**RESEARCH ARTICLE** 

# Diagnostic value of smartphone in obstructive sleep apnea syndrome: A systematic review and meta-analysis

#### Do Hyun Kim<sup>1</sup>, Sung Won Kim<sup>1</sup>, Se Hwan Hwang<sup>2</sup>\*

1 Department of Otolaryngology-Head and Neck Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, 2 Department of Otolaryngology-Head and Neck Surgery, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

\* yellobird@catholic.ac.kr

# Abstract

# Objectives

To assess the diagnostic utility of smartphone-based measurement in detecting moderate to severe obstructive sleep apnea syndrome (OSAS).

# Methods

Six databases were thoroughly reviewed. Random-effect models were used to estimate the summary sensitivity, specificity, negative predictive value, positive predictive value, diagnostic odds ratio, summary receiver operating characteristic curve and measured the areas under the curve. To assess the accuracy and precision, pooled mean difference and standard deviation of apnea hypopnea index (AHI) between smartphone and polysomnography (95% limits of agreement) across studies were calculated using the random-effects model. Study methodological quality was evaluated using the QUADAS-2 tool.

# Results

Eleven studies were analyzed. The smartphone diagnostic odds ratio for moderate-tosevere OSAS (apnea/hypopnea index > 15) was 57.3873 (95% confidence interval [CI]: [34.7462; 94.7815]). The area under the summary receiver operating characteristic curve was 0.917. The sensitivity, specificity, negative predictive value, and positive predictive value were 0.9064 [0.8789; 0.9282], 0.8801 [0.8227; 0.9207], 0.9049 [0.8556; 0.9386], and 0.8844 [0.8234; 0.9263], respectively. We performed subgroup analysis based on the various OSAS detection methods (motion, sound, oximetry, and combinations thereof). Although the diagnostic odds ratios, specificities, and negative predictive values varied significantly (all p < 0.05), all methods afforded good sensitivity (> 80%). The sensitivities and positive predictive values were similar for the various methods (both p > 0.05). The mean difference with standard deviation in the AHI between smartphone and polysomnography was -0.6845 ± 1.611 events/h [-3.8426; 2.4735].



# G OPEN ACCESS

**Citation:** Kim DH, Kim SW, Hwang SH (2022) Diagnostic value of smartphone in obstructive sleep apnea syndrome: A systematic review and meta-analysis. PLoS ONE 17(5): e0268585. https:// doi.org/10.1371/journal.pone.0268585

Editor: Thomas Penzel, Charité -Universitätsmedizin Berlin, GERMANY

Received: October 21, 2021

Accepted: May 3, 2022

Published: May 19, 2022

**Copyright:** © 2022 Kim et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

**Funding:** The authors received no specific funding for this work.

**Competing interests:** The authors have declared that no competing interests exist.

## Conclusions

Smartphone could be used to screen the moderate-to-severe OSAS. The mean difference between smartphones and polysomnography AHI measurements was small, though limits of agreement was wide. Therefore, clinicians should be cautious when making clinical decisions based on these devices.

#### Introduction

Obstructive sleep apnea syndrome (OSAS) is a disorder associated with periodic breathing cessation, significantly reducing the quality of life, and increasing cardiovascular disease and mortality [1, 2]. The prevalence of OSAS is 9 to 38% in the general population and has increased in recent years [2, 3]. Attended polysomnography (PSG) in a sleep laboratory is currently the gold-standard tool for OSAS diagnosis. PSG data are used to assess apnea/hypopnea events, oxygen desaturations, and arousal frequency. The number of apnea and hypopnea events per hour (the apnea/hypopnea index [AHI]) is a measure of sleep apnea severity [4]. However, the costs of a special room, monitoring facilities, and specialized personnel limit access for many potential patients. Furthermore, PSG evaluations are usually limited to one night, associated with false- negatives; significant variations in OSAS severity have been observed over multiple nights. OSAS must become easily and cheaply detectable [5]. Today, smartphones can collect sound, movement, and oximeter data [6-8]. Therefore, there were reports comparing PSG and portable devices to evaluate the sleep environment in a more patient-friendly environment, away from the inconvenient and artificial sleep environment of the PSG setting [5-15]. Among portable devices, many recent apps for sleep tests use a smartphone computer and sensors [16–19]. Currently, no meta-analysis either supports or does not support the suggestion that smartphones could effectively screen for OSA. Therefore, we performed a meta-analysis that can intuitively compare and evaluate the diagnostic accuracy and utility of smartphones using various sensing devices in terms of OSAS screening.

## Materials and methods

#### Search strategy and study selection

We retrieved clinical data from PubMed, Embase, the Web of Science, SCOPUS, the Cochrane Central Register of Controlled Trials, and Google Scholar from the dates of inception to May 2021. The population, intervention, comparison, and outcome (PICO) parameters were: P, patients with suspected OSA who evaluated sleep disorder with PSG and smartphone; I, biological data measured by the smartphone; C, sleep data measured by PSG; and O, the AHI. Only papers written in English were considered. The search terms were: "sleep disturbed breathing," "obstructive sleep apnea," "smartphone," "polysomnography," "mobile," and "screening." The reference lists were checked to ensure that no relevant studies were omitted. The titles and abstracts of all candidate studies were systematically reviewed by two independent reviewers.

#### Selection criteria

The inclusion criteria were: 1) a study analyzing sleep with mobile phone device and/or accessories; 2) a cohort study; 3) a comparison between a smartphone and PSG (the reference); and 4) an article containing sensitivity and specificity values data. The exclusion criteria were: 1) case reports; 2) review articles; 3) diagnosis or screening of OSAS with other portable devices except smartphone; and 4) insufficient data. The search strategy is shown in Fig 1.

#### Data extraction and bias assessment

Two reviewers (SWK and SHH) independently selected and compared eligible studies, then extracted data using standardized forms. We collected study identification, publication year, study design, enrolled number of patients, mean AHI, Sex ratio, apnea detecting mechanism, cut off values of AHI, and 2x2 table outcomes. At each stage, the papers selected by two reviewers were compared, and if the selected articles were inconsistent, a final decision was made through panel discussion with the third reviewer (DHK). The bias assessment was performed in the same way. The search terms and queries were presented in S1 Table.

We analyzed the predictive power of sleep analysis by a smartphone (i.e., the diagnostic odds ratio [DOR]), then constructed summary receiver operating characteristic (SROC) curves and measured the areas under the curves (AUCs) [5–15]. Moderate to severe OSAS (AHI  $\geq$  15) was defined based on PSG. True-positive, true-negative, false-positive, and false-negative values were collected for the calculation of AUCs and DORs. To calculate the accuracy and precision of smartphone compared to PSG, we extracted mean difference and standard deviation (SD) of mean differences between the PSG-AHI and smartphone-AHI measurements from a single study. They were pooled in meta-analysis to yield a summary estimate (weighted mean difference) [5, 6, 13]. The quality of each study was analyzed using the Quality Assessment of Diagnostic Accuracy Studies ver. 2 (QUADAS-2) tool [20].

#### Statistical analysis and measurement of outcomes

Meta-analysis was conducted using R statistical software (R Foundation for Statistical Computing, Vienna, Austria [version 3.6.3]). Explore the cause of significant between-study heterogeneity among the studies, subgroup analyses were performed (motion, sound, oximetry, and combinations thereof). We generated forest plots of sensitivities, specificities, and negative predictive values, as well as SROC curves.

Heterogeneity was calculated with the I<sup>2</sup> test: The I<sup>2</sup> test describes the rate of variation across studies caused by heterogeneity rather than probabilistic chance; the measure ranges from 0 (no heterogeneity) to 100 (maximum heterogeneity). When significant heterogeneity among outcomes was found (defined as I<sup>2</sup> > 50), the random-effects model was used according to DerSimonian-Laird. Those outcomes that did not present a significant level of heterogeneity (I<sup>2</sup> < 50) were analyzed with the fixed-effects model. The fixed-effects model uses the inverse variance approach, and it is assumed that all studies come from a common population. Sensitivity analyses were performed to determine the effects of individual studies on the overall meta-analysis results.

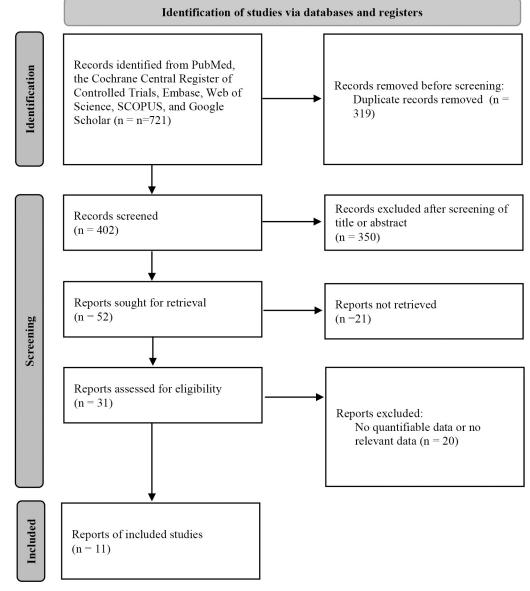
We used Begg's funnel plot and Egger's test simultaneously to detect publication bias. The trim-and-fill method also was done to indicate the significance of publication bias as well as provide bias-adjusted results.

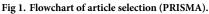
#### Results

In total, 11 studies with 1,644 participants were included. Study characteristics and bias assessments are presented in S2 and S3 Tables. Egger's test (p > 0.05) and Begg's funnel plot (S1 Fig) on these measurements suggested that a bias source was not evident in this sample of studies.

# Diagnostic accuracy of smartphones in terms of moderate-to-severe obstructive sleep apnea syndrome

Eleven studies were analyzed. The smartphone DOR for moderate-to-severe OSAS (AHI > 15) was 57.3873 (95% confidence interval [CI]: 34.7462; 94.7815,  $I^2 = 24.3\%$ ) (Fig 2).





https://doi.org/10.1371/journal.pone.0268585.g001

The area under the SROC curve was 0.917 (Fig 3). The correlation between sensitivity and the false-positive rate was 0.137, indicating that heterogeneity was absent. The sensitivity, specificity, negative predictive value, and positive predictive value were 0.9064 ([0.8789; 0.9282],  $I^2 = 0.0\%$ ), 0.8801 ([0.8227; 0.9207],  $I^2 = 61.7\%$ ), 0.9049 ([0.8556; 0.9386],  $I^2 = 54.9\%$ ), and 0.8844 ([0.8234; 0.9263],  $I^2 = 66.3\%$ ), respectively (Fig 4). The overall pooled random-effects mean difference (smartphone—polysomnography) and SD were -0.6845 ([-3.8426; 2.4735],  $I^2 = 92.9\%$ ) (Fig 5).

