Review Article for Sleep Section

Technologic advances in the assessment and management of obstructive sleep apnoea beyond the apnoea-hypopnoea index: a narrative review

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Abstract: Obstructive sleep apnoea (OSA) is a growing and serious worldwide health problem with significant health and socioeconomic consequences. Current diagnostic testing strategies are limited by cost, access to resources and over reliance on one measure, namely the apnoea-hypopnoea frequency per hour (AHI). Recent evidence supports moving away from the AHI as the principle measure of OSA severity towards a more personalised approach to OSA diagnosis and treatment that includes phenotypic and biological traits. Novel advances in technology include the use of signals such as heart rate variability (HRV), oximetry and peripheral arterial tonometry (PAT) as alternative or additional measures. Ubiquitous use of smartphones and developments in wearable technology have also led to increased availability of applications and devices to facilitate home screening of at-risk populations, although current evidence indicates relatively poor accuracy in comparison with the traditional gold standard polysomnography (PSG). In this review, we evaluate the current strategies for diagnosing OSA in the context of their limitations, potential physiological targets as alternatives to AHI and the role of novel technology in OSA. We also evaluate the current evidence for using newer technologies in OSA diagnosis, the physiological targets such as smartphone applications and wearable technology. Future developments in OSA diagnosis and assessment will likely focus increasingly on systemic effects of sleep disordered breathing (SDB) such as changes in nocturnal oxygen and blood pressure (BP); and may also include other factors such as circulating biomarkers. These developments will likely require a re-evaluation of the diagnostic and grading criteria for clinically significant OSA.

Keywords: Obstructive sleep apnoea (OSA); diagnosis; screening; wearable technology; smartphones; beyond the apnoea-hypopnoea index (beyond the AHI)

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Introduction

Obstructive sleep apnoea (OSA) is a serious and worldwide health problem that affects at least 10% of the general population (1,2), although a large percentage of patients with moderate to severe disease remain undiagnosed (3,4). OSA is highly prevalent in adults (14% in men, 5% in females), especially mild-moderate severity and is becoming more prevalent due in part to the increasing prevalence of obesity in the developed world (5,6). The global prevalence is thought to be 1 billion, with general population prevalence estimates exceeding 50% in some countries (7). This represents a challenge for diagnosis, as the current gold standard diagnostic test is overnight polysomnography (PSG) in a sleep laboratory, which is labour intensive and expensive (8).

OSA is characterised by recurrent upper airway

obstruction (UAO) during sleep triggering episodes of apnoea and hypopnoea that leads to sleep fragmentation, non-restorative sleep and excessive daytime somnolence (EDS) (9). The cessation in airflow causes intermittent hypoxia (IH) (10) which is thought to be a major pathogenic mechanism for the adverse complications associated with OSA (11) including cardiovascular complications and increased mortality (12,13). Increasingly, it is recognised that various phenotypic traits are important contributors to OSA for most patients, which include a low respiratory arousal threshold, loop gain, and anatomical factors that narrow the upper airway (14). Clinical symptoms, the presence of certain biomarkers and co-morbidities are also significant variables (15).

OSA contributes to a significant health burden in society due to the strong association with cardiovascular disease [hypertension (HTN), coronary artery disease, congestive cardiac failure], stroke, metabolic syndrome and type 2 diabetes mellitus (12,16). OSA, independent of age, sex and obesity is also associated with reduced quality of life secondary to EDS (17), motor vehicle accidents (18), depression and cognitive decline (19).

Currently, disease severity is measured using the apnoea-hypopnoea index (AHI) as determined from a sleep study. However, recent evidence suggests a poor association between daytime symptoms (e.g., EDS) and the severity of OSA recorded in a sleep study (20), and there is a growing call to move away from the AHI as the principle measure of OSA severity towards a more personalised approach to OSA diagnosis and treatment (15). The global individual and socioeconomic burden of OSA, evidence for poor correlation of daytime symptoms with AHI, and limitations of AHI in terms of disease severity has led to emerging trends for the practice of personalized medicine within OSA and the development of simpler, more convenient objective methods of diagnosis. Recent reviews (15,21,22) highlight the need to move away from sole use of AHI as indicator and predictor of adverse outcome in OSA and instead consider individual risk factors, clinical history and co-morbid disease in the diagnosis and treatment of OSA. Other signals such as heart rate variability (HRV), pulse transit time (PTT), oximetry and the use of biomotion sensors may allow for an improved and phenotypic diagnosis. Home sleep apnoea testing (HSAT) and wearable technologies may help improve access to diagnosis and treatment adherence. Finally, technological advances in telemedicine may strengthen inter-departmental collaboration to improve overall care of OSA patients.

In this paper, we review the current diagnostic strategies for OSA in the context of their limitations, the role of emerging technology and potential physiological targets. We review the current evidence for using newer technologies in OSA diagnosis such as smartphone applications and wearable technology.

We present the following article/case in accordance with the Narrative Review Checklist (available at http://dx.doi.org/10.21037/jtd-sleep-2020-003).

Clinical and pathophysiologic phenotypes

OSA patients typically present with EDS, frequent awakenings, bed partner reports of frequent choking/gasping during sleep, and loud snoring (8). Patients often complain of morning headache, dry mouth and nonrestorative sleep, and may have a diagnosis of systolic HTN or co-morbid cardiovascular disease. Evidence from epidemiological studies indicate that not all patients complain of EDS or fatigue and some patients report only minimal symptoms (23). Furthermore, clinical history and symptoms are now recognised as an important phenotypic variable in the individualised approach to the diagnosis and treatment of OSA (24) with different characteristics requiring tailored treatment plans (15,21). Nonetheless, undiagnosed and untreated OSA is a significant burden on the healthcare system, with increased healthcare utilization seen in those with untreated disease (25).

