apnoea, AUROC = area under receiver operator curve, CI = confidence interval, SE = standard error.

in these patients [90,91] and the biological mechanisms that may underlie the associations between insomnia and heart failure [92]. The studies described in this paper indicate a growing evidence base showing that interventions such as cognitive behaviour therapy have beneficial effects on important outcomes such as perceived sleep quality, sleep duration anxiety, depression and fatigue [47,48,93].

It is important to assess sleep quality in cardiac patients since there is evidence that improving the quality of sleep, rather than simply increasing sleep duration, is important to the quality of life and recovery [64]. It has also been recognised that conditions such as OSA can severely affect sleep quality which is associated with clinical depression [94] and reduced exercise capacity [95], and it is therefore important to screen for sleep quality in conjunction with OSA screening. The AASM have recommended the PSQI as a standard measure of sleep satisfaction or quality [85]and is the most commonly used measure of sleep quality in the cardiac patient population. Although the PSQI is mostly used as a global score (eg, to assess the relationship of median sleep quality score with depression [60]) the multidimensional aspects have been confirmed with cardiac patients, with the individual dimensions such as sleep efficiency also proving to be useful in evaluation of quality of sleep [64] With the recognised need for briefer instruments that have practical utility in clinical settings [17], relatively new instruments such as the FOSQ-10 [78] (ten items) have proven to be promising in replicating dimensions obtained in longer instruments.

Having surveyed the sleep disturbance screening instruments in current use with cardiac patients we are in a position to make some recommendations on what instrument should be used (see Table 4). Given the high prevalence of OSA [3], insomnia [4,5] or possibly COMISA [96] in patients living with CVD, it may be advisable to screen for both OSA and insomnia rather than focus on a single condition which may inadvertently lead to inadequate or incorrect diagnosis and suboptimal treatment [16].

Table 4
Recommended available screening instrument for given diagnostic categories.

Sleep Disorder	ACS/Post-Surgical/Atrial fibrillation	Heart Failure
Obstructive Sleep Apnoea	Stop-BANG score 2 step method (Chung et al. [104]) 0–2 = confident low risk 3–4 = intermediate risk (step 2)[a] ≥5 = confident high risk (consider supplementing with administration of ESS and FOSQ-10) Atrial fibrillation – use objective measure if practical	Use PSG or portable at home monitor
Central Sleep Apnoea	Use objective measure (PSG or portable home monitor)	Use objective measure (PSG)
Insomnia	Insomnia Severity Index	ISI
Sleep Quality	Pittsburgh Sleep Quality Index Functional Outcomes of Sleep-10	PSQI FOSQ-10
Daytime Sleepiness	Epworth Sleepiness Scale	ESS

Abbreviations: ACS: acute coronary syndrome; CSA: central sleep apnoea; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; FOSQ-10: Functional Outcomes of Sleep Questionnaire; ESS: Epworth Sleepiness Scale; PSG: polysomnography.

[a] See (Chung et al. [104]) for further instructions.

Given the high prevalence of OSA and low specificity of screening tools reported here, a conclusion could be reached that ideally all patients should be directly referred to objective assessment. Indeed, some of the authors in the papers under review here have concluded the same [41,97] or suggest changes to cut-off scores to improve specificity and predictive value [39]. A recent European Respiratory Taskforce on OSA and driving risk concluded that “questionnaires do not reliably rule in or rule out the presence of OSA” [98].In practical terms however, it could be argued that any potential increase in predictive ability offered by objective measures should be balanced against practical considerations such as the increased burden on the health care team to collect clinical variables [99], costs of sleep studies [100] and recognition that objective sleep measurement may need to be completed on multiple occasions due to night to night variability of OSA [101,102]. The AASM Clinical Practice Guidelines recommend clinical pathways that include “use of tools or questionnaires that capture clinically important information that is reviewed by a board-certified sleep medicine physician prior to testing”p.485 [103]. They further state that these questionnaires should not be used for final diagnosis. Similarly, the Australasian Sleep Association state that these tools may assist clinicians in determining who is likely to have moderate to severe OSA and who may be suitable to proceed directly to objective sleep studies [18]. We believe this should be the approach here. The tools are a practical means of assessing pre-test probability of moderate to severe OSA in settings such as cardiac rehabilitation but should certainly not be considered diagnostic endpoints.

With consideration of the aforementioned caveats for OSA screening, we recommend the Stop-Bang given its superior sensitivity and DOR compared to the BQ. It should be noted that the Stop-Bang has also been recommended for routine preoperative assessment for cardiac patients in a recent review led by interventional cardiologists [1]. However, given the poor specificity of the Stop-Bang, however it is advised to apply the author's current two-step method for assessing risk [104]. With this method if a patient's Stop-Bang score is 2 or lower, they are considered to be at low risk of OSA, and the possibility of those patients having more severe levels of sleep apnoea can be confidently ruled out. Conversely, when a patient has a STOP-Bang score of 5–8, we can be highly confident that the patient actually has moderate to severe OSA. Patients who fall in the middle with STOP-Bang scores of 3 or 4 can be further classified as having a higher risk for moderate to severe OSA if one of four further conditions are present ((1) the combination of a STOP score of ≥2 plus BMI > 35 kg/m2; (2) a STOP score of ≥2 plus male gender; (3) a STOP score of ≥2 plus neck circumference > 40 cm (16 in); or (4) a STOP-Bang score of ≥3 plus serum HCO3- ≥ 28 mmol/L [104]. This two-step algorithm is yet to be validated with cardiac patients, however, so caution is advised if patients score in this middle range and it may advisable to undertake objective measurement if practical. Some researchers have suggested that questionnaire screening with atrial fibrillation patients is inadequate given such low specificity and recommend objective monitoring [41]. Since central sleep apnoea with Cheyne Stokes respiration (CSA-CSR) is common in patients experiencing heart failure [105], comprehensive objective measurement which includes assessment of oscillatory or periodic breathing patterns is recommended. It should also be noted that many of the newer or lesser known screening instruments, such as the OSA-50 [106], have not yet been validated with cardiac patients and may still prove to have good diagnostic accuracy. Other efforts to develop and improve tools and screening algorithms for OSA are still underway [79]. Given implications for prognosis and associated psychosocial outcomes, it is also recommended to accompany OSA screening with assessment of daytime sleepiness (ESS) and sleep quality (PSQI or FOSQ-10). Despite the lack of validation studies for cardiac patients, for insomnia screening, it is our opinion that the ISI can still be recommended since it has achieved excellent validation across a wide range of patient groups. The AIS is also a possibility here with comparable diagnostic ability and clinical utility to the ISI but does not have the proven track record of the ISI with cardiac patients. For sleep quality, the PSQI has been the dominant instrument and is probably preferred if assessment of insomnia and sleep quality is required without administering the ISI. For briefer screening the FOSQ-10 is recommended as an accompaniment to the Stop-Bang when screening for OSA or the ISI if screening for insomnia.

This meta-analysis has a number of limitations. First, the meta-analysis of diagnostic accuracy was limited to diagnostic categories and level of severity where a sufficient number of included studies and given instruments were available, in this case moderate OSA (AHI ≥15) with the BQ and Stop-Bang. It is likely and evident from published results (see Table 2) that specificity may be improved when the target condition is mild (OSA AHI ≥5 [41,107,108] or AHI ≥10 [43]). Second, the heterogeneity observed in the meta-analysis for the Stop-Bang was high. We ruled out the possibility of this being due to a threshold effect or diagnostic category, but there are many other clinical (eg, variation in co-morbidities) or study variables (eg, sample size, age and sex distribution variation) that could potentially affect these pooled analyses. We used the random effects method, which is more suitable when heterogeneity exists but clearly, further validation studies are required to improve the robustness of these findings. Third, the review of insomnia and sleep quality instruments is based on diagnostic accuracy obtained in other patient groups together with qualitative assessment of their use with cardiac patients. Finally, there is a recency bias against instruments that have been validated or used in other patient populations but have yet to be used with cardiac patients or are currently under development.

5. Conclusion

The currently available, and most frequently used, instruments (the BQ and Stop-Bang) can identify those cardiac patients most likely to have moderate OSA, but tend to have poor specificity which may result in a large number of false positives. Results from any screening tool are a practical means of assessing pre-test probability of moderate to severe OSA which should be confirmed by objective measurement. Although insomnia instruments are yet to be specifically validated with cardiac patients, the existing evidence from a wide range of other patient populations and widespread use in a variety of settings point to good diagnostic ability and practical utility with the dominant instrument, the ISI. Both categories of instrument can be supplemented with measures of daytime sleepiness and sleep quality in order to obtain a more comprehensive picture of the impact of the sleep disorders upon prognosis and rehabilitation prospects.