Subgroup analysis was performed according to the mode of detection of apnea severity (using motion, sound, oximetry, and combinations thereof) because high heterogeneity in terms of diagnostic accuracy was evident (Table 1). In terms of specificity, motion or oximetry methods (motion 96%; motion and oximetry 100%; oximetry 88%) were better than the other

	Experin Events		Events	ontrol Total	Odds Ratio OR	95%-CI	Weight
g2 = Motion							
Nandakumar 2015	15	15	0	22	1395.000	[26.251; 74132.451]	1.5%
Lvon 2019	16	20	1	74		[ 30.559; 2790.182]	4.3%
Lyon 2019	32	33	2	35		[ 45.599; 6113.830]	3.7%
Random effects model Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,		68		131		[100.409; 2147.927]	9.6%
g2 = Motion and oximete							
Chang 2020	42		3	14	279.286	[13.441; 5803.369]	2.5%
Random effects model		42		14	279.286	[13.441; 5803.369]	2.5%
Heterogeneity: not applicable							
g2 = Motion and sound							
Bonnesen 2018	9	13	1	10	20.250	[ 1.878; 218.390]	3.9%
Tiron 2020	35	47	4	81	56.146	[16.910; 186.421]	11.6%
Tiron 2020	53	65	7	55	30.286	[11.023; 83.207]	14.3%
Random effects model		125		146	36.740	[17.614; 76.634]	29.9%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,	p = 0.65						
g2 = Oximeter							
Pinheiro 2020	139	156	12	148	92.667	[42.655; 201.316]	18.8%
Random effects model		156		148	92.667	[ 42.655; 201.316]	18.8%
Heterogeneity: not applicable							
g2 = Sound							
Abeyratne 2013	11	13	3	11	14.667	[ 1.970; 109.204]	5.3%
Nakano 2014	25	29	4	21	26.562	[ 5.829; 121.049]	8.3%
Akhter 2018	52	55	7	30	56.952	[13.510; 240.092]	9.0%
Swarnkar 2018	34	38	5	35	51.000	[12.533; 207.531]	9.3%
Narayan 2019	31	40	2	19	29.278	[ 5.666; 151.293]	7.3%
Random effects model		175		116	35.421	[ 17.600; 71.286]	39.2%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,	p = 0.81						
Random effects model		566		555	57.387	[ 34.746; 94.782]	100.0%
Heterogeneity: $I^2 = 24\%$ , $\tau^2 = 0$ Residual heterogeneity: $I^2 = 0$ %					.001 0.1 1 10 1000		

Fig 2. Forest plot of the diagnostic odds ratios of the included studies.

https://doi.org/10.1371/journal.pone.0268585.g002

methods (82 and 81%; p = 0.0085). In terms of the negative predictive value, motion or oximetry methods (motion 97%; motion and sound 92%; and oximeter 92%) were better than the other methods (78 and 81%; p = 0.0015). In terms of the DOR, motion or oximetry methods (motion 464.4033; motion and oximetry 279.2857; and oximetry 92.6667) were better than the other methods (36.7401 and 35.4208; p = 0.0117). In contrast, the specificity and both negative and positive predictive values were similar (80–100%, all p > 0.05) for all methods. However, although only single study used only oximetry, it was clear that smartphones afforded good diagnostic accuracies (in terms of sensitivity, specificity, negative predictive value, and positive predictive value; all 80–100%) when screening for moderate-to-severe OSAS.

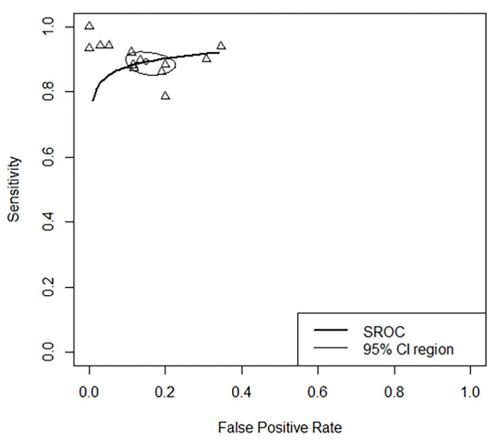
#### Sensitivity analyses

We evaluated differences in pooled estimates by repeating the meta-analysis, omitting study one at a time. All results were consistent with the above results (S2 Fig).

# Discussion

In this study, the smartphone diagnostic accuracy exhibited a pooled sensitivity of 0.90, a pooled specificity of 0.88, a pooled negative predictive value of 0.90, a pooled positive predictive value of 0.88, and an AUC of 0.92. All AUCs under SROC curves were 0.9–1.00, suggesting excellent diagnostic accuracy. The sensitivity in terms of moderate-to-severe OSA was good (90%). The specificity in terms of the absence of moderate-to-severe OSA was 88%; the false-negative rate was thus very low. These results mean that smartphone-based OSAS screening would be useful for patients with moderate-to-severe OSAS. The high negative predictive value suggests that only 10% of smartphone-positive patients would have false-positive diagnoses, compared with patients diagnosed on the basis of clinical examination or history-taking.

Attended full PSG is the gold-standard tool for OSAS diagnosis. However, the patient must sleep in an unfamiliar specialized room with 22 wires attached; these collect neurological,



# SROC curve (bivariate model)

Fig 3. Area under the summary receiver operating characteristic curves of included studies.

https://doi.org/10.1371/journal.pone.0268585.g003

cardiac, and respiratory data. The process can cause serious discomfort and anxiety; the patient may not be able to sleep as usual. Therefore, some clinics prescribe sleeping pills, which distort analysis. Moreover, few hospitals feature full PSG, particularly in rural areas, and PSG is expensive [21, 22]. There is an urgent need for portable devices that are accurate, convenient, and measure only key biological signals [23, 24].

Smartphones feature various apps [25]. Internal sensors and external (connectable) devices measure blood oxygen, pulse, body movement (using accelerometers or sonars), and breath sounds during sleep [12]. Studies using oximeter/accelerometer combinations to diagnose sleep apnea found that body position data aided in respiratory movement assessment [26, 27]. Breathing sounds during sleep also aid in OSAS diagnosis. Snoring differs between healthy people and sleep apnea patients; the noises alone accurately separate the groups [28]. In addition, various recent apps feature algorithms analyzing oxygen saturation, body position during sleep, and sleep breathing sounds [5–10, 12, 14, 15, 29]. Furthermore, because smartphones use motion, sound, oximetry, and combinations thereof to detect abnormal sleep, we evaluated the effects of the various methods on diagnostic accuracy; we performed subgroup analysis.

Recent studies have compared the reliabilities of such apps to the reliability of PSG [5, 8, 16–19]. Because moderate-to-severe OSA ([AHI  $\geq$  15/h) is associated with high risks of cardiovascular morbidity and mortality, and thus requires treatment [30], many studies have sought to clinically validate apps by screening for such OSA [5–10, 12, 14, 15, 29].

Study		4	Proportio	n 95%-CI	B	Events Total		Proportion	
g2 = Motion			1		g2 = Motion		1		
Nandakumar 2015	15 1	5	1.00	0 [0.782; 1.000]	Nandakumar 2015	22 22		1.000	[0.
Lyon 2019	16 1	7	. 0.9	1 [0.713; 0.999]	Lyon 2019	73 77		0.948	01
Lyon 2019	32 3			1 [0.803; 0.993]	Lyon 2019	33 34		0.971	
Random effects model				5 [0.868; 0.985]	Random effects mode			0.962	
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$		0		ia [o.ooo, o.ooo]	Heterogeneity: $I^2 = 0\%$ , $\pi^2$			0.002	for
g2 = Motion and oxime Chang 2020	42 4	·		3 [0.817; 0.986]	g2 = Motion and oxim- Chang 2020	eter 11 11		1.000	10 3
Random effects model		s		3 [0.813; 0.978]	Random effects mod			1.000	
Heterogeneity: not applicable				(	Heterogeneity: not applicabl				1
g2 = Motion and sound Bonnesen 2018	9 1			0 [0.555; 0.997]	g2 = Motion and soun Bonnesen 2018	d 9 13 —		0.692	10.2
Tiron 2020	35 3			7 [0.758; 0.971]	Tiron 2020	77 89		0.865	
Tiron 2020	53 6			3 [0.774; 0.952]	Tiron 2020	48 60	100	0.800	
Random effects model Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$		9	0.8	0 [0.816; 0.936]	Random effects mode Heterogeneity: $I^2 = 0\%$ , $\tau^2$		~	0.827	[0.7
Heterogeneity: 7 = 0%, 1 = 1	0, p = 0.97				reservageneity: 7 = 0%, 4	0, p = 0.25			
g2 = Oximeter					g2 = Oximeter				-
Pinheiro 2020	139 15			[1 [0.865; 0.958]	Pinheiro 2020	136 153		0.889	
Random effects model	1 15	1 -	0.93	[1 [0.865; 0.954]	Random effects mode	el 153		0.889	[0.8
Heterogeneity: not applicable					Heterogeneity: not applicable				
g2 = Sound					g2 = Sound				
Abeyratne 2013	11 1	4	0.7	6 [0.492; 0.953]	Abeyratne 2013	8 10		0.800	[0.4
Nakano 2014	25 2	9		2 [0.683; 0.961]	Nakano 2014	17 21		0.810	
Akhter 2018	52 5			[0.771; 0.951]	Akhter 2018	23 26		0.885	
Swarnkar 2018	34 3			2 [0.726; 0.957]	Swarnkar 2018	30 34		0.882	
Swarnkar 2018 Naravan 2019	34 3			2 [0.726; 0.957]	Swarnkar 2018 Narayan 2019	30 34 17 26	100	0.882	
Random effects model			0.8	9 [0.822; 0.920]	Random effects mod			0.815	[0.7
Heterogeneity: $I^2 = 0\%$ , $\pi^2 = 0$	0. p = 0.69				Heterogeneity: $I^2 = 25\%$ , $\pi^2$	= 0.1023, p = 0.21			
Random effects model	54	5	0.9	6 [0.879; 0.928]	Random effects mode	el 576		0.880	[0.8
	0. p = 0.92					+0.3731 # +0.04			
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ Residual heterogeneity: $I^2 = 0$		0.5 0.6 0.7 0.8	0.9 1		Heterogeneity: J <sup>2</sup> = 62%, x <sup>2</sup> Residual heterogeneity: J <sup>2</sup> =	= 0.3731, p = 0.04	0.5 0.6 0.7 0.8 0.9 1		
Heterogeneity: /2 = 0%, x2 = 0		0.5 0.6 0.7 0.8			Heterogeneity: $I^2 = 62\%$ , $\tau^2$	= 0.3731, p = 0.04	0.5 0.6 0.7 0.8 0.9 1		
Heterogeneity: /2 = 0%, x2 = 0					Heterogeneity: I <sup>2</sup> = 62%, v <sup>2</sup> Residual heterogeneity: I <sup>2</sup> = <b>Study</b>	= 0.3731, p = 0.04		Proportion	
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ Residual heterogeneity: $I^2 = 0$	0%, p = 0.97		0.9 1 Proporti	on 95%-CI	Heterogeneity: /² + 62%, -² Residual heterogeneity: /² + <b>D</b> g2 = Motion	= 0.3731, p = 0.04 10%, p = 0.35 0.4 Events Total			
Heterogeneity: <i>I</i> <sup>2</sup> = 0%, x <sup>2</sup> = ( Residual heterogeneity: <i>I</i> <sup>2</sup> = 0 <b>Study</b>	5%. p = 0.97 Events To		0.9 1 Proporti		Heteropeneity: I <sup>2</sup> = 62%, -t <sup>2</sup> Residual heteropeneity: I <sup>2</sup> + Study	= 0.3731, p = 0.04 10%, p = 0.35 0.4		Proportion	[0.78
Heterogeneity: J <sup>2</sup> = 0%, c <sup>2</sup> = ( Residual heterogeneity: J <sup>2</sup> = 0 <b>Study</b> g2 = Motion Nandakumar 2015	2%, p = 0.97 Events To 22	al	Proporti	on 95%-Cl	Heterogeneity: /² = 62%, - Residual heterogeneity: /² = Study g2 = Motion Nandakumar 2015	= 0.3731, p = 0.04 10%, p = 0.35 0.4 Events Total		1.000	
Heterogeneity: I <sup>2</sup> = 05s, s <sup>2</sup> = ( Residual heterogeneity: I <sup>2</sup> = 0 Study g2 = Motion Nandakumar 2015 Lyon 2019	2%, p = 0.97 Events To 22 73	al 22 74	0.9 1 Proporti	on 95%-Cl	Heterogeneity: J <sup>2</sup> + 625, s <sup>2</sup> Residual heterogeneity: J <sup>2</sup> + <b>D</b> Study g2 = Motion NandaLumar 2015 Lyon 2019	= 0.3731. p = 0.04 1075. p = 0.35 Events Total 15 15 16 20		1.000	[0.56
Heterogeneity: I <sup>2</sup> = 05, s <sup>2</sup> = ( Residual heterogeneity: I <sup>2</sup> = 0 Study g <sup>2</sup> = Motion Nandakumar 2015 Lyon 2019 Lyon 2019	2%, p = 0.97 Events To 22 73 33	al 22 74 35 —	Proporti	on 95%-Cl 00 [0.846; 1.000] 866 [0.927; 1.000] 43 [0.808; 0.993]	Heteropanelty: i <sup>2</sup> = 02%, i <sup>2</sup> Residual heteropanelty: i <sup>2</sup> = <b>D</b> Study g2 = Motion Nandakumar 2015 Lyon 2019 Lyon 2019	* 0.3731, p * 0.04 10%, p * 0.35 Events Total 15 15 16 20 32 33		1.000 0.800 0.970	[0.56
Heterogeneity: <i>I</i> <sup>2</sup> = 05, <i>s</i> <sup>2</sup> = ( Residual heterogeneity: <i>I</i> <sup>2</sup> = 0 Study 02 = Motion Nandakumar 2015 Lyon 2019 Lyon 2019 Random effects mode	Events To 22 73 33	al 22 74	Proporti	on 95%-Cl	Hateropenety, r <sup>2</sup> + 62%, r <sup>2</sup> Residual heteropenety, r <sup>2</sup> + <b>D</b> g2 = Motion Nandakumar 2015 Lyon 2019 Random effects mod	= 0.3731, p = 0.04 10%, p = 0.35 Events Total 15 15 16 20 32 33 cl 66		1.000	[0.56
Heterogeneity: I <sup>2</sup> = 05, s <sup>2</sup> = ( Residual heterogeneity: I <sup>2</sup> = 0 Study g <sup>2</sup> = Motion Nandakumar 2015 Lyon 2019 Lyon 2019	Events To 22 73 33	al 22 74 35 —	Proporti	on 95%-Cl 00 [0.846; 1.000] 866 [0.927; 1.000] 43 [0.808; 0.993]	Heteropanelty: i <sup>2</sup> = 02%, i <sup>2</sup> Residual heteropanelty: i <sup>2</sup> = <b>D</b> Study g2 = Motion Nandakumar 2015 Lyon 2019 Lyon 2019	= 0.3731, p = 0.04 10%, p = 0.35 Events Total 15 15 16 20 32 33 cl 66		1.000 0.800 0.970	[0.56
Heterogeneity: $t^2 = 05$ , $s^2 = 1$ Residual heterogeneity: $t^2 = 0$ Study g2 = Motion Nandakumar 2015 Lyon 2019 Lyon 2019 Heterogeneity: $t^2 = 05$ , $s^2 = 1$ g2 = Motion and oximme	Events To 22 73 33 11 1 0. p = 0.49 ster	al 22 26 55 — 11	Proporti	on 95%-Cl 00 [0.846; 1.000] 88 [0.927; 1.000] 43 [0.808; 0.993] 77 [0.931; 0.993]	Heterogenery, if a 25% of Residual heterogenery, if a D Study Q2 = Motion Nandatume? 2015 Lyna 2019 Bandom offects mod Heterogenery, if a 25% of Q2 = Motion and own	= 0.3731, p = 0.04 10%, p = 0.35 Events Total 15 15 16 20 32 33 el 68 = 0.9681, p = 0.20 eter		1.000 0.800 0.970 0.946	[0.56 [0.84
Heterogeneity: $r^2 = 05, r^2 = 1$ Rasidual heterogeneity: $r^2 = 0$ Study Q2 = Motion Nandakumar 2015 Lyon 2019 Random effects mode Heterogeneity: $r^2 = 05, r^2 =$ Q2 = Motion and oxime Chang 2020	Events To 22 73 33 11 1 0, p = 0.49 21	al 12 15 — 11	Proporti	on 95%-C1 00 [0.846; 1.000] 885 [0.927; 1.000] 143 [0.806; 0.993] 777 [0.931; 0.993] 886 [0.492; 0.953]	Heterogenery, if a 251, c <sup>2</sup> Residual heterogenery, if a D Study 02 = Motion Handshumer 2015 Lyon 2016 Lyon 2016 Canadon effects mod Heterogenery, if a 251, c <sup>2</sup> 02 = Motion and oxim Chang 2020	* 0.3731, p * 0.04 10%, p * 0.35 Events Total 15 15 16 20 32 33 el 68 = 0.9681, p = 0.20		1.000 0.800 0.970 0.946	[0.56 [0.84 [0.74
Heterogeneity: $t^2 = 05$ , $s^2 = 1$ Residual heterogeneity: $t^2 = 0$ Study g2 = Motion Nandakumar 2015 Lyon 2019 Lyon 2019 Heterogeneity: $t^2 = 05$ , $s^2 = 1$ g2 = Motion and oximme	Events To 22 73 33 11 1 0, p = 0.49 24 11	al 22 26 55 — 11	Proporti	on 95%-Cl 00 [0.846; 1.000] 88 [0.927; 1.000] 43 [0.808; 0.993] 77 [0.931; 0.993]	Heterogenery, if + 255, c <sup>2</sup> Residual heterosenery, i <sup>2</sup> + D Study Q2 = Motion Nac6doumer 2015 Lyse 2019 Eandom effects mod Heterogenery, i <sup>2</sup> + 255, c <sup>2</sup> g <sup>2</sup> = Motion and outin Chang 2020 Bandom effect <del>s mod</del>	= 0.331, p = 0.4 105, p = 0.35 0.4 Events Total 15 15 16 20 32 33 el 68 ≈ 0.5051, p = 0.20 eter 42 42 42		1.000 0.800 0.970 0.946	[0.56 [0.84 [0.74]
Heterogeneity: $r^2 = 05, r^2 = 1$ Rasidual heterogeneity: $r^2 = 0$ Study Q2 = Motion Nandakumar 2015 Lyon 2019 Random effects mode Heterogeneity: $r^2 = 05, r^2 =$ Q2 = Motion and oxime Chang 2020	22 22 73 33 1 1 0, p = 0.49 ster 11	al 12 15 — 11	Proporti	on 95%-C1 00 [0.846; 1.000] 885 [0.927; 1.000] 143 [0.806; 0.993] 777 [0.931; 0.993] 886 [0.492; 0.953]	Heterogenery, if a 251, c <sup>2</sup> Residual heterogenery, if a D Study 02 = Motion Handshumer 2015 Lyon 2016 Lyon 2016 Canadon effects mod Heterogenery, if a 251, c <sup>2</sup> 02 = Motion and oxim Chang 2020	= 0.331, p = 0.4 105, p = 0.35 0.4 Events Total 15 15 16 20 32 33 el 68 ≈ 0.5051, p = 0.20 eter 42 42 42		1.000 0.800 0.970 0.946	[0.56 [0.84 [0.74
Helenspenity, r <sup>2</sup> + 05, 4 <sup>2</sup> + Readual Helenspenity, r <sup>2</sup> + 0 Study g2 = Motion Nandakimarg 2015 Lynn 2019 Random effects model meangenety, r <sup>2</sup> + 05, 4 <sup>2</sup> g2 = Motion and oxime Chang 2020 Random effects model Helenspenity, rei apticabil	22 73 33 10. p = 0.49 10. p = 0.49 ster 11	al 12 15 — 11	Proporti	on 95%-C1 00 [0.846; 1.000] 885 [0.927; 1.000] 143 [0.806; 0.993] 777 [0.931; 0.993] 886 [0.492; 0.953]	B B B B B B B B B B B B B B	+ 0.331, p + 0.4 10%, p + 0.35 0.4 Events Total 15 15 16 20 32 33 cl 60 + 0.5031, p + 0.20 eter 42 42 + 2 + 2 + 2 + 2 + 2 + 2 + 2 +		1.000 0.800 0.970 0.946	[0.56 [0.84 [0.74