Author contributions

ML. Ideas; formulation or evolution of overarching research goals and aims; data/evidence collection; Development or design of methodology; formal analysis; Writing - Original Draft; Visualization. AJ. Writing - review & editing, Validation. AB, DK, AD. Review & Editing; Supervision.

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Conflict of interest

None of the authors has any conflict of interest to disclose.

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Appendix A

Supplemental Table 1
PubMed Search Strategy.

Search ((((((((myocardial infarction [MeSH Terms]) OR ((acute[Title/abstract]) AND (coronary[Title/abstract]) AND (syndrome[Title/abstract])) OR (((myocard*[Title/abstract]) OR (heart[Title/abstract])) AND (infarct*[Title/abstract])) OR (STEMI[Title/abstract]) OR (((STelevation[Title/abstract]) OR (ST elevation[Title/abstract]) OR (ST-segmentelevation[Title/abstract]) OR (ST segment-elevation[Title/abstract]) OR (STsegment elevation[Title/abstract]) OR (ST segment elevation[Title/abstract])) AND (infarct*[Title/abstract])) OR (NSTEMI[Title/abstract]) OR (((Non-STelevation[Title/abstract]) OR (Non ST elevation[Title/abstract]) OR (Non-ST elevation[Title/abstract]) OR (Non ST-elevation[Title/abstract]) OR (Non STsegment-elevation[Title/abstract]) OR (Non ST segment-elevation[Title/abstract]) OR (Non ST-segment elevation[Title/abstract]) OR (Non ST segment elevation [Title/abstract]) OR (Non-ST-segment-elevation[Title/abstract]) OR (Non- ST-segment elevation[Title/abstract]) OR (Non-ST segment elevation[Title/abstract])) AND (infarct*[Title/abstract])) OR (acute coronary syndrome [MeSH Terms]) OR (cardiac rehabilitation[MeSH Terms]))) OR (((percutaneous coronary[MeSH Terms]) OR (stents[MeSH Terms]) OR (balloon dilatation [MeSH Terms]) OR (Myocardial revascularization [MeSH Terms]) OR (angioplast* [Title/abstract]) OR ((percutaneous[Title/abstract]) AND (coronary[Title/abstract]) AND (intervention[Title/abstract])) OR ((percutaneous[Title/abstract]) AND (coronary[Title/abstract]) AND (revascularization[Title/abstract])) OR ((percutaneous[Title/abstract]) AND (coronary[Title/abstract]) AND (revascularisation[Title/abstract])) OR (revascularization*[Title/abstract]) OR (revascularisation*[Title/abstract]) OR (reperfusion*[Title/abstract]) OR (stent*[Title/abstract]) OR (balloon*[Title/abstract]) OR (dilatat*[Title/abstract]) OR (transluminal*[Title/abstract]) OR ((coronary[Title/abstract]) AND atherectom*[Title/abstract]))))
AND (#1 OR #2)) AND ((instrumentation[sh] OR methods[sh] OR "Validation Studies"[pt] OR "Comparative Study"[pt] OR "psychometrics"[MeSH] OR specificity [tiab] OR “receiver operator” [tiab] OR “diagnostic accuracy” [tiab] OR psychometr*[tiab] OR clinimetr*[tw] OR clinometr*[tw] OR "outcome assessment (health care)"[MeSH] OR "outcome assessment"[tiab] OR "outcome measure*"[tw] OR "observer variation"[MeSH] OR "observer variation"[tiab] OR "Health Status Indicators"[Mesh] OR "reproducibility of results"[MeSH] OR reproducib*[tiab] OR "discriminant analysis"[MeSH] OR reliab*[tiab] OR unreliab*[tiab] OR valid*[tiab] OR "coefficient of variation"[tiab] OR coefficient[tiab] OR homogeneity[tiab] OR homogeneous [tiab] OR "internal consistency"[tiab] OR (cronbach*[tiab] AND (alpha[tiab] OR alphas[tiab])) OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab])) OR agreement[tw] OR precision[tw] OR imprecision [tw] OR "precise values"[tw] OR test-retest[tiab] OR (test[tiab] AND retest [tiab]) OR (reliab*[tiab] AND (test[tiab] OR retest[tiab])) OR stability[tiab] OR interrater[tiab] OR inter-rater[tiab] OR intrarater[tiab] OR intra-rater[tiab] OR intertester[tiab] OR inter-tester[tiab] OR intratester[tiab] OR intra-tester [tiab] OR interobserver[tiab] OR inter-observer[tiab] OR intraobserver[tiab] OR intra-observer[tiab] OR intertechnician[tiab] OR inter-technician[tiab] OR intratechnician[tiab] OR intra-technician[tiab] OR interexaminer[tiab] OR inter-examiner[tiab] OR intraexaminer[tiab] OR intra-examiner[tiab] OR interassay[tiab] OR inter-assay[tiab] OR intraassay[tiab] OR intra-assay[tiab] OR interindividual[tiab] OR inter-individual[tiab] OR intraindividual[tiab] OR intra-individual[tiab] OR interparticipant[tiab] OR inter-participant[tiab] OR intraparticipant[tiab] OR intra-participant[tiab] OR kappa[tiab] OR kappa's [tiab] OR kappas[tiab] OR repeatab*[tw] OR ((replicab*[tw] OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR results [tw] OR test[tw] OR tests[tw])) OR generaliza*[tiab] OR generalisa*[tiab] OR concordance[tiab] OR (intraclass[tiab] AND correlation*[tiab]) OR discriminative[tiab] OR "known group"[tiab] OR "factor analysis"[tiab] OR "factor analyses"[tiab] OR "factor structure"[tiab] OR "factor structures"[tiab] OR dimension*[tiab] OR subscale*[tiab] OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab])) OR "item discriminant"[tiab] OR "interscale correlation*"[tiab] OR error[tiab] OR errors[tiab] OR "individual variability"[tiab] OR "interval variability"[tiab] OR "rate variability"[tiab] OR (variability[tiab] AND (analysis[tiab] OR values[tiab])) OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab])) OR "standard error of measurement"[tiab] OR sensitiv*[tiab] OR responsive*[tiab] OR (limit[tiab] AND detection[tiab]) OR "minimal detectable concentration"[tiab] OR interpretab*[tiab] OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND (important[tiab] OR significant[tiab] OR detectable [tiab]) AND (change[tiab] OR difference[tiab])) OR (small*[tiab] AND (real [tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR "meaningful change"[tiab] OR "ceiling effect"[tiab] OR "floor effect"[tiab] OR "Item response model"[tiab] OR IRT[tiab] OR Rasch[tiab] OR "Differential item functioning"[tiab] OR DIF[tiab] OR "computer adaptive testing"[tiab] OR "item bank"[tiab] OR "cross-cultural equivalence"[tiab])))
AND (#3 and #4)) AND (obstructive sleep apnoea (all fields) OR sleep apnea, obstructive (mesh terms) OR sleep (all fields) and apnea (all fields) and obstructive (all fields) OR obstructive sleep apnea (all fields) OR obstructive (all fields) and sleep (all fields) and apnea (all fields) sleep apnoea (all fields) OR sleep apnea syndromes (mesh terms) OR sleep (all fields) and apnea (all fields) and syndromes (all fields) OR sleep apnea syndromes (all fields) OR sleep (all fields) and apnea (all fields) OR sleep apnea (all fields) obstructive sleep apnoea syndrome (all fields) OR sleep apnea, obstructive (mesh terms) OR sleep (all fields) and apnea (all fields) and obstructive (all fields) OR obstructive sleep apnea (all fields) OR obstructive (all fields) OR "Sleep Initiation and Maintenance Disorders"[Mesh] OR insomnia*[tw] OR Sleep Apnea Syndromes[mh] OR "sleep apnea"[tiab] OR "sleep disordered breathing"[tiab] OR obstructive sleep apnea syndrome (all fields) OR "Sleep"[Mesh] OR Sleep*[tw])) OR “sleep quality” [tiab] OR “STOP-bang” [tiab] OR “berlin questionnaire” [tiab] OR “Insomnia Severity Index” [tiab] OR “Pittsburgh Sleep Quality Index” [tiab] OR “Functional Outcomes of Sleep” [tiab] OR OSA50 [tiab] OR “Insomnia Scale” [tiab] OR “Sleep Scale” [tiab] OR “sleep questionnaire” [tiab]

Supplemental Table 2
Characteristics of the included study populations.