Heenspendty, r <sup>2</sup> + 05, 4 + r Radical Heenspender, r <sup>2</sup> + 0 Study g2 = Motion Nandaturer 2015 Lyon 2019 Random effects mode Heenspendy, r <sup>2</sup> + 05, 4 <sup>2</sup> g2 = Motion and oxime Chang 2020 Random effects mode Heenspendy, re asplastic g2 = Motion and source	$K_{1,p} = 0.97$ Events To 22 73 33 11 0, p + 0.49 ster 11 11 0	al 22 74 75 75 71	Proport	on 95%-Cl 00 [0.846; 1.000] 06 [0.927; 1.000] 13 [0.806; 0.993] 77 [0.931; 0.993] 06 [0.462; 0.953] 06 [0.566; 0.529]	Bescauteners, i <sup>2</sup> + St. <sup>2</sup> , Restaut teuroparety, i <sup>2</sup> + Backarner 2015 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Random effects amod memography for appendix Random effects amod Random eff	+ 0.331; p + 0.04 10%, p + 0.35 10%, p + 0.35 15 15 16 20 32 33 16 68 + 0.981; p + 0.20 eter 42 42 42 42 42 42 42		1.000 0.800 0.970 0.946 1.000	[0.56 [0.84 [0.74
Heinsgeneby, r <sup>2</sup> + 05, s <sup>2</sup> + 7 Residual heinsgeneby, r <sup>2</sup> + 02 Study g <sup>2</sup> + Molion Nandakumer 2015 Lynn 2019 Lynn 2019 Bandom effects mode Heinsgeneby, rel appleab Chap 2020 Random effects mode Heinsgeneby, rel appleab Heinsgeneby, rel appleab Bonesen 2016	Wx, p = 0.97           Events To           22           73           33           1           1           10, p = 0.49           otter           11           10           9	al 22 74 75 71 74 74 74 74 74 74 74 74 74 74 74 74 74	Proport	on 95%-Cl 00 [0.846; 1.000] 13 [0.806; 0.993] 17 [0.931; 0.993] 18 [0.492; 0.953] 18 [0.492; 0.953] 10 [0.556; 0.927] 10 [0.555; 0.997]	D Study Study D Study St	+ 0.331, p + 0.04 10%, p + 0.35 0.4 Events Total 15 15 16 20 32 33 el 60 + 0.5031, p + 0.20 eter 42 42 - - - - - - - - - - - - -		1.000 0.800 0.970 0.946 1.000 1.000	[0.56 [0.84 [0.74 [0.91 [0.00
Hereageneby, $r^2 + 05$ , $q^2 + 1$ Residual termination of $r^2 + 0$ Study $q^2 = Motion$ Nandakumar 2015 Lyon 2019 Lyon 2019 Exandone effects mode Interrogeney <i>res</i> , $r^2 = 0$ , $q^2 = 0$ Randone effects mode Interrogeney <i>res</i> replace Randone effects mode Benesen 2018 Benesen 2018	%, p = 0.57           Events To           22           33           1	al 22 74 75 76 76 76 76 76 76 76 76 76 76 76 76 76	Proporti	on         95%-C1           000         (0.846; 1.000)           060         (0.927; 1.000)           431         (0.806; 0.993)           77         (0.931; 0.993)           96         (0.492; 0.953)           96         (0.506; 0.923)           96         (0.556; 0.997)           91         (0.555; 0.997)           91         (0.556; 0.997)           91         (0.556; 0.997)	D Staty Basedu Hencenety, if 4 Staty D Staty Sav Motion Lyso 2019 Random effects and management, if a 2019 Random effects and management, if a 2012 gr - Motion and atom Chang 2020 Random effects and change 2020 Random effects and Random e	+ 0.331; p + 0.04 105; p + 0.35 105; p + 0.35 15 15 15 16 20 32 33 10 60 42 22 32 33 10 60 42 47		1.000 0.800 0.970 0.946 1.000 1.000	[0.56 [0.84 [0.74 [0.74 [0.91 [0.00
Heerspeety, r <sup>2</sup> + 05, r <sup>2</sup> + 7 Restaat heerspeety, r <sup>2</sup> + 02 Study g 2 + Motion Nandaiume 2015 Lynn 2019 Lynn 2019 Lynn 2019 Random effects mode Heerspeety, rel aptication Q + Motion and source Bandom effects mode Heerspeety, rel aptication g 2 + Motion and source Banesse 2018 Tren 2020	$K_{1, p} = 0.57$ Events To 22 73 3 11 1 0, p = 0.49 2 2 7 3 3 3 1 1 1 1 1 1 1 1 1 1 1 1 2 4 5 2 2 7 7 7 4 5	al 22 74 15 14 14 14 10 10 15 55	Proport	on 95%-Cl 00 [0.846; 1.000] 08 [0.927, 1.000] 19 [0.807, 1.000] 19 [0.805, 0.993] 10 [0.931; 0.293] 08 [0.492, 0.953] 09 [0.555; 0.997] 15 [0.875; 0.947] 15 [0.755; 0.947]	D Study Bescal Hersenery, if v Study D Study Backstone 2015 (spen 2019) Backstone 2015 (spen 2019) Backstone 2015 (spen 2019) Backstone differs mode menoperacy if v Str., if Chap 2020 Random of Effects mode menoperacy on application (spen 2010) Backstone and some menoperacy on application (spen 2010) Backstone 2010 There 2020 There 2020	$\begin{array}{c} * 0.3731, p + 0.04 \\ 1056, p + 0.36 \\ \hline \\ $		1.000 0.800 0.970 0.946 1.000 1.000	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70
Heuropenby, $r^2 + 05$ , $q^2 + Residual heuropenby, r^2 + 05, q^2 + Residual heuropenby, r^2 + 05Studyg^2 = MotionNandakumar 2015Lyon 2019Lyon 2017Random effects modeRandom Lyon (fects mode$	$K_{1,p} = 0.57$ Events To 22 33 11 1 10, $p = 0.49$ tter 11 11 11 11 11 11 11 11 11 11 11 11 11	al 22 24 25 25 26 26 27 26 27 27 27 27 27 27 27 27 27 27	Proport	on         95%-C1           000         (0.846; 1.000)           060         (0.927; 1.000)           431         (0.806; 0.993)           77         (0.931; 0.993)           96         (0.492; 0.953)           96         (0.506; 0.923)           96         (0.556; 0.997)           91         (0.555; 0.997)           91         (0.556; 0.997)           91         (0.556; 0.997)	Basedur Henegonery, 7 + 627, Budy D Study D Suby	* 0.373/; * p. * 0.04 105%, p * 0.35 Events Total 15 15 16 16 20 32 33 el 68 42 42 42 42 43 9 13 		1.000 0.800 0.970 0.946 1.000 1.000	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70
Heerspeety, r <sup>2</sup> + 05, r <sup>2</sup> + 7 Restaat heerspeety, r <sup>2</sup> + 02 Study g 2 + Motion Nandaiume 2015 Lynn 2019 Lynn 2019 Lynn 2019 Random effects mode Heerspeety, rel aptication Q + Motion and source Bandom effects mode Heerspeety, rel aptication g 2 + Motion and source Banesse 2018 Tren 2020	$K_{1,p} = 0.57$ Events To 22 33 11 1 10, $p = 0.49$ tter 11 11 11 11 11 11 11 11 11 11 11 11 11	al 22 24 25 25 26 26 27 26 27 27 27 27 27 27 27 27 27 27	Proport	on 95%-Cl 00 [0.846; 1.000] 08 [0.927, 1.000] 19 [0.807, 1.000] 19 [0.805, 0.993] 10 [0.931; 0.293] 08 [0.492, 0.953] 09 [0.555; 0.997] 15 [0.875; 0.947] 15 [0.755; 0.947]	Bescart Heregoeney, r <sup>2</sup> etc. <sup>2</sup> , Andrew Bescart Heregoeney, r <sup>2</sup> etc. <sup>2</sup> Box Support Heredonica 2016 Heredonica 2016 Heredonica 2016 Constraints and action Constraints and action Constraints and action Reservery, r <sup>2</sup> etc. <sup>2</sup> , Addition and action Reservery, r <sup>2</sup> etc. <sup>2</sup> , Additional Heredonica 2016 Tree 2020 Heredonica 2016 Heredonica 2016 Heredonica 2016	* 0.373/; * p. * 0.04 105%, p * 0.35 Events Total 15 15 16 16 20 32 33 el 68 68 69 12 42 42 42 42 49 9 13 		1.000 0.800 0.970 0.946 1.000 1.000	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70
Heursgeatery, P <sup>2</sup> + 05, V <sup>2</sup> + 1 Study Q <sup>2</sup> + Motion Nandakumz 2015 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Bandom effects mode Instancement, Pix studies Bonesen 2018 Tren 2020 Tren 2020 Tren 2020 Q <sup>2</sup> - Motion and x <sup>2</sup> Studies (Studies) Studies (Studies) Studies (Studies) Studies) Studies (Studies) Studie	22 73 33 10, p = 0.49 11 10 77 4 9 77 73 33 11 11 11 12 13 14 11 14 14 15 16 11 16 17 10 17 10 10 10 10 10 10 10 10 10 10	al 22 74 75 75 74 74 74 74 75 75 75 75 75 75 75 75 75 75 75 75 75	Proport	on         95%-CI           00         [0.846; 1.000]         [0.827; 1.000]           04         [0.826; 0.993]         [0.866; 0.993]           97         [0.931; 0.993]         [0.866; 0.993]           96         [0.492; 0.953]         [0.555; 0.997]           96         [0.492; 0.953]         [0.555; 0.997]           97         [0.555; 0.997]         [0.855; 0.997]           91         [0.854; 0.355]         [0.854]	Bescala Helespeetry, if etc.3 Helescala Helespeetry, if a Starby D Starby C Starby Starby<	$\begin{array}{c} \circ 0.373, p = 0.04 \\ \hline 1050, p = 0.35 \\ \hline 1050, p = 0.35 \\ \hline 1050, p = 0.35 \\ \hline 1050, p = 0.20 \\ \hline 105$		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70 [0.69
Heenspeaks, r <sup>2</sup> + 05, s <sup>2</sup> + 1 Readaitespeaks, r <sup>2</sup> + 0 Study (3 - Motion Incohamer 2015 Lyon 2019 Random effects mode Insenspeaky, r <sup>2</sup> + 05, s <sup>2</sup> + (3 - Motion and souther (3 - Motion and souther) (3 - Motion and souther (3 - Motion and souther (3 - Motion and souther) (3 - Motio	22 73 33 1 1, , , , , + 0.49 1 4 9 77 48 9 77 48 9 77 48 9 77 48 9 77 48 9 77 10 11 11 11 12 13 13 11 11 11 13 13 13 11 11	al 22 74 75 71 74 74 74 74 75 75 75 75 75 75 75 75 75 75 75 75 75	Proport	on         95%-CI           000         10.846, 1.000]           10.927, 1.000]         10.927, 1.000]           43         10.806, 0.993]           77         10.931, 0.993]           66         [0.452, 0.953]           66         [0.452, 0.953]           71         [0.356, 0.997]           61         [0.555, 0.997]           61         [0.854, 0.3647]           18         [0.864, 0.366]           19         [0.863, 0.957]	Bescar Heregoner, P. * 547, * B. Stat. B. St	• 0.3731, p = 0.04     • 0.3731, p = 0.04     • 0.4      Events Total     15    15     16    20     32    33 el     60     • 0.5031, p = 0.20 eter     42    42 e      4     9    13     53    46 et     125 et     12		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70 [0.69
Heursgeatery, P <sup>2</sup> + 05, V <sup>2</sup> + 1 Study Q <sup>2</sup> + Motion Nandakumz 2015 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Q <sup>2</sup> + Motion and x <sup>2</sup> Bandom effects mode Instancement, Pix studies Bonesen 2018 Tren 2020 Tren 2020 Tren 2020 Q <sup>2</sup> - Motion and x <sup>2</sup> Studies (Studies) Studies (Studies) Studies (Studies) Studies) Studies (Studies) Studie	22 73 33 1 1, , , , , + 0.49 1 4 9 77 48 9 77 48 9 77 48 9 77 48 9 77 48 9 77 10 11 11 11 12 13 13 11 11 11 13 13 13 11 11	al 22 74 75 75 74 74 74 74 75 75 75 75 75 75 75 75 75 75 75 75 75	Proport	on         95%-CI           00         [0.846; 1.000]         [0.827; 1.000]           04         [0.826; 0.993]         [0.866; 0.993]           97         [0.931; 0.993]         [0.866; 0.993]           96         [0.492; 0.953]         [0.555; 0.997]           96         [0.492; 0.953]         [0.555; 0.997]           97         [0.555; 0.997]         [0.855; 0.997]           91         [0.854; 0.355]         [0.854]	Basedur Henergenery, 7 et 92. Basedur Henergenery, 7 et Basedur Henergenery, 7 et Basedur Henergenery, 7 et Lyse 2019 Random et Betes and et and attesta mod mangenery, 7 et 32. 24 - Motion Random et Betes and et	$\begin{array}{c} \bullet 0.3731, p = 0.04 \\ \hline 1054, p = 0.04 \\ \hline 10$		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70 [0.69
Heenspeaks, r <sup>2</sup> + 05, s <sup>2</sup> + 1 Readaitespeaks, r <sup>2</sup> + 0 Study (3 - Motion Incohamer 2015 Lyon 2019 Random effects mode Insenspeaky, r <sup>2</sup> + 05, s <sup>2</sup> + (3 - Motion and souther (3 - Motion and souther) (3 - Motion and souther (3 - Motion and souther (3 - Motion and souther) (3 - Motio	YML, p = 0.97           Events         To           22         73           33         33           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1	al 22 74 75 71 74 74 74 74 75 75 75 75 75 75 75 75 75 75 75 75 75	Proport	on         95%-CI           000         10.846, 1.000]           10.927, 1.000]         10.927, 1.000]           43         10.806, 0.993]           77         10.931, 0.993]           66         [0.452, 0.953]           66         [0.452, 0.953]           71         [0.356, 0.997]           61         [0.555, 0.997]           61         [0.854, 0.3647]           18         [0.864, 0.366]           19         [0.863, 0.957]	Bescar Heregoner, P. * 547, * B. Stat. B. St	$\begin{array}{c} \bullet 0.3731, p = 0.04 \\ \hline 1054, p = 0.04 \\ \hline 10$		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776	[0.56 [0.84 [0.74 [0.91 [0.00 [0.38 [0.59 [0.70 [0.69
Henregevery, P = 05, 4 + 7 Study g = Motion Nandakure 2015 Lyon 2019 Lyon 2019 Lyo	YML, p = 0.97           Events         To           22         73           33         33           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1           1         1	al 22 74 75 71 74 74 74 74 75 75 75 75 75 75 75 75 75 75 75 75 75	Proport	on         95%-CI           000         10.846, 1.000]           10.927, 1.000]         10.927, 1.000]           43         10.806, 0.993]           77         10.931, 0.993]           66         [0.452, 0.953]           66         [0.452, 0.953]           71         [0.356, 0.997]           61         [0.555, 0.997]           61         [0.854, 0.3647]           18         [0.864, 0.366]           19         [0.863, 0.957]	Bescar Heeropere, 7 <sup>2</sup> etc. <sup>2</sup> , <sup>2</sup> Bescar Heeropere, 7 <sup>2</sup> etc. <sup>2</sup> Budy Budy Backbone 2015 Lyon 2019 Backbone Hitchis and example of Hitchis and Joann Galaction and Joann Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Tren 2020 Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Hitchis and Joann Backbone Alford Hitchis Backbone Al	+ 0.2372 (p + 0.04 + 0.2372 (p + 0.04 <b>Events Total</b> 15 15 16 20 16 22 30 16 22 30 17 20 20 17 20		1.000 0.900 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891	[0.56 [0.84 [0.74] [0.91 [0.00] [0.38 [0.59 [0.70 [0.69] [0.69] [0.83
Heurspeakers, P <sup>2</sup> + 05, <sup>2</sup> + 1 20 - 20 - 20 - 20 - 20 - 20 - 20 - 20 -	$\begin{array}{c} \text{Events To} \\ 22 \\ 73 \\ 33 \\ 1 \\ 0, p = 0.40 \\ \text{ster} \\ 11 \\ 1 \\ 0 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ $	al 22 74 155 — 14 14 14 156 10 11 155 15 15 15 15 15 15 15 1		on         95%-C1           00         (2.46;1.000)           00         (2.46;1.000)           00         (2.46;1.000)           00         (2.46;1.000)           00         (2.46;0.000)           00         (2.46;0.000)           00         (0.26;0.000)           00         (0.26;0.000)           00         (0.26;0.000)           01         (0.26;0.000)           10         (0.26;0.000)           19         (0.26;0.000)	Bescar Henespeer, if etc. Bescar Henespeer, if etc. Budy Budy Suby	$\begin{array}{c} \bullet 0.3731, p = 0.04 \\ \hline 1054, p = 0.04 \\ \hline 10$		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776	[0.56 [0.84 [0.74] [0.91 [0.00] [0.38 [0.59 [0.70 [0.69] [0.69] [0.83
Henrogeney, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Readout heavy p <sup>2</sup> + 05, q <sup>2</sup> + 0 Study g <sup>2</sup> - Motion Nandahame 2015 Lyon 2019 Random effects mode Henrogeney, P <sup>2</sup> + 05, q <sup>2</sup> + g <sup>2</sup> - Motion and South Charg 2020 Random effects mode Henrogeney, ret applicat g <sup>2</sup> - Motion and South Henrogeney, ret applicat Bonessen 2015 Then 2020 Random effects mode Henrogeney, P <sup>2</sup> + 115, q <sup>2</sup> g <sup>2</sup> - 2000 Random effects mode Henrogeney, P <sup>2</sup> + 115, q <sup>2</sup> Random effects mode	Events To 22 23 10, $p = 0.43$ eter 11 1 24 5 5 5 1 1 1 1 1 1 1 1 1 1 1 1 1	al 22 24 24 24 24 24 24 24 24 24		on         35%-CI           00         (0.844: 10.001)           00         (0.844: 10.001)           01         (0.844: 10.001)           02         (0.827: 10.002)           03         (0.842: 0.853)           04         (0.842: 0.853)           05         (0.842: 0.853)           01         (0.556: 0.897)           02         (0.556: 0.897)           11         (0.856: 0.856)           12         (0.845: 0.856)           13         (0.845: 0.857)           14         (0.845: 0.857)           15         (0.845: 0.857)           16         (0.845)           17         (0.345: 0.857)	Bescar Heeropere, 7 <sup>2</sup> etc. <sup>2</sup> , <sup>2</sup> Bescar Heeropere, 7 <sup>2</sup> etc. <sup>2</sup> Budy Budy Backbone 2015 Lyon 2019 Backbone Hitchis and example of Hitchis and Joann Galaction and Joann Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Tren 2020 Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Alford Hitchis Backbone Hitchis and Joann Backbone Alford Hitchis Backbone Al	+ 0.2372 (p + 0.04 + 0.2372 (p + 0.04 <b>Events Total</b> 15 15 16 20 16 22 30 16 22 30 17 20 20 17 20		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891	[0.56 [0.84 [0.74] [0.91 [0.00] [0.59 [0.70 [0.69] [0.83 [0.83] [0.83]
Heursgearby, $r^2 + 05$ , $r^2 + 1$ Study $q^2 + Motion$ Nandakumy 2015 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Lyon 2019 Q <sup>2</sup> + Motion and Cate the model Heursgearp, $r^2 + 50$ , $r^2 = 0$ Random effects model Heursgearp, $r^2 + 50$ , $r^2 = 0$ Bonosen 2018 Tren 2020 Tren 2020 Tren 2020 Photos	22, 23 22, 23 1, 3, 1 1, 0, p + 0.49 1, 0, p + 0.49 1, 1 1,			on         95%-CI           00         (2.84; 1.00)           00         (2.84; 1.00)           00         (2.84; 1.00)           00         (2.84; 1.00)           00         (2.84; 1.00)           00         (2.84; 0.93)           07         (0.350; 0.93)           00         (2.85; 0.93)           01         (2.85; 0.93)           11         (0.86; 0.93)           19         (0.86; 0.93)           27         (0.300; 0.94)           (1.93)         (0.34); 0.94)	D Staty 2 - Motion Staty D Staty 2 - Motion Staty 2 - Motion Staty S	$\begin{array}{c} + 2375 (p + 0.04) \\ + 2375 (p + 0.03) \\ \hline \\ $		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891 0.891	[0.56 [0.84 [0.74] [0.91] [0.91] [0.93 [0.59] [0.83 [0.83] [0.83] [0.83]
Heenspeed, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Readaul helsy, P <sup>2</sup> + 05, q <sup>2</sup> + 2 Study g <sup>2</sup> - Motion Incohamer 2015 Lyon 2019 Endome effects mode Interspeedy, P <sup>2</sup> + 05, q <sup>2</sup> + g <sup>2</sup> - Motion and solime g <sup>2</sup> - Motion and solime Bonnesen 2018 Tero 2020 Bonnesen 2018 Rendom effects mode Interspeedy, ret apticati tero 2020 Rendom effects mode Interspeedy, ret apticati g <sup>2</sup> - Motion and Solime Photero 2020 Random effects mode Rendom effects Rendom effects R	Events To 22 23 33 11 0, p = 0.43 eter 11 1 2 2 33 1 1 1 1 1 1 1 1 1 1 1 1 1			on         35%-C1           00         (0.844: 1.000)           00         (0.844: 1.000)           01         (0.844: 1.000)           01         (0.847: 1.000)           01         (0.847: 1.000)           02         (0.842: 0.053)           03         (0.842: 0.053)           04         (0.842: 0.053)           05         (0.842: 0.053)           10         (0.842: 0.053)           11         (0.842: 0.053)           12         (0.842: 0.053)           19         (0.842: 0.043)           10         (0.842: 0.043)           11         (0.842: 0.044)           12         (0.340: 0.044)           10         (0.840: 0.044)           10         (0.840: 0.044)	Bescar Heresoner, Pr 5 - 55, 2 Bescar Heresoner, Pr 4 Bury	+ 0.373 (p + 0.04 (vents Total 15 15 2 15 2		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891 0.891 0.891	[0.56 [0.84 [0.74 [0.91] [0.00 [0.59 [0.70 [0.69 [0.83 [0.83 [0.83