Study	Measures	N	Age Mean (SD, range) yr	Gender % female	Cardiac diagnosis	Sleep Disorder/ domain of interest	Setting	Country	Patient selection	Study design	Response rate	Study quality rating
Shapira-Daniels et al. (2020) [97]	STOP-BANG	188	62 ± 11	35	Afib	OSA	Two tertiary referral hospitals where catheter ablation of AF is routinely performed	USA	Consecutively recruited	prospective cohort study	89%	4
Mohammadieh et al. (2019) [43]	STOP-BANG ESS	72	Average age 60.4 years (SD 11.6, range 18+	33	Afib	OSA	Hospital clinic	Australia	Randomised	prospective observational diagnostic accuracy study	Ongoing study (interim results presented)	4
Calcaianu et al. (2019) [125]	BQ ESS PSQI	53	59.5 ± 10	22	ACS/PCI	OSA	Cardiac Intensive Care Unit	France	Consecutively recruited	prospective cohort study	42%	4
Kadhim et al. (2019) [126]	ESS	442	60 ± 11	31	Afib	Sleepiness			Consecutively recruited		85%	4
Mason et al. (2018) [39]		122	70.3 (0.80)	12	CABGS	OSA	specialist cardiothoracic center	UK	without previous diagnosis of OSA, undergoing elective CABG	prospective observational cohort	80%	4
Reuter et al. (2018) [127]	STOP-BANG BQ	89	59 ± 15	39	MI AFib HF	OSA	Hypertension clinic at university hospital	Germany	recruited from an outpatient hypertension clinic	prospective cohort study	79%	3
Abumuamar et al. (2018) [41]	STOP-BANG	95	65(12) OSA, 54 (14) non-OSA	25	Afib	OSA	two major specialized arrhythmia clinics	Canada	consecutively recruited	prospective cohort study	77%	4
Jonasson et al. (2017) [129]	STOP-BANG NoSAS	160	69.5 (9.4)	5	Afib	OSA	Community cardiology clinic	Canada	consecutively recruited	prospective cohort study	86%	3
Cho et al. (2017) [128]	BQ	52	Range 25–82	19	ACS/PCI	OSA	5 days after PCI	South Korea	consecutively recruited	prospective observational diagnostic accuracy study	Not stated	3
Lee et al. (2016) [132]	BQ ESS	1311	58.2 ± 10	15	ACS/PCI	OSA	Within 7 days of PCI	5 country	consecutively recruited	prospective, multicenter registry	75%	4
Nunes et al. (2015) [40]	Stop STOP-BANG BQ	40	56 ± 7	27	CABGS	OSA	patients referred for CABG at tertiary University Hospital	Brazil	consecutively recruited	Prospective matched cohort	40%	3
Zhao et al. (2015) [131]	BQ ESS	160	62.2 ± 9	14	Afib	OSA	scheduled to undergo an elective CABG within the next 7 days	Singapore	consecutively recruited	prospective cohort study	94%	4
Szymanski et al. (2015) [130]	OSACS score BQ ESS	158	57.1 ± 9	32	ACS	OSA	Cardiology Intensive Care Unit	Poland	consecutively recruited	prospective cohort study	Not stated	4

(*continued on next page*)

Supplemental Table 2 (*continued*)

Study	Measures	N	Age Mean (SD, range) yr	Gender % female	Cardiac diagnosis	Sleep Disorder/ domain of interest	Setting	Country	Patient selection	Study design	Response rate	Study quality rating
Pittman et al. (2014) [133]	STOP-BANG	101	62.2 (8.5)	45	Afib	OSA	Hospital clinic	UK	Patients with paroxysmal AF undergoing ablation were approached	prospective observational cohort	44%	3
Danzi-Soares et al. (2012) [42]	BQ	70	58 ± 7	24	CABGS	OSA	single outpatient clinic	Brazil	consecutive patients with severe CAD, above 40 years of age	cross-sectional	70%	5
Laporta et al. (2012) [135]	BQ	91	67.7 ± 11.8	0	CVD veterans with documented history of MI, PCI or CABGS	OSA	VA cardiology clinic	USA	Consecutive recruitment	cross-sectional	55%	3
Martinez et al. (2012) [134]	BQ	57	54 ± 7	54	Angina	OSA	Patients undergoing diagnostic cineangiography	Brazil	consecutively recruited	Secondary analysis of cross-sectional study	11%	2
Sert Kuniyoshi et al. (2011) [129]	BQ	99	62 (13)	19	MI	OSA	In-hospital cardiology service	US	recruitment was based on availability of research personnel and patients consenting to participate	cross-sectional	Not reported	3
Capodanno et al. (2011) [45]	ESS	332	65.5 ± 10.0	28	angiographically confirmed CAD	OSA/Daytime Sleepiness	During hospital stay	Italy	consecutively recruited	prospective cohort study	88%	3

Supplemental Table 3
Diagnostic accuracy data used for pooled analysis.

Author-date	TP	FP	FN	TN	Test	AHI	Diag	Female%	Qual	Ref
Mason 2018	44	51	2	2	2	5	1	12	22	3
Mason 2018	15	13	32	40	3	5	1	12	22	3
Sert-K 2011	34	49	15	23	1	5	1	19	22	1
Danzi-S 2012	44	5	17	4	1	5	1	24	24	1
Abumuamar 2018	72	9	9	5	2	5	2	25	23	2
Abumuamar 2018	11	2	70	12	3	5	2	25	23	2
Pittman 2013	44	32	1	24	2	5	2	45	14	3
Laporta 2012	55	14	13	9	1	5	1	0	25	1
Mason 2018	12	103	0	7	2	15	1	12	22	1
Mason 2018	9	25	3	85	3	15	1	12	22	1
Reuter 2018	22	29	8	21	1	15	1	39	22	2
Reuter 2018	31	46	1	7	2	15	1	39	22	2
Sert-K 2011	30	34	16	19	1	15	1	19	22	1
Nunes 2015	14	14	7	5	1	15	1	27	23	1
Nunes 2015	21	18	0	1	2	15	1	27	23	1
Nunes 2015	6	5	15	14	3	15	1	27	23	1
Danzi-S 2012	28	21	10	11	1	15	1	24	24	1
Martinez 2012	18	16	7	16	1	15	1	54	21	2
Abumuamar 2018	57	31	0	7	2	15	2	25	23	2
Abumuamar 2018	8	5	49	33	3	15	2	25	23	2
Sert-K 2011	15	49	6	29	1	30	1	19	22	1
Cho 2017	11	11	8	22	1	15	1		15	1
Cho 2017	10	17	9	16	2	15	1		15	1
Laporta 2012	45	24	8	14	1	10	1	0	25	1
Lee 2016	256	199	338	518	1	15	1		15	2
Zhao 2015	60	12	66	22	1	5	1	14	15	2
Calcaianu 2019	18	1	21	13	1	15	1	22	24	1
Shapira-Daniels 2020	126	19	29	14	2	5	2	35	23	2

Abbreviations: TP True positive FP False positive FN False Negative TN True Negative; AHI: apnoea-hypopnoea index; Reference: 1 = Polysomnogaphy, 2 = Portable home monitoring 3 = other.

Supplemental Table 4
Studies assessing obstructive sleep apnoea in patients with cardiac disease using subjective instruments.

Study (First author and year of publication)	Instruments	Study design	Patients	Findings
Shapira-Daniels et al. (2020) [97]	Stop-Bang	Prospective cohort study	188 consecutive patients with AF without a prior diagnosis of sleep apnea	Prevalence of sleep apnoea was high (82%). In a multivariate analysis, the STOP-BANG was not predictive for sleep apnoea. Symptoms of sleep apnoea including snoring, daytime fatigue, or witnessed apneic episodes were equally present in AF patients with and without a positive sleep study.
Aung et al. (2020) [136]	Berlin Questionnaire	multicenter prospective cohort study	163 patients who had undergone PCI in the prior 6–36 months	Patients with OSA during REM sleep were more likely to be categorized as high-risk for OSA based on the Berlin Questionnaire (42.4% vs 19.4%) than those not exhibiting OSA during REM sleep.
Mohammadieh et al. (2019) [43]	Stop-Bang Berlin Questionnaire ESS	Prospective cohort study	100 patients with AF	Increasing the cutoff value of the Stop-Bang to ≥ 5 improved specificity but lowered sensitivity. The BQ demonstrated moderate sensitivity and specificity in detecting OSA
Imes et al. (2019) [137]	Berlin Questionnaire ESS	Secondary analysis of baseline data from a multi-center, randomised clinical trial	126 stable coronary artery disease patients	Berlin Questionnaire was used as screening for further home sleep study. Authors found no difference in endothelial function across OSA severity, as measured by AHI with this testing.
Calcaianu et al. (2019) [125]	Berlin Questionnaire ESS	Prospective cohort study	53 ACS patients referred to PCI followed up at 2 months after the ACS	Higher degree of apnoea was associated with more severe cardiac impairment, as well as higher hypoxemia and arousal index. Sleepiness as assessed by the ESS did not correlate with AHI
Mason et al. (2018) [39]	Stop-Bang	Prospective observational cohort study	122 CABGS patients	The STOP-Bang questionnaire had poor diagnostic accuracy in detecting sleep apnoea. Many patients had false-positive results when the generally accepted cut-off value of 3 or greater was used. However, STOP-bang scores less than 2 allowed for confident exclusion of moderate/severe sleep apnoea in patients but only 5% of patients scored at that level.
von Känel et al. (2018) [138]	Stop	Prospective cohort study	190 myocardial infarction patients	A high risk of OSA as determined by STOP scores was associated with markers of neuroendocrine dysregulation

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Supplemental Table 4 (*continued*)

Study (First author and year of publication)	Instruments	Study design	Patients	Findings
Abumuamar et al. (2018) [41]	Stop-Bang	Prospective cohort study	95 Atrial fibrillation patients	The STOP-BANG questionnaire was sensitive but had low specificity with a high false positive rate. "we recommend the use of a level II sleep study regardless of the results of the screening questionnaire."
Karimi et al. (2018) [139]	Stop-Bang	Retrospective observational study	1593 cardiac surgery patients	Patients at high risk for OSA as measured by the STOP-BANG pre-surgery were at increased risk for post-operative atrial fibrillation
Diken et al. (2018) [140]	Stop-Bang	Prospective cohort study	61 CABGS patients	High risk for OSA, as determined by the preoperative STOP-BANG, was associated with increased incidences of postoperative hypoxia and CPAP use, and increased ICU length of stay
Reuter et al. (2018) [127]	Stop-Bang Berlin Questionnaire ESS	Prospective cohort study	85 CVD patients	Due to the very high amount of false positive results, both the BQ and SB do not allow a reliable differentiation between people with or without SDB
Cho et al. (2017) [128]	Stop-Bang Berlin Questionnaire ESS	Prospective cohort study	52 ACS patients	The BQ has slightly superior predictive value compared to STOP-BANG
Maia et al. (2017) [141]	Berlin Questionnaire	Longitudinal cohort study using registry data	639 cases of ACS 30 days after the index event.	High risk for OSA was as an independent predictor of non-fatal reinfarction or CHD mortality in post-ACS individuals in a long-term follow-up (mean 2.6 years)
Jonasson et al. (2017) [142]	Stop-Bang NoSAS ESS	Cross-sectional study	160 Atrial fibrillation patients	Performance of the Stop-Bang and NoSaS was modest. Daytime sleepiness did not differ between severity levels of OSA
Li et al. (2017) [143]	Berlin Questionnaire	Case–control study	115 patients undergoing PCI	There was a significant association between OSA and early stent thrombosis.
Barger et al. (2017) [144]	Berlin Questionnaire	Multinational, double-blind, placebo-controlled trial	13,026 patients with diagnosis of ACS $\leq$30	Patients who reported <6 h sleep per night had a 29% higher risk of MCE compared with those with longer sleep. Patients who screened positive for OSA had a 12% higher risk of MCE than those who did not screen positive
Lee et al. (2016) [132]	Berlin Questionnaire	Prospective, multicenter registry study	1311 PCI patients	Only 52% of the patients with PSG confirmed OSA were classified as high risk by the Berlin questionnaire, and only 24% had excessive daytime sleepiness
Marzolini et al. (2016) [145]	Stop-Bang ESS	Prospective cohort study	211 cardiac rehabilitation patients & 84 diabetic	A de novo diagnosis in 10.2% of all patients screened by questionnaires, and a diagnosis in 13.1% of those who scored high on the screening questionnaire.
Kua et al. (2016) [146]	Berlin Questionnaire	Prospective cohort study	150 CABGS patients	Sleep apnoea as assessed by overnight sleep study (Watch-PAT) was able to predict acute kidney injury after CABGS. High risk score on the BQ was not predictive.
Loo et al. (2016) [147]	Stop-Bang Berlin Questionnaire ESS	Prospective cohort study	209 cardiac rehabilitation patients	Using the WatchPAT device as the diagnostic reference, neither the Berlin Questionnaire nor the STOP-BANG Questionnaire could discriminate the SDB group from the non-SDB group
Nunes et al. (2015) [40]	Stop-Bang Berlin Questionnaire	Prospective cohort study	40 consecutive patients referred for CABG	Populations of patients with established cardiovascular disease are in general less sleepy, and questionnaires to detect OSA are probably less useful. Instruments showed high sensitivity but low specificity. The BQ showed very poor specificity.
Khan et al. (2015) [148]	Berlin Questionnaire	Cross-sectional study	200 CAD patients	52% of CAD patients were at high risk for OSA according to BQ scores. Those at risk for OSA also had significantly higher Beck Anxiety Inventory scores
Szymanski et al. (2015) [130]	Berlin Questionnaire OSACS score	Prospective cohort study	158 ACS patients	34% of patients were at high risk for OSA according to BQ scores
Ghazal et al. (2015) [149]	Berlin Questionnaire	Cross-sectional study	127 patients with chronic stable angina	Prevalence of risk of OSA was 65%. The Gensini score (degree of angiographic atherosclerosis)was significantly higher in patients with high OSA probability
Costa et al. (2015) [150]	Berlin Questionnaire ESS	Randomised Controlled Trial	500 cardiology outpatients with one of 5 diagnostic areas (hypertension, coronary, arrhythmia, heart failure, valvular heart disease)	50% of patients with several cardiovascular diseases receiving regular treatment were at high risk for OSA, but the majority of them were unaware. Only 53% of the high risk patients reported high levels of excessive daytime sleepiness.
Andrechuk & Ceolim (2015) [151]	Berlin Questionnaire	Cross-sectional study	113 myocardial infarction patients	60% of patients were identified as being at high risk for OSA within 3 days of hospital admission.
Foldvary-Schaefer et al. (2015) [152]	Epworth Sleepiness Scale (ESS), Berlin scale, Sleep Apnea Scale of the Sleep Disorders Questionnaire (SA/SDQ), and Global Sleep Assessment Questionnaire (GSAQ)	Prospective cohort study	107 CABGS patients	There were no significant differences in post-operative outcomes between patients with OSA and without but this may have been due to small sample size. The instrument outcomes were not reported in detail.

Supplemental Table 4 (*continued*)