Heursgearby, $r^2 + 05$ , $r^2 + 1$ Study $q^2 + Motion$ Nandakumy 2015 Lyon 2019 Random effects mode Heursgeary, $r^2 + 05$ , $r^2 = 0$ Random effects mode Heursgeary, $r^2 + 05$ , $r^2 = 0$ Random effects mode Heursgeary, $r^2 + 15$ , $r^2$ $q^2 + Motion and source Bonosen 2018 Tren 2020 Random effects mode Heursgeary, r^2 + 15, r^2Random effects modeHeursgeary, r^2 + 15, r^2Random effects modeHeursgeary, r^2 + 15, r^2Random effects modeHeursgeary, est applicablePholes 2020Random effects modeHeursgeary, est applicablePholes 2020Random effects modeHeursgeary, est applicableq^2 - 5 sourceq^2 - 5 s$	22:         23:           23:         33:           1:         1:           0:         p = 0.49:           rter         11:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:	al 22 24 24 24 25 25 26 26 26 26 26 26 26 26 26 26		on         59%-CI           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           01         [3.64, 0.000]           02         [3.64, 0.000]           06         [1.64, 0.000]           06         [1.64, 0.000]           07         [1.55, 0.000]           19         [1.64, 0.000]           22         [1.36, 0.000]           23         [1.64, 0.000]           24         [1.66, 0.000]           19         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]	Bescard Hencement, /* 6.47 Budy D Study D Suby Suby Suby Suby Suby Substance 2016 Substance 2016 Substance 2018 Substance 2018 S	+ 0.2372 (p + 0.04 (p + 0.15) (p + 0.04 (p + 0.15) (p + 0.04 (p + 0.15) (p + 0.04 (p + 0.05) (p + 0.25) (p + 0.05) (p + 0.25) (p + 0.25) (p + 0.05) (p + 0.25) (p + 0.25) (p + 0.25) (p + 0.05) (p + 0.25) (p + 0		1.000 0.800 0.970 0.946 1.000 1.000 1.000 0.692 0.745 0.891 0.891 0.891 0.891 0.891 0.891	[0.56 [0.84 [0.74 [0.91] [0.00 [0.59 [0.70 [0.69 [0.83 [0.83 [0.83 [0.83 [0.84 [0.68] [0.84 [0.84 [0.84]
Heinspecker, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Study g <sup>2</sup> + Motion Nandakumz 2015 Lyon 2019 Random effects mode Interpreter and the state of the state Interpreter and the state Interpreter an	22:         23:           23:         33:           1:         1:           0:         p = 0.49:           rter         11:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:           1:         1:			on         59%-CI           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           01         [3.64, 0.000]           02         [3.64, 0.000]           06         [1.64, 0.000]           06         [1.64, 0.000]           07         [1.55, 0.000]           19         [1.64, 0.000]           22         [1.36, 0.000]           23         [1.64, 0.000]           24         [1.66, 0.000]           19         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]	D Staty Basedonetty, 7 + 55, 7 Basedonetty, 7 + Basedonetty, 7 + Basedonetty, 7 + Basedonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Randonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Randonetty, 7 + 55, 7	+ 2373(p+0.04) <b>Events Total</b> 15 15 16 15 16 15 16 22 33 18 42 23 19		1.000 0.800 0.970 0.946 1.000 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891 0.891 0.891 0.846 0.846 0.945 0.945	[0.56 [0.84 [0.74] [0.91] [0.00] [0.38 [0.59 [0.70] [0.69] [0.63] [0.83 [0.84 [0.84 [0.84 [0.84] [0.64]
Heenspeerly, r <sup>2</sup> + 05, s <sup>2</sup> + 1 Readout helps, r <sup>2</sup> + 05, s <sup>2</sup> + 0 Study (3 - Motion and Souther Lyon 2019 Random effects model Heanspeerly, r <sup>2</sup> + 05, s <sup>2</sup> + 02 + Motion and Souther (3 - Motion and Souther Bandom effects model Heanspeerly, r <sup>2</sup> + 05, s <sup>2</sup> + Random effects model Bandom effects model Bandom effects model Bandom effects model Bandom effects model Bandom effects model Bandom effects model Heanspeerly respective Random effects model Random effects model	$\begin{array}{c} \mathbf{Events} & \mathbf{To}\\ \mathbf{Events} & \mathbf{To}\\ 22\\ 72\\ 33\\ 1\\ $	al 22 24 24 24 25 25 26 26 26 26 26 26 26 26 26 26		on         95%-CI           00         (3.64, 1.000)           00         (3.64, 1.000)           01         (3.64, 1.000)           01         (3.64, 1.000)           02         (3.64, 1.000)           03         (1.642, 0.653)           03         (1.642, 0.653)           04         (1.642, 0.653)           05         (1.642, 0.653)           10         (1.642, 0.653)           110         (1.642, 0.653)           110         (1.642, 0.653)           110         (1.643, 0.653)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.	Bescar Herespeer, if etc. Rescar Herespeer, if etc. Budy Budy Budy Herespeers, if etc. Budy Herespeers, if etc. Herespeers, if etc. Heresp	• 0.0370 (p = 0.04 (vents Total 15 15 16 15 16 15 16 15 16 25 16 23 16 42 16 15 16 25 16 23 16 42 17 42 17 42 17 15 17 1		1.000 0.800 0.970 0.946 1.000 1.000 1.000 0.692 0.745 0.891 0.891 0.891 0.891 0.891 0.891	[0.56 [0.84 [0.74] [0.91] [0.00] [0.38 [0.59 [0.70] [0.69] [0.63] [0.83 [0.84 [0.84 [0.84 [0.84] [0.64]
Heinspecker, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Study g <sup>2</sup> + Motion Nandakumz 2015 Lyon 2019 Random effects mode Interpreter and the state of the state Interpreter and the state Interpreter an	$\begin{array}{c} {\rm Events} \ {\rm To}\\ {\rm Events} \ {\rm To}\\ 22\\ 73\\ 33\\ 1\\ 0, p + 0, 40\\ 11\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1$			on         59%-CI           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           00         [3.64, 1.000]           01         [3.64, 0.000]           02         [3.64, 0.000]           06         [1.64, 0.000]           06         [1.64, 0.000]           07         [1.55, 0.000]           19         [1.64, 0.000]           22         [1.36, 0.000]           23         [1.64, 0.000]           24         [1.66, 0.000]           19         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]           27         [1.66, 0.000]	D Staty Basedonetty, 7 + 55, 7 Basedonetty, 7 + Basedonetty, 7 + Basedonetty, 7 + Basedonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Randonetty, 7 + 55, 7 Charge 2020 Randonetty, 7 + 55, 7 Randonetty, 7 + 55, 7	• 0.0370 (p = 0.04 (vents Total 15 15 16 15 16 15 16 15 16 25 16 23 16 42 16 15 16 25 16 23 16 42 17 42 17 42 17 15 17 1		1.000 0.800 0.970 0.946 1.000 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891 0.891 0.891 0.846 0.846 0.945 0.945	[0.56 [0.84 [0.74] [0.91] [0.00] [0.38 [0.59 [0.70] [0.69] [0.63] [0.83 [0.84 [0.84 [0.84 [0.84] [0.64]
Henregenety, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Readed Henregenety, P <sup>2</sup> + 05, q <sup>2</sup> + 2 Study g <sup>2</sup> - Motion Nandahamar 2015 Lyon 2019 Random effects mode Henregenety, P <sup>2</sup> + 05, q <sup>2</sup> + g <sup>2</sup> - Motion and South Charge 2020 Random effects mode Henregenety, P4 support g <sup>2</sup> - Motion and South Random effects mode Henregenety, P4 support Random effects mode Henregenety, P4 support Nakaro 2014 Random effects mode Henregenety, P4 support Random effects mode Nakaro 2014 Random effects mode Henregenety, P4 support Random effects mode Henregenety, P4 support Random effects mode	$\begin{array}{c} {\rm Events} & {\rm TO}\\ {\rm Events} & {\rm TO}\\ 22\\ 73\\ 33\\ 1\\ 0, p + 0, 40\\ {\rm ster}\\ {\rm th}\\ {\rm th}$			on         35%-CI           600         (0.844: 10.001)           600         (0.844: 10.001)           610         (0.844: 10.001)           610         (0.842: 0.932)           77         (0.351: 0.632)           640         (0.442: 0.9431)           100         (0.555: 0.6497)           100         (0.555: 0.6497)           101         (0.845: 0.9531)           119         (0.845: 0.9531)           127         (0.345: 0.9543)           101         (0.845: 0.9543)           101         (0.845: 0.9543)           101         (0.845: 0.9543)           101         (0.845: 0.9543)           101         (0.845: 0.9543)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)           101         (0.845: 0.9542)	Bescart Herespeer, if etc. Bescart Herespeer, if etc. Brand Market State Brand Herespeer, if etc. Brand Herespeer, if	+0.373 (p + 0.04 (vents Total 15 15 45 15 15 5 15 20 16 20		1.000 0.800 0.970 0.946 1.000 1.000 0.692 0.745 0.815 0.811 0.891 0.891 0.891 0.891 0.891 0.891 0.891 0.895 0.775 0.876	[0.56 [0.84 [0.74] [0.91] [0.00] [0.38 [0.59 [0.70 [0.69] [0.83] [0.83] [0.83] [0.83] [0.83] [0.84] [0.84] [0.84] [0.84]
Henregenety, P <sup>2</sup> + 05, q <sup>2</sup> + 1 Rescalarestrether, P <sup>2</sup> + 05 Study Q <sup>2</sup> - Motion Nandakume 2015 Lyon 2019 Random, effects model Henregenety, P <sup>2</sup> + 05, q <sup>2</sup> Random, effects model Henregenety, Pit subject Random, effects model Henregenety, Pit subject Random, effects model Henregenety, Pit + 15, q <sup>2</sup> Q <sup>2</sup> - Motion and south Random, effects model Henregenety, Pit + 15, q <sup>2</sup> Q <sup>2</sup> - Motion and south Random, effects model Henregenety, Pit + 15, q <sup>2</sup> Q <sup>2</sup> - Souther Panlero 2020 Random, effects model Henregenety, Pit + 15, q <sup>2</sup> Random, effects model	200			on         95%-CI           00         (3.64, 1.000)           00         (3.64, 1.000)           01         (3.64, 1.000)           01         (3.64, 1.000)           02         (3.64, 1.000)           03         (1.642, 0.653)           03         (1.642, 0.653)           04         (1.642, 0.653)           05         (1.642, 0.653)           10         (1.642, 0.653)           110         (1.642, 0.653)           110         (1.642, 0.653)           110         (1.643, 0.653)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           110         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.643)           111         (1.643, 0.	Bescar Herespeer, if etc. Rescar Herespeer, if etc. Budy Budy Budy Herespeers, if etc. Budy Herespeers, if etc. Herespeers, if etc. Heresp	+ 0.2372, (p + 0.04 <b>i</b> + 0.2372, (p + 0.04) <b>i i</b> + 0.051 <b>i</b> +		1.000 0.800 0.970 0.946 1.000 1.000 1.000 0.692 0.745 0.815 0.776 0.891 0.891 0.891 0.891 0.846 0.846 0.945 0.945	[0.56: [0.84] [0.74] [0.911 [0.001 [0.59] [0