Study (First author and year of publication)	Instruments	Study design	Patients	Findings
Zhao et al. (2015) [131]	Berlin Questionnaire	Prospective observational study	171 patients listed for elective CABGS	BQ high risk was not significantly associated with apnoea as assessed by an in hospital overnight sleep study using a wrist-worn portable device
Pittman et al. (2013) [133]	Stop-Bang	Cross-sectional study	101 patients with paroxysmal AF undergoing ablation	The STOP-BANG questionnaire has a high sensitivity for detecting sleep apnoea in AF patients
Amra et al. (2014) [153]	Berlin Questionnaire	Prospective study	61 CABGS elective candidates	40% of patients had a high risk for OSA and risk was associated with BMI, hypertension and dyslipidemia
van Oosten et al. (2013) [154]	modified Berlin questionnaire.	Prospective single-center	277 patients with CABGS	Risk of OSA was found to be a strong predictor of post-CABG AF which in turn was found to be associated with increased length of stay.
Mungan et al. (2013) [155]	Berlin Questionnaire ESS	Case control study	73 CABGS patients	There was a higher prevalence of high risk for OSA in the postoperative atrial fibrillation group than control (58% vs 34%; p: 0.044)
Danzi-Soares et al. (2012) [42]	Berlin Questionnaire ESS	Cross-sectional study	70 CABGS patients	The BQ was a reasonable tool for screening for OSA while portable monitoring was acceptable for diagnosis
Martinez et al. (2012) [134]	Berlin Questionnaire	Secondary analysis of cross-sectional study	57 angina patients	The association between high risk for OSA in BQ and the AHI in the portable monitoring, is non-significant, either as continuous variable, or as binary variable, either using a cut point of $\geq$5/h or of $\geq$15/h. After adjusting for age, gender, and BMI, the high risk for in BQ becomes significantly associated to AHI$\geq$15
Laporta et al. (2012) [135]	Berlin Questionnaire Clinical decision-support system (CDSS)	Cross-sectional study	91 male veteran CVD patients	Prevalence of OSA was 75% (AHI $\geq$5). A handheld clinical decision-support system (CDSS) tool was superior to the BQ in diagnostic accuracy
Massierer et al. (2012) [156]	Berlin Questionnaire	Case-control study	328 CHD patients	individuals with a BQ positive result for OSA had an OR (71% higher risk) of displaying significant coronary lesions. (53% after adjustment for sociodemographics, smoking & diabetes)
Correia et al. (2012) [157]	Berlin Questionnaire	Prospective cohort study	168 ACS patients	
Capodanno et al. (2011) [45]	ESS	Cross-sectional study	376 CAD patients	In CAD patients there is a disconnection between self-reported daily sleepiness and true apnoea episodes assessed by polysomnography
Patidar et al. (2011) [158]	Modified Berlin Questionnaire, Quebec Sleep Questionnaire to assess sleep-related quality of life	Cross-sectional survey in India	50 Heart failure patients	Proportion with high risk of OSA in the HF patients was 18% which is lower than in Western countries.
Sharma & Parker (2011) [159]	Berlin Questionnaire	Cross-sectional study	98 cardiac rehabilitation patients	(44%) patients were found to have high risk for OSA as predicted by the Berlin Questionnaire. From the 15 patients who underwent a PSG 13 had a positive study with an AHI>5
Sert-Kuniyoshi et al. (2011b) [108]	Berlin Questionnaire	Prospective cohort study	338 cardiac rehabilitation patients	52% patients were at high risk for OSA as determined by BQ. A significant percentage of patients at high-risk decline further evaluation. 53% out of 74 who did complete their PSG evaluation were found to have OSA with an AHI>5
Sert-Kuniyoshi et al. (2011a) [129]	Berlin Questionnaire	Cross-sectional study	99 patients who had an MI 1–3 months previously	The BQ performed with modest sensitivity, but the specificity was poor, suggesting that the BQ is not ideal in identifying SDB in patients with a recent MI.
Jesus et al. (2010) [160]	Berlin Questionnaire	Prospective cohort study	200 ACS patients	47% patients assessed by the BQ were likely to have OSA. High risk for OSA was associated with a non-significant higher mortality (4.25% vs 0.94%; $p = 0.189$), but a significant higher incidence of composite cardiovascular events.

Abbreviations: BQ Berlin Questionnaire; ESS Epworth Sleepiness Scale; OSA obstructive sleep apnoea; ACS acute coronary syndrome; CABGS coronary artery bypass graft surgery; CAD coronary artery disease; HD heart failure; MI myocardial infarction; AF atrial fibrillation; AHI apnoea-hypopnoea index; SDB sleep disordered breathing; PSG polysomnography; BMI body mass index; MCE major cardiovascular events; ICU intensive care unit; CPAP continuous positive airway pressure REM rapid eye movement sleep.

Supplemental Table 5
Studies assessing insomnia in patients with cardiac disease.

Study	Instruments	Study design	Patients	Findings
Oh et al. (2020) [161]	Insomnia Severity Index	Cross-sectional survey and retrospective chart review	193 patients with cardiovascular disease at a tertiary referral cardiology clinic	Clinically significant insomnia (16% of patients) was significantly associated with heart disease, prior myocardial infarction or cerebrovascular accident, and heart failure. Left ventricular ejection fraction was significantly associated with insomnia
Siebmanns et al. (2020) [162]	Insomnia Severity Index	Qualitative study	20 CVD patients	Patients with CVD and insomnia experienced both physical and cognitive distress from their heart condition, with high levels of concern about consequences, but also showed that behavioral and social disturbances affected their sleep
Waterman et al. (2020) [163]	"insomnia index" created from "Hamilton Depression Rating Scale sleep questions	RCT comparing usual care vs nurse led collaborative care for depression	Post CABGS patients that were depressed (n = 152) versus not depressed (n = 150)	At baseline, 63% of participants who were depressed vs 12% of those who were not depressed reported insomnia. Insomnia index change score indicated beneficial effects of collaborative care.
Lin et al. (2020) [164]	Insomnia Severity Index	18 month longitudinal study	468 Heart failure patients	eHealth literacy had direct and indirect effects (through insomnia and psychological distress) on medication adherence and quality of life.
Javaheri et al. (2020) [48]	Insomnia Severity Index	Pragmatic randomized controlled pilot study	34 comorbid CHD and insomnia patients	Web-based CBT-I resulted in clinically meaningful improvement in insomnia severity.
Zhang et al. (2019) [165]	Athens Insomnia Scale	Cross-sectional	184 ACS patients	Higher AIS scores were observed or STEMI patients followed by NSTEMI patients with unstable angina patients having the lowest score,
Redeker et al. (2019) [93]	Insomnia Severity Index, Pittsburgh Sleep Quality Index, Dysfunctional Beliefs and Attitudes about Sleep (DBAS) and Sleep Disturbance Questionnaires (SDQ),	RCT CBT-I (n = 30) or attention control (HF self-management education, n = 21)	Stable New York Heart Association Class II-III Heart Failure patients (total n = 51	Improvements in dysfunctional cognitions were associated with improved sleep quality, insomnia severity, sleep latency and decreased fatigue, depression, and anxiety, with sustained effects at six months.
Heenan et al. (2019) [47]	Insomnia Severity Index	Pre and post study of single group of patients	47 comorbid CVD and insomnia patients	CBT-I group intervention tailored for cardiac patients improved sleep and significantly lower levels of anxiety and depression.
Harris et al. (2019) [46]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	RCT evaluating Brief Behavioral Treatment for Insomnia (BBTI)	23 comorbid heart failure and insomnia patients	BBTI participants experienced reduced insomnia and increased sleep quality and efficiency
Edwards et al. (2019) [91]	Insomnia Severity Index	Cross-sectional survey	117 female cardiac outpatients	Percentage of patients reporting symptoms of clinical insomnia (50%) was higher than those reporting anxiety (42%) or depression (20%)
Munkhaugen et al. (2018) [166]	Bergen Insomnia Scale	Cross-sectional explorative study, data from hospital records	1083 patients undergoing a first or recurrent coronary event or treatment (ie, AMI, CABGS, or PCI)	There was a higher prevalence of insomnia among CHD patients with comorbid type 2 diabetes patients compared with prediabetic patients
von Känel et al. (2018) [138]	Jenkins Sleep Scale	Prospective cohort study	190 myocardial infarction patients	Insomnia symptoms, particularly problems initiating or maintaining sleep, showed a relation with reduced sympathetic nervous system activity
Rouleau et al. (2017) [167]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	Longitudinal (12 weeks) study of single cohort of cardiac rehabilitation participants	80 cardiac rehabilitation participants	Completion of exercise-based CR among CVD patients was associated with both improvements in insomnia symptoms.
Peersen et al. (2017) [168]	Insomnia (Bergen Insomnia Scale)	Cross-sectional study – part of NOR-COR study	99 CHD patients (MI, CABGS & PCI)	High test-retest (6 days) reliability (0.92) for the Bergen Insomnia scale
Da Costa et al. (2017) [5]	Insomnia Severity Index, Dysfunctional Beliefs and Attitudes about Sleep (DBAS)	Cross-sectional study	209 recent myocardial infarction patients	Younger age, use of prescribed medication for sleep, more depressive symptoms, and greater dysfunctional beliefs about sleep were associated with insomnia
Chimluang et al. (2017) [169]	Insomnia Severity Index, Dysfunctional Beliefs and Attitudes about Sleep (DBAS)	Predictive correlational study	340 heart failure patients	Anxiety, depression and DBAS were associated with insomnia. Age, gender, sleep disorder breathing, and sleep hygiene were not significant predictors of insomnia.
Horsley et al. (2016) [170]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	Cross-sectional study of single cohort of cardiac rehabilitation	121 cardiac rehabilitation participants	There was an association between difficulty falling asleep and 1-min heart