**Fig 4.** Forest plots of the sensitivities (A), specificities (B), negative predictive values (C), and positive predictive values (D) of the included studies.

https://doi.org/10.1371/journal.pone.0268585.g004

Smartphones may usefully screen for OSAS among individuals who may be unaware of a problem, such as singles with no consistent bed partners. It is thus easy to screen patients with high risks of cardiovascular and cerebrovascular diseases because of hypoxia during sleep [8]. In addition, smartphones could be useful to follow-up patients wearing oral devices or who have undergone upper airway surgery. According to the recent development of devices and algorithms, the Respiratory Event Index (REI), which performs automatic scoring by coupling

Study	Total	Mean Difference	MD	95%-CI	Weight (fixed)	Weight (random)
Nakano 2014	50	·	-6.10	[-8.79: -3.41]	7.2%	23.1%
Lvon 2019	94	4=		[-0.54; 2.34]	24.8%	26.2%
Lyon 2019	68		-1.10	[-3.65; 1.45]	8.0%	23.5%
Pinheiro 2020	304			[ 1.83; 3.69]	60.1%	27.1%
Fixed effect model	516	-\$	1.36	[0.64; 2.08]	100.0%	
Random effects mod	el		-0.68	[-3.84; 2.47]		100.0%
Heterogeneity: $I^2 = 93\%$ ,	$\tau^2 = 9.3507, p <$	0.01				
- , , ,		-5 0 5				

Fig 5. Overall pooled random-effects mean difference of apnea hypopnea index between smartphone and polysomnography across studies.

https://doi.org/10.1371/journal.pone.0268585.g005

Subgroup	Study (n)	DOR [95% CIs]; I <sup>2</sup>	Sensitivity [95% CIs]; I <sup>2</sup>	Specificity [95% CIs]; I <sup>2</sup>	NPV; I <sup>2</sup>	PPV; I <sup>2</sup>
methods of screening the moderate to severe OSAS	11	57.3873 [34.7462; 94.7815]; 24.3%	0.9064 [0.8789; 0.9282]; 0.0%;	0.8801 [0.8227; 0.9207]; 61.7%;	0.9049 [0.8556; 0.9386]; 54.9%	0.8844 [0.8234; 0.9263]; 66.3%
Motion	3	464.4033 [100.4086; 2147.9273]; 0.0%	0.9545 [0.8683; 0.9853]; 0.0%	0.9624 [0.9129; 0.9843]; 0.0%	0.9771 [0.9314; 0.9926]; 0.0%	0.9460 [0.7465; 0.9905]; 52.1%
Motion and oximeter	1	279.2857 [13.4406; 5803.3689]; NA	0.9333 [0.8127; 0.9783]; NA	1.0000 [0.0000; 1.0000]; NA	0.7857 [0.5057; 0.9293]; NA	1.0000 [0.0000; 1.0000]; NA
Motion and sound	3	36.7401 [17.6141; 76.6336]; 0.0%	0.8899 [0.8161; 0.9364]; 0.0%	0.8272 [0.7610; 0.8779]; 0.0%	0.9177 [0.8539; 0.9551]; 10.6%	0.7760 [0.6947; 0.8406]; 0.0%
Oximeter	1	92.6667 [42.6548; 201.3163]; NA	0.9205 [0.8653; 0.9543]; NA	0.8889 [0.8285; 0.9298]; NA	0.9189 [0.8627; 0.9534];NA	0.8910 [0.8317; 0.9312]; NA
Sound	5	35.4208 [17.5999; 71.2864]; 0.0%	0.8793 [0.8220; 0.9200]; 0.0%	0.8149 [0.7157; 0.8851]; 24.8%	0.8190 [0.7382; 0.8789]; 0.0%	0.8759 [0.8023; 0.9247]; 28.7%

#### Table 1. Subgroup analysis according to detection method.

DOR; diagnostic odds ratio, CI; confidence interval, NPV; negative predictive value, PPV; positive predictive value, AUC; area under the curve.

https://doi.org/10.1371/journal.pone.0268585.t001

heart rate variability and oxygen saturation changes using a device such as a smartphone, has a good correlation with AHI and can be used as a useful tool to evaluate the patient's hypoxic burden [31–34]. However, the apps allow only self-problem checking, not counseling. Additionally, clinicians should be aware that smartphones simply reveal good correlations between sleep data and the AHI, but do not integrate all of the important PSG findings. For example, OSAS is a heterogeneous disease that can show multiple phenotypes [35, 36]. When measured through smartphones, patients with disrupted sleep with insomnia might not be measured properly.

On subgroup analysis of the detection methods, all approaches exhibited similar (and good) sensitivities and specificities (80–100%), but methods employing pulse oximetry or motion detection tended to be more diagnostically accurate. A pulse oximeter measures blood oxygen levels non-invasively and continuously [37]. A strong correlation between the AHI and oxygen desaturation was reported in a group of patients with suspected sleep apnea [38]. Moreover, most movement during sleep reflects the respiratory efforts of the torso, which are critical for sleep apnea detection; movement-based apnea estimation is strongly correlated with PSG data, particularly for patients with moderate-to-severe OSA [39]. The use of pulse oximetry or motion detection is optimal.

Another measurement of this meta-analysis assessed the agreement between smartphone and PSG AHI measurements. The mean difference was small (around -0.7) but the limits of agreement was wide (around 6.2). It could mean that smartphone measured AHI seemed significantly close to the true value from PSG but the variability of repeated values due to random error in the smartphone looked considerable. An AHI measured by smartphone may be accurate but imprecise meaning that resultant values are close to the true value but can be inconsistent. Therefore, clinicians need to be cautious when making clinical decision. Also, because the results were based on only four studies, more work is required to support them.

This study had some limitations. First, we analyzed only a limited number of studies, despite extensive searching. To our knowledge, there have been few relevant studies. Therefore, more work is required. Second, high heterogeneity was evident in studies evaluating whether smartphones could screen for moderate-to-severe OSAS, reflecting the use of different detection methods in and OSAS definitions. Also, PSG used as a control group was mostly type I full PSG, but the type was not specified in three studies. It is possible that an unidentified PSG may have influenced the results. These must be standardized in future studies. Based on our results, and despite the limitations, smartphones serve as useful adjuncts when screening for moderate-to-severe OSAS. Smartphones cannot replace PSG. However, smartphones greatly aid in large-scale screening, thus detecting OSAS patients who are prone to misdiagnosis and OSAS patients in regions with poor or inaccessible medical facilities; they can avoid the need for expensive equipment and rooms, as well as specialized personnel.

# Conclusion

Smartphone-based OSAS screening would be useful for patients with moderate-to-severe OSAS. While various OSAS detection methods exhibited similar sensitivity and specificity, using pulse oximetry or motion detection tended to be more accurate diagnostically. Smartphone-based OSAS screening cannot replace PSG, but greatly aids in large-scale screening, thus detecting OSAS patients who are prone to misdiagnosis and OSAS patients in regions with poor or inaccessible medical facilities. However, assessing the agreement between smartphone and PSG AHI measurements, the wide limits of agreement mean clinicians should be cautious when making clinical decisions based on these devices. Further studies are needed, and smartphone detection methods must be strictly standardized.

# **Supporting information**

**S1 Checklist. PRISMA-DTA checklist.** (DOC)

**S1 Table. Search terms and queries.** (DOCX)

**S2** Table. Study characteristics. (DOCX)

**S3 Table. Methodological qualities of all included studies.** (DOCX)

**S1 Fig.** Begg's funnel plot analyses for sensitivity (A), specificity (B), negative predictive value (C), positive predictive value (D), and diagnostic odds ratio (E). (TIF)

**S2 Fig.** Sensitivity analyses for sensitivity (A), specificity (B), negative predictive value (C), positive predictive value (D), and diagnostic odds ratio (E). (TIF)

# **Author Contributions**

Conceptualization: Do Hyun Kim, Se Hwan Hwang.

Data curation: Do Hyun Kim, Sung Won Kim.

Formal analysis: Do Hyun Kim, Sung Won Kim, Se Hwan Hwang.

Investigation: Do Hyun Kim, Sung Won Kim, Se Hwan Hwang.

Methodology: Sung Won Kim.

Project administration: Se Hwan Hwang.

Resources: Do Hyun Kim, Sung Won Kim.

Software: Sung Won Kim.

Supervision: Se Hwan Hwang.

Validation: Do Hyun Kim, Sung Won Kim.

Visualization: Do Hyun Kim, Sung Won Kim.

Writing - original draft: Do Hyun Kim, Se Hwan Hwang.

Writing - review & editing: Do Hyun Kim, Sung Won Kim, Se Hwan Hwang.