Supplemental Table 5 (*continued*)

Study	Instruments	Study design	Patients	Findings
		participants assessed prior to 12-week program		rate recovery (HRR), (an index of parasympathetic tone)
Jeon & Redeker (2016) [171]	Pittsburgh Sleep Quality Index, Insomnia Symptoms from the Sleep Habits Questionnaire	Secondary analysis of data from a cross-sectional, observational study	173 stable heart failure patients	Daytime symptoms mediated the relationship between sleep disturbance and functional performance.
Rouleau et al. (2015) [172]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	Cross-sectional study of single cohort of cardiac rehabilitation participants.	57 male cardiac rehabilitation participants	CR patients that reported insomnia symptoms experienced daytime mood disturbances but benefited from potential mood-elevating properties of exercise.
Redeker et al. (2015) [49]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	Pilot randomised controlled trial	52 stable heart failure patients	CBT-I was feasible and acceptable and had a statistically significant effect on insomnia and fatigue, while controlling for the effects of comorbidity and age.
Ozdemir et al. (2015) [173]	Insomnia Severity Index	Prospective cross-sectional study	120 patients undergoing elective coronary angiography	There were no significant changes in ISI score from pre to post angiography.
Coryell et al. (2013) [4]	Insomnia Severity Index	Cross-sectional study conducted during hospitalisation	102 ACS patients	Insomnia was present in over one-third of ACS patients during hospitalisation. Insomnia was not associated with sleep apnoea. A quarter of patients with insomnia did not report symptoms of depression
Cserep et al. (2010)	Athens Insomnia Scale	Prospective cohort study	197 CABGS patients	Sleeping disorders were associated independently with the occurrence of long term (3 years after surgery) major adverse outcomes after adjustment for covariates

Abbreviations: PSQI Pittsburgh Sleep Quality Index; AIS Athens Insomnia Scale VASS Visual Analogue Sleep Scale; BQ Berlin Questionnaire; ESS Epworth Sleepiness Scale; OSA obstructive sleep apnoea; ACS acute coronary syndrome; CABGS coronary artery bypass graft surgery; CAD coronary artery disease; HD heart failure; MI myocardial infarction; AMI acute myocardial infarction; AF atrial fibrillation; AHI apnoea-hypopnoea index; SDB sleep disordered breathing; PSG polysomnography; BMI body mass index; MCE major cardiovascular events; CCU coronary care unit; ICU intensive care unit; CPAP continuous positive airway pressure REM rapid eye movement sleep; QOL quality of life; PTSD post-traumatic stress disorder; NSTEMI Non-ST-elevation myocardial infarction; CBT-I Cognitive behavioural therapy for insomnia.

Supplemental Table 6
Studies assessing subjective sleep quality in cardiac patients (2009 to November 2019).

Study	Instruments	Study design	Patients	Findings
Muthukrishnan et al. (2020) [174]	Pittsburgh Sleep Quality Index	Prospective cohort study	187 CABGS patients, average 3 months after surgery	78% reported poor sleep quality. Preoperative state anxiety was the strongest predictor of poor sleep quality
Wang et al. (2020) [175]	Pittsburgh Sleep Quality Index	Prospective randomized controlled parallel-group clinical trial (intervention was ICU diaries)	126 cardiac surgery patients followed up at 1 month and 3 months post-surgery	Those who kept an ICU diary experienced improved sleep quality scores in the 3 months post-ICU compared to those who did not keep a diary
Bang et al. (2020) [176]	Korea sleep scale Sleep satisfaction	Single-blind, randomised controlled trial	42 cardiac surgery patients	Patients who had an auricular acupressure intervention had higher sleep quality scores than control patients
Romero et al. (2020) [177]	Pittsburgh Sleep Quality Index	Prospective observational cohort study.	576 patients evaluated in hospital for ACS	Short sleep duration as assessed by 2 questions from the PSQI was associated with increased risk of all-cause readmission within 6 months of discharge
Mahran et al. (2020) [178]	Richards-Campbell Sleep Questionnaire	Prospective, parallel-group, randomised controlled trial	70 cardiac surgery patients	The use of nocturnal eye masks was associated with improved sleep quality in postoperative cardiac patients
Manzoli et al. (2020) [179]	Visual Analogue Sleep Scale	clinical validation study	75 ACS patients	The VASS was considered easy to administer but the nurse diagnosticians perceived some difficulty from the patients in understanding and completing the scale items
Kjellsdotter et al. (2020) [180]	Uppsala Sleep Inventory Vicious Cycle of Sleeplessness Scale	Observational case—control design	859 stable CAD patients	Type D personality was not a predictor for too little sleep in CAD patients. Resilience to stress is more related to sleeplessness behavior.
Zhang et al. (2019) [165]	Pittsburgh Sleep Quality Index	Cross-sectional	184 ACS patients	Higher PSQI scores (lower sleep quality) was observed in STEMI patients compared to NSTEMI and unstable angina patients
Tsai et al. (2019) [181]	Cardiac Symptom Survey	Prospective cohort study	198 CABGS patients	Patients who had had fewer vessels bypassed were more likely to have a poor sleep problem trajectory
Tan et al. (2019) [64]	Pittsburgh Sleep Quality Index	Cross-sectional	167 CHD patients at community-based cardiac rehabilitation program	Perceived sleep quality, but not sleep efficiency, was significantly associated with emotional, physical, and social quality of life in cardiac patients
Hojskov et al. (2019) [72]	Pittsburgh Sleep Quality Index	Randomised controlled trial	326 CABGS patients	There were improvements in sleep quality as a result of the intervention but these were non-significant

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Supplemental Table 6 (*continued*)