#### References

- Strollo PJ Jr., Rogers RM. Obstructive sleep apnea. N Engl J Med. 1996; 334:99–104. https://doi.org/ 10.1056/NEJM199601113340207 PMID: 8531966
- Lee JJ, Sundar KM. Evaluation and Management of Adults with Obstructive Sleep Apnea Syndrome. Lung. 2021; 199:87–101. https://doi.org/10.1007/s00408-021-00426-w PMID: 33713177
- Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017; 34:70– 81. https://doi.org/10.1016/j.smrv.2016.07.002 PMID: 27568340
- Garde A, Dekhordi P, Ansermino JM, Dumont GA. Identifying individual sleep apnea/hypoapnea epochs using smartphone-based pulse oximetry. Annu Int Conf IEEE Eng Med Biol Soc. 2016; 2016:3195–3198. https://doi.org/10.1109/EMBC.2016.7591408 PMID: 28268987
- Lyon G, Tiron R, Zaffaroni A, Osman A, Kilroy H, Lederer K, et al. Detection of Sleep Apnea Using Sonar Smartphone Technology. Annu Int Conf IEEE Eng Med Biol Soc. 2019; 2019:7193–7196. https://doi.org/10.1109/EMBC.2019.8857836 PMID: 31947494
- Nakano H, Hirayama K, Sadamitsu Y, Toshimitsu A, Fujita H, Shin S, et al. Monitoring sound to quantify snoring and sleep apnea severity using a smartphone: proof of concept. J Clin Sleep Med. 2014; 10:73–78. https://doi.org/10.5664/jcsm.3364 PMID: 24426823
- Akhter S, Abeyratne UR, Swarnkar V, Hukins C. Snore Sound Analysis Can Detect the Presence of Obstructive Sleep Apnea Specific to NREM or REM Sleep. J Clin Sleep Med. 2018; 14:991–1003. https://doi.org/10.5664/jcsm.7168 PMID: 29852905
- Chang HC, Wu HT, Huang PC, Ma HP, Lo YL, Huang YH. Portable Sleep Apnea Syndrome Screening and Event Detection Using Long Short-Term Memory Recurrent Neural Network. Sensors (Basel). 2020; 20 https://doi.org/10.3390/s20216067 PMID: 33113849
- Abeyratne U, Swarnkar V, Hukins C, Keenan E, Duce B. An android smart phone APP for the snore sound based diagnosis of sleep apnea. Sleep and Biological Rhythms. 2013; 11:21. <u>https://doi.org/10.1111/sbr.12028</u>
- Bonnesen MP, Sorensen HBD, Jennum P. Mobile Apnea Screening System for at-home Recording and Analysis of Sleep Apnea Severity. Annu Int Conf IEEE Eng Med Biol Soc. 2018; 2018:457–460. https://doi.org/10.1109/EMBC.2018.8512335 PMID: 30440433
- Nandakumar R, Gollakota S, Watson N. Contactless Sleep Apnea Detection on Smartphones. Proceedings of the 13th Annual International Conference on Mobile Systems, Applications, and Services. Florence, Italy: Association for Computing Machinery; 2015. pp. 45–57.
- Narayan S, Shivdare P, Niranjan T, Williams K, Freudman J, Sehra R. Noncontact identification of sleep-disturbed breathing from smartphone-recorded sounds validated by polysomnography. Sleep Breath. 2019; 23:269–279. https://doi.org/10.1007/s11325-018-1695-6 PMID: 30022325
- Pinheiro GDL, Cruz AF, Domingues DM, Genta PR, Drager LF, Strollo PJ, et al. Validation of an Overnight Wireless High-Resolution Oximeter plus Cloud-Based Algorithm for the Diagnosis of Obstructive Sleep Apnea. Clinics (Sao Paulo). 2020; 75:e2414. https://doi.org/10.6061/clinics/2020/e2414 PMID: 33263626
- Swarnkar V, Abeyratne U, Duce B, Hukins C. Smartphones-based diagnosis of sleep apnoea using the nocturnal respiratory sound spectrum from breathing to snoring. Journal of Sleep Research. 2018; 27 https://doi.org/10.1111/jsr.12766
- Tiron R, Lyon G, Kilroy H, Osman A, Kelly N, O'Mahony N, et al. Screening for obstructive sleep apnea with novel hybrid acoustic smartphone app technology. J Thorac Dis. 2020; 12:4476–4495. https://doi. org/10.21037/jtd-20-804 PMID: 32944361
- Fino E, Mazzetti M. Monitoring healthy and disturbed sleep through smartphone applications: a review of experimental evidence. Sleep Breath. 2019; 23:13–24. https://doi.org/10.1007/s11325-018-1661-3 PMID: 29687190

- O'Mahony AM, Garvey JF, McNicholas WT. Technologic advances in the assessment and management of obstructive sleep apnoea beyond the apnoea-hypopnoea index: a narrative review. J Thorac Dis. 2020; 12:5020–5038. https://doi.org/10.21037/jtd-sleep-2020-003 PMID: 33145074
- 18. Duggal C, Pang KP, Rotenberg BW. Can Smartphone Apps Be Used to Screen for Obstructive Sleep Apnea. Laryngoscope. 2021; 131:3–4. https://doi.org/10.1002/lary.28673 PMID: 32297977
- Penzel T, Glos M, Fietze I. New Trends and New Technologies in Sleep Medicine: Expanding Accessibility. Sleep Med Clin. 2021; 16:475–483. https://doi.org/10.1016/j.jsmc.2021.05.010 PMID: 34325824
- Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011; 155:529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009 PMID: 22007046
- Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999; 22:667–689. PMID: 10450601
- 22. Hamada M, lida M. Home monitoring using portable polygraphy for perioperative assessment of pediatric obstructive sleep apnea syndrome. Tokai J Exp Clin Med. 2012; 37:66–70. PMID: 23032246
- Manoni A, Loreti F, Radicioni V, Pellegrino D, Della Torre L, Gumiero A, et al. A New Wearable System for Home Sleep Apnea Testing, Screening, and Classification. Sensors (Basel, Switzerland). 2020; 20:7014. https://doi.org/10.3390/s20247014 PMID: 33302407
- Burgos A, Goñi A, Illarramendi A, Bermúdez J. Real-time detection of apneas on a PDA. IEEE Trans Inf Technol Biomed. 2010; 14:995–1002. https://doi.org/10.1109/TITB.2009.2034975 PMID: 19887328
- Ong AA, Gillespie MB. Overview of smartphone applications for sleep analysis. World J Otorhinolaryngol Head Neck Surg. 2016; 2:45–49. https://doi.org/10.1016/j.wjorl.2016.02.001 PMID: 29204548
- Lee Y, Jung S, Seo Y, Chung W. Measurement of Motion Activity during Ambulatory Using Pulse Oximeter and Triaxial Accelerometer. 2008 Third International Conference on Convergence and Hybrid Information Technology; 2008. pp. 436–441.
- Cao Z, Zhu R, Que RY. A wireless portable system with microsensors for monitoring respiratory diseases. IEEE Trans Biomed Eng. 2012; 59:3110–3116. https://doi.org/10.1109/TBME.2012.2211354 PMID: 22875237
- Solà-Soler J, Fiz JA, Morera J, Jané R. Multiclass classification of subjects with sleep apnoea-hypopnoea syndrome through snoring analysis. Medical engineering & physics. 2012; 34:1213–1220. <u>https://</u> doi.org/10.1016/j.medengphy.2011.12.008 PMID: 22226588
- Behar J, Roebuck A, Shahid M, Daly J, Hallack A, Palmius N, et al. SleepAp: an automated obstructive sleep apnoea screening application for smartphones. IEEE J Biomed Health Inform. 2015; 19:325– 331. https://doi.org/10.1109/JBHI.2014.2307913 PMID: 25561453
- Kendzerska T, Gershon AS, Hawker G, Leung RS, Tomlinson G. Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med. 2014; 11:e1001599. https://doi.org/10.1371/journal.pmed.1001599 PMID: 24503600
- Magnusdottir S, Hilmisson H. Ambulatory screening tool for sleep apnea: analyzing a single-lead electrocardiogram signal (ECG). Sleep Breath. 2018; 22:421–429. <u>https://doi.org/10.1007/s11325-017-1566-6 PMID: 28884264</u>
- Gu W, Leung L, Kwok KC, Wu IC, Folz RJ, Chiang AA. Belun Ring Platform: a novel home sleep apnea testing system for assessment of obstructive sleep apnea. J Clin Sleep Med. 2020; 16:1611–1617. https://doi.org/10.5664/jcsm.8592 PMID: 32464087
- Hilmisson H, Lange N, Duntley SP. Sleep apnea detection: accuracy of using automated ECG analysis compared to manually scored polysomnography (apnea hypopnea index). Sleep and Breathing. 2019; 23:125–133. https://doi.org/10.1007/s11325-018-1672-0 PMID: 29808290
- Huhtakangas JK, Huhtakangas J, Bloigu R, Saaresranta T. Unattended sleep study in screening for sleep apnea in the acute phase of ischemic stroke. Sleep Med. 2020; 65:121–126. https://doi.org/10. 1016/j.sleep.2019.08.002 PMID: 31751906
- Malhotra A, Mesarwi O, Pepin JL, Owens RL. Endotypes and phenotypes in obstructive sleep apnea. Curr Opin Pulm Med. 2020; 26:609–614. <u>https://doi.org/10.1097/MCP.00000000000724</u> PMID: 32890019
- Zinchuk A, Yaggi HK. Phenotypic Subtypes of OSA: A Challenge and Opportunity for Precision Medicine. Chest. 2020; 157:403–420. https://doi.org/10.1016/j.chest.2019.09.002 PMID: 31539538
- Chung F, Liao P, Elsaid H, Islam S, Shapiro CM, Sun Y. Oxygen desaturation index from nocturnal oximetry: a sensitive and specific tool to detect sleep-disordered breathing in surgical patients. Anesth Analg. 2012; 114:993–1000. https://doi.org/10.1213/ANE.0b013e318248f4f5 PMID: 22366847

- Temirbekov D, Güneş S, Yazıcı ZM, Sayın İ. The Ignored Parameter in the Diagnosis of Obstructive Sleep Apnea Syndrome: The Oxygen Desaturation Index. Turkish archives of otorhinolaryngology. 2018; 56:1–6. https://doi.org/10.5152/tao.2018.3025 PMID: 29988275
- Zaffaroni A, Kent B, O'Hare E, Heneghan C, Boyle P, O'Connell G, et al. Assessment of sleep-disordered breathing using a non-contact bio-motion sensor. J Sleep Res. 2013; 22:231–236. https://doi. org/10.1111/j.1365-2869.2012.01056.x PMID: 23176607