Study	Instruments	Study design	Patients	Findings
Kurose et al. (2019) [67]	Pittsburgh Sleep Quality Index	Cross-sectional multi-centre	102 elderly patients with CVD undergoing phase III cardiac rehabilitation	Locomotive activity and exercise tolerance was associated with sleep latency
Conley et al. (2019) [182]	Pittsburgh Sleep Quality Index, and Sleep Habits Questionnaire	Retrospective analysis of a cross-sectional study	173 stable heart failure patients	Pain was associated with subjective sleep quality and daytime sleep characteristics and the use of sleep medication but not sleep duration or continuity
Calcaianu et al. (2019) [125]	Pittsburgh Sleep Quality Index	Prospective cohort study	53 ACS patients referred to PCI followed up at 2 months after the ACS	At two months after ACS the there was a trend ($p = 0.08$) for sleep quality of OSA patients to be worse than non-OSA patients
Zhu et al. (2019) [183]	Single question “During the past month, how would you rate your sleep quality overall?” based on a 4-point rating scale ranging from very poor to very good.	Cross-sectional study	4043 ACS patients from 16 hospitals across China	There was significant association of greater depression with physical inactivity and poor sleep quality
Risom et al. (2018) [184]	Pittsburgh Sleep Quality Index	Explorative study using data from randomised rehabilitation trial	210 atrial fibrillation patients	85% of all atrial fibrillation patients reported poor sleep quality at 1 month, and 55% reported poor sleep quality at 6 months
Walter et al. (2018) [185]	Pittsburgh Sleep Quality Index	secondary analysis of a prospective observational study	267 stable heart failure patients	Cognitive function was not associated with sleep quality or daytime sleepiness
Song & Wu (2018) [186]	Pittsburgh Sleep Quality Index	Cross-sectional	160 heart failure patients	Vitamin D deficiency was associated with poor sleep quality. In mediation analysis, the relationship between vitamin D deficiency and cognitive function was mediated by sleep quality among older adults with HF
Santos et al. (2018) [187]	Pittsburgh Sleep Quality Index	Prospective cohort study	32 heart failure patients	Non-pharmacological interventions improved quality of sleep but not statistically significant
Ghavami et al. (2018) [188]	Pittsburgh Sleep Quality Index	Randomised-controlled study	146 CABGS patients	A self-care intervention based on sleep hygiene was associated with improved sleep quality scores post-surgery
Juskiene et al. (2018) [65]	Pittsburgh Sleep Quality Index	Cross-sectional study	879 CAD patients attending cardiac rehabilitation program	Type D and negative affectivity were associated with worse subjective sleep quality in patients with OSA and without OSA. The mediational analysis revealed that type D and NA were indirectly associated with sleep quality through anxiety and depression symptoms regardless of presence of OSA
Casida et al. (2018) [189]	Verran Snyder-Halpern Visual Analogue Sleep Scale	Exploratory repeated-measures	38 cardiac surgery patients	Night-time care routine interactions affected daytime sleepiness but not night-time sleep effectiveness of patients
Caruana et al. (2018) [190]	Pittsburgh Sleep Quality Index Insomnia Severity Index Richards-Campbell Sleep Questionnaire (RCSQ) Sleep in the Intensive Care Unit Questionnaire (SICQ)	Prospective observational study while the patient was in the ICU and the hospital ward and at 2 and 6 months after hospital discharge	101 CABGS patients	Poor sleep quality at 6 months was associated with prehospital insomnia. Sleep quality in the ICU, in the hospital ward, and at home 2 and 6 months after hospital discharge was poor
Diaz-Alonso et al. (2018) [191]	Pittsburgh Sleep Quality Index, Richards-Campbell Sleep Questionnaire	RCT in ICU setting	40 valve cardiac surgery patients	Sleep quality in the ICU was measured with the Richards-Campbell Sleep Questionnaire and usual sleep quality with the PSQI. A nurse intervention prior to ICU admission did not increase patients' sleep quality
Fukuoka et al. (2017) [192]	Pittsburgh Sleep Quality Index	Cross-sectional study	44 ACS and 117 stable angina patients	The PSQI and ESS could not differentiate patients with SDB from those without
Mehra at al (2017) [74]	Functional Outcomes of Sleep Questionnaire (FOSQ)	Cross-sectional study	26 stable heart failure patients	Objective sleepiness was not associated with subjective sleepiness as measured by FOSQ or ESS
Navarro-García et al. (2017) [193]	Richards-Campbell Sleep Questionnaire	Observational, descriptive and cross-sectional study	66 cardiac surgery patients	Sources of sleep disturbing factors in the ICU were discomfort with the different devices, pain, environmental noise and voices of the professionals
Sable et al. (2017) [194]	Pittsburgh Sleep Quality Index	quasi-experimental study	30 heart failure patients	Back massage improved duration and quality of sleep in HF patients
Peric et al. (2017) [63]	Nottingham Health Profile Questionnaire (Sleep 5 items)	Longitudinal cohort (2 year follow-up)	208 CABGS patients	Sleep was an independent predictor of quality of life improvement after 2 years post CABGS
Matsuda et al. (2017) [60]	Pittsburgh Sleep Quality Index	Cross-sectional	1071 patients admitted for CVD at a university hospital	43 percent of patients had poor sleep quality which was associated with depression and anxiety
Karadag et al. (2017) [73]	Pittsburgh Sleep Quality Index	Randomised controlled study	60 patients in coronary ICU	Lavender essential oil increased quality of sleep and reduced level of anxiety in patients in ICU
Choudhury et al. (2017) [195]	Pittsburgh Sleep Quality Index	Prospective clinical study	156 elective CABGS patients	Poor sleep quality assessed 2–3 days before admission was associated with a higher incidence of adverse perioperative events
Byun et al. (2017) [59]	Pittsburgh Sleep Quality Index	Cross-sectional	105 heart failure patients	Poor nighttime sleep quality was associated with cognitive impairment in older patients (≥60 years)
		Case-control study		

Supplemental Table 6 (*continued*)

Study	Instruments	Study design	Patients	Findings
Awotidebe et al. (2017) [196]	Pittsburgh Sleep Quality Index		50 heart failure patients matched with healthy controls	Patients with heart failure demonstrated lower functional capacity and poorer sleep quality than controls
Yilmaz et al. (2016) [56]	Pittsburgh Sleep Quality Index	Case-control study	52 CABGS patients	The severity of angina pectoris in the preoperative period is independently associated with worse sleep quality after elective CABGS
Doering et al. (2016) [197]	Pittsburgh Sleep Quality Index	Secondary analysis from a randomised controlled trial	53 cardiac surgery patients	CBT for depression was associated with improved pain scores, but not sleep disturbance as assessed by the PSQI
Ammouri et al. (2016) [198]	Cardiac Symptom Survey	Descriptive, cross-sectional design	100 post-CABGS patients	Difficulty sleeping was significantly prevalent among post-CABG patients who were women and illiterate and those with no interest to seek information about CABG experiences.
Masterson Creber et al. (2016) [199]	Pittsburgh Sleep Quality Index	Cross-sectional	280 heart failure patients	Although sleep quality was poor, exercise may help to promote behavioral alertness and reduce daytime sleepiness in adults with heart failure
Le Grande et al. (2016) [200]	Sleep disturbance measured Beck Depression Inventory (v.2) item 16	Secondary analysis of longitudinal study	134 CHD patients (MI & CABGS)	Sleep disturbance at 4 months post-event was associated with reduced treatment adherence and self-efficacy, and higher anxiety and depression scores at 12 months
Lee et al. (2016) [57]	Pittsburgh Sleep Quality Index	Longitudinal study	204 heart failure patients	63% of patients reported poor sleep quality. This was associated with poor cardiac event-free survival
Jeon & Redeker (2016) [171]	Pittsburgh Sleep Quality Index, Insomnia Symptoms from the Sleep Habits Questionnaire	Secondary analysis of data from a cross-sectional, observational study	173 stable heart failure patients	Daytime symptoms mediated the relationship between sleep disturbance and functional performance.
Gatti et al. (2016) [201]	Pittsburgh Sleep Quality Index	randomised controlled trial	15 heart failure patients	Poor sleep quality as indicated by the PSQI was reported
Gostoli et al. (2016) [70]	Pittsburgh Sleep Quality Index	Longitudinal study	108 CVD patients attending cardiac rehabilitation & 85 non-attenders	Cardiac rehabilitation was associated with maintenance of physical activity, improvement of behavioural aspects related to food consumption, stress management, and sleep quality
Johansson et al. (2015) [202]	One item “Was your sleep restless?” from the Center for Epidemiological Studies Depression Scale (CES-D)	Secondary analysis of randomised multicenter trial (COACH)	499 Heart failure patients with assessment at two time points (baseline and 12 months)	1 year after discharge from hospital, one-third of the patients still reported a sleep problem. Continued sleep problem was associated with rehospitalisations.
Fritschi et al. (2015) [203]	Pittsburgh Sleep Quality Index	Secondary analysis of data obtained from an observational study	173 stable Class II-IV HF patients	HF patients with diabetes had longer sleep latency and spent a greater percentage of time awake after sleep onset than the HF patients who did not have diabetes
Ranjbaran et al. (2015) [204]	Pittsburgh Sleep Quality Index	Randomised clinical trial	100 CABGS patients	An 8-week educational intervention resulted in improved sleep quality compared to controls
Yang et al. (2015) [61]	Pittsburgh Sleep Quality Index	Descriptive correlational design	87 CABGS patients	Poorer sleep quality correlated with older age, poorer heart function, anxiety and depression
Redeker et al. (2015) [49]	Insomnia Severity Index, Pittsburgh Sleep Quality Index	Pilot randomised controlled trial	52 stable heart failure patients	CBT-I was feasible and acceptable and had a statistically significant effect on insomnia and fatigue, while controlling for the effects of comorbidity and age.
Dianatkhah et al. (2015) [205]	Groningen Sleep Quality Score	Randomised double-blind study	145 CABG patients	Receiving 3 mg of melatonin instead of 10 mg of Oxazepam daily, from 3 days before surgery. was associated with improved sleep quality
Suna et al. (2015) [95]	Pittsburgh Sleep Quality Index	Sub-study of a multisite randomised controlled trial	106 heart failure patients	Improved sleep quality correlated with improved exercise capacity and reduced depressive symptoms, but not with changes in body mass index or resting heart rate
Nasir et al. (2015) [206]	Pittsburgh Sleep Quality Index	Cross-sectional study	40 heart failure patients	There was a significant relationship between sleep quality and depression
Fredriksson-Larsson et al. (2015) [207]	Pittsburgh Sleep Quality Index	Cross-sectional study	142 MI patients (2 months post MI)	Sleep quality was associated with fatigue, but the association was not statistically significant
Moon et al. (2015) [208]	Pittsburgh Sleep Quality Index	Descriptive, cross-sectional study	68 heart failure patients	Sleep quality was not associated with cognitive function.
Javadi et al. (2015) [52]	Pittsburgh Sleep Quality Index	Cross-sectional survey study	240 heart failure patients	Age, sex, educational level, smoking, and obesity were the most significant factors affecting sleep quality
Babaii et al. (2015) [71]	Pittsburgh Sleep Quality Index	Randomised controlled trial	60 cardiac patients in coronary care unit	Using an eye mask significantly improved the sleep quality in the CCU
Poole et al. (2014) [209]	Jenkins Sleep Problems Scale	prospective longitudinal design	230 CABGS patients	Greater sleep complaints in the month before surgery were associated with poorer physical HRQoL, greater physical symptoms and greater sensory pain in the 2 months after CABGS
Szymanski et al. (2014) [55]	Pittsburgh Sleep Quality Index	Cross-sectional study	177 consecutive patients, with non-valvular atrial fibrillation	Poor sleep quality was present in almost half of all patients. Those with poor sleep quality were more often females, were older, and had higher systolic blood pressure. PSQI scores were related to degree of severity of AF symptoms (EHRA score).
		Cross-sectional study		

(*continued on next page*)

Supplemental Table 6 (*continued*)

Study	Instruments	Study design	Patients	Findings
Banack et al. (2014) [210]	Pittsburgh Sleep Quality Index		259 Cardiac rehabilitation participants	Disturbed sleep was strongly associated with depressive symptoms and decreased health-related quality of life
Johansson et al. (2014) [211]	Uppsala Sleep Inventory	randomised pretest-posttest control design	47 cardiac surgery patients	A nurse-led individualised education programme to promote self-care of sleep was associated with improved sleep quality at follow-up compared to a control group
Geovanini et al. (2014) [212]	Pittsburgh Sleep Quality Index	Cross-sectional two-group study	70 patients with refractory angina & 70 patients with stable CAD	Patients with refractory angina reported worse quality of sleep then stable CAD patients.
Wang et al. (2014) [75]	Pittsburgh Sleep Quality Index	Experimental pretest and repeated posttest design	128 patients with coronary heart disease	Relaxation training at night was better than morning with shorter sleep latency, fewer awakenings, higher sleep quality, and use of significantly fewer sleep medications
Moradi et al. (2014) [53]	Pittsburgh Sleep Quality Index	Cross-sectional study	200 heart failure patients	79% of patients reported poor sleep quality. Age, gender, educational level, number of hospitalizations, diuretic use, and left ventricular ejection fraction affected PSQI scores
Shaffer et al. (2013) [66]	Pittsburgh Sleep Quality Index	Coss-sectional study	188 Acute Coronary Syndrome patients	ACS-induced PTSD symptoms may be associated with poor sleep, which may explain why PTSD confers increased cardiovascular risk after ACS
Riegal et al. (2013) [213]	Pittsburgh Sleep Quality Index	Cross-sectional study	280 systolic or diastolic heart failure patients	Only 16% of patients reported daytime dysfunction due to poor sleep quality.
Chen et al. (2013) [214]	Pittsburgh Sleep Quality Index	Cross-sectional and correlational study	133 heart failure patients	One quarter of participants reported subjective excessive daytime sleepiness, suggesting that recognition of this symptom should be incorporated into HF management
Assari et al. (2013) [50]	Pittsburgh Sleep Quality Index	Cross sectional study	717 CAD patients	Among female but not male patients with CAD, low education and income were associated with poor sleep quality.
Alosco et al. (2013) [215]	Pittsburgh Sleep Quality Index	Cross sectional study	53 heart failure patients	75% of patients reported impaired sleep. Decreased cerebral perfusion and greater white matter hyperintensities were associated with poor sleep quality
Ryu et al. (2012) [216]	modified Verran and Synder-Halpern (VSH) sleeping scale	Experimental study	58 patients prior to PCI	Earphone-delivered sleep-inducing music significantly increased the quantity and quality of sleep compared to the use of ear plugs in the CCU
Riegel et al. (2012) [58]	Pittsburgh Sleep Quality Index	Cross sectional study	266 heart failure patients	Factors associated with sleep dysfunction in HF include medications with sleepiness as a side-effect, depression, poorer health perceptions, and better sleep hygiene.
Norra et al. (2012) [217]	Pittsburgh Sleep Quality Index	Cross sectional study	94 cardiac patients with CVD	Significant correlation between increased depressive symptoms and poor subjective sleep quality and daytime dysfunction
Fink et al. (2012) [218]	Pittsburgh Sleep Quality Index	Cross sectional study	59 heart failure patients	Patients with HF had significantly greater fatigue and depressive symptoms and poorer sleep quality compared to healthy control subjects
Selvi et al. (2011) [219]	Pittsburgh Sleep Quality Index	Cross sectional study	219 MI patients in CCU	Those who had AMI when asleep had poorer subjective sleep quality than those who had their AMI when awake
Johansson et al. (2011) [220]	Uppsala Sleep Inventory	Prospective matched cohort	880 CAD patients	Patients with CAD had close to 2 h shorter sleep duration, lower sleep efficiency, and severely non-rested insomnia compared with the general population
Liu et al. (2011) [221]	Pittsburgh Sleep Quality Index	Cross-sectional correlational design	88 stable heart failure patients	Poor quality sleep independently predicted physical and psychological domains of QOL, whereas daytime sleepiness independently predicted the environmental QOL
Gau et al. (2011) [51]	Pittsburgh Sleep Quality Index	two-group, cross-sectional study	126 heart failure patients	The prevalence of insomnia was 44% for the elderly group and 31% for the younger group. The major determinants of poor night sleep quality in the elderly group were dyspnea and long sleep latency,
Duarte Freitas et al. (2011) [69]	Pittsburgh Sleep Quality Index	Observational cohort study	101 patients attending 4 week cardiac rehabilitation program	There were significant improvements in sleep quality following the cardiac rehabilitation program.
Cross et al. (2010) [222]	Pittsburgh Sleep Quality Index	Two-group, cross-sectional study	30 CAD & 30 ICD patients	CAD patients reported poorer sleep quality than ICD patients
Wang et al. (2010) [54]	Pittsburgh Sleep Quality Index	predictive correlational design	101 heart failure patients	81% of participants reported poor sleep quality. Factors related to sleep quality were gender, perceived health, depressive mood, and the number of comorbidities.
Johansson et al. (2010) [223]	Uppsala Sleep Inventory	cross sectional cohort study	36 heart failure patients matched with community sample	HF patients had more difficulty maintaining sleep than age/gender matched community elderly participants. Sleep disordered breathing had no association to any of the insomnia symptoms
Redeker et al. (2010) [224]	Pittsburgh Sleep Quality Index	Cross-sectional, observational study	170 stable chronic heart failure patients	Severe SDB was associated with poor physical function but not with daytime symptoms or self-reported sleep,

Supplemental Table 6 (*continued*)

Study	Instruments	Study design	Patients	Findings
				despite poorer objective sleep quality in patients with SDB
Redeker et al. (2010) [10]	Pittsburgh Sleep Quality Index	Cross-sectional, observational study	173 stable chronic heart failure patients	Over half of HF patients reported insomnia symptom and these were associated with daytime symptoms and decrements in functional performance
Czarnecka et al. (2010) [225]	Pittsburgh Sleep Quality Index	Observational cohort study	27 heart failure patients	Cardiac Resynchronization Therapy decreased central sleep apnoea and improved quality of sleep and daytime sleepiness
Zimmerman et al. (2010) [226]	Cardiac Symptom Survey	Secondary analysis of randomised controlled trial	226 CABHS patients	There were three patient clusters of symptom burden with one cluster characterized by high sleep disturbance
Chen et al. (2010) [227]	Pittsburgh Sleep Quality Index	Cross-sectional, descriptive correlational design	125 heart failure patients	Subjective sleep quality was a significant predictor of quality of life

Abbreviations: PSQI Pittsburgh Sleep Quality Index; VASS Visual Analogue Sleep Scale; BQ Berlin Questionnaire; ESS Epworth Sleepiness Scale; OSA obstructive sleep apnoea; ACS acute coronary syndrome; CABGS coronary artery bypass graft surgery; CAD coronary artery disease; HD heart failure; MI myocardial infarction; AMI acute myocardial infarction; AF atrial fibrillation; AHI apnoea-hypopnoea index; SDB sleep disordered breathing; PSG polysomnography; BMI body mass index; MCE major cardiovascular events; CCU coronary care unit; ICU intensive care unit; CPAP continuous positive airway pressure REM rapid eye movement sleep; QOL quality of life; PTSD post-traumatic stress disorder.

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