More recently, Randerath *et al.* (15) presented conclusions from an expert review of the challenges in OSA management. The expert consensus was that a revision to the diagnostic criteria for OSA is required to include factors that reflect different clinical and pathophysiological phenotypes, and relevant comorbidities such as non-dipping nocturnal blood pressure (BP), which are not currently part of the diagnostic criteria. PSG will objectively measure AHI but fails to demonstrate an individual's susceptibility for systemic effects of recurrent hypoxia due to OSA or the underlying pathophysiology. For instance, in older adults, airway anatomy/collapsibility plays a relatively greater pathogenetic role (26). Molecular markers or biomarkers that result from end-organ strain or damage inflicted by factors such as IH represent another variable to consider. These differences have clinical relevance and may influence treatment options (14). Going forward, management should be linked to the underlying clinical and pathophysiological phenotype and assess additional factors to the AHI such as acute systemic effects and associated relevant comorbidity (*Figure 1*).

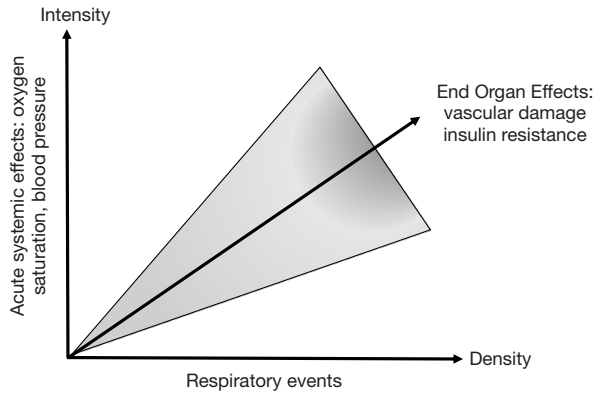

Figure 1 Graphic representation of a three-dimensional model of OSA disease severity. The X-axis represents respiratory events such as apnoeas and hypopnoeas; the Y-axis represents the acute systemic effects of sleep-disordered breathing such as oxygen desaturation and increased blood pressure. The intermediate axis represents end-organ effects such as vascular and metabolic, predisposing to comorbidities such as hypertension and diabetes. The grey triangular zone is intended to convey the variability in susceptibility to comorbidity. OSA, obstructive sleep apnoea.

Diagnostic strategies in OSA

Traditional measures

Current guidelines describe optimum methods for testing of patients suspected of OSA (8). Patients presenting with symptoms of EDS and clinical features as highlighted above should be suspected as having OSA, particularly in the setting of risk factors such as advanced age, male gender and obesity (5,8). PSG in conjunction with a sleep-focused clinical review is the gold standard for the diagnosis of OSA and represents the reference method for the quantitative study of sleep (8). PSG is labour intensive, involving the continuous recording of electroencephalography, electrooculography, electromyography, and electrocardiography (ECG) to determine sleep stages, arousals, movement and sleep related cardiac arrhythmia, respectively. A nasal pressure sensor and a thermistor detect airflow and respiratory inductive plethysmography detect thoracic movements. Pulse oximetry is also utilised to monitor oxygen saturations and heart rate (HR). PSG is typically performed in a sleep laboratory setting with a technician in attendance. The increasing prevalence of OSA (5,27), cumbersome set up, and concern that PSG testing is not cost effective (28) has led to the emergence of alternative types of testing including portable HSAT in recent years.

HSAT

HSAT can be performed in the patient's home, is cheaper and convenient. HSAT will record between four and seven variables that include respiratory effort, airflow, HR or ECG, arterial oxygen saturation, snoring, body position and movement. Newer devices have improved diagnostic accuracy and many devices have now been validated against PSG (29), thus providing a more convenient and cost-effective diagnostic option. Also, HSAT can record several nights of sleep, which is advantageous as night-to-night variability is a feature of OSA and tends to be most relevant in patients with mild disease (30,31).

Despite the convenience of HSAT, these devices typically underestimate the AHI, increasing the likelihood of a false negative result due to the inability of HSAT to record total sleep time (TST) and detect arousals (32,33). Fewer physiological variables are measured which can lead to misinterpretation of results and may miss coexisting sleep disorders such as insomnia, periodic limb movements and parasomnias. The American Academy of Sleep Medicine (AASM) recommends the use of HSAT for OSA diagnosis in selected populations, but advises against its use as a population screening tool (34).

However, current OSA severity thresholds based on AHI level also need to be revised, especially since recent general population studies suggest that up to 50% of the general population have significant OSA based on AHI (23). Furthermore, the disparity between AHI and symptom level evokes concerns regarding the sole assessment of OSA by PSG. Thus, a move toward multi-modality testing using novel technologies that encompass clinical, phenotypical and objective measurements is needed, employing additional markers of disease severity than the AHI.

Technological developments in sleep assessment

Emerging innovative technology allows more in-depth information to be gathered from more sophisticated algorithms and systems. Traditional PSG remains the "gold standard", but new technologies such as novel sensors, WiFI, remote monitoring and wearable devices provide exciting potential alternatives to PSG (*Figure 2*). Integration of these technologies has the potential to improve patient care and allow more readable accessibility of diagnostic tests to allow quicker diagnosis and ultimately treatment of patients with OSA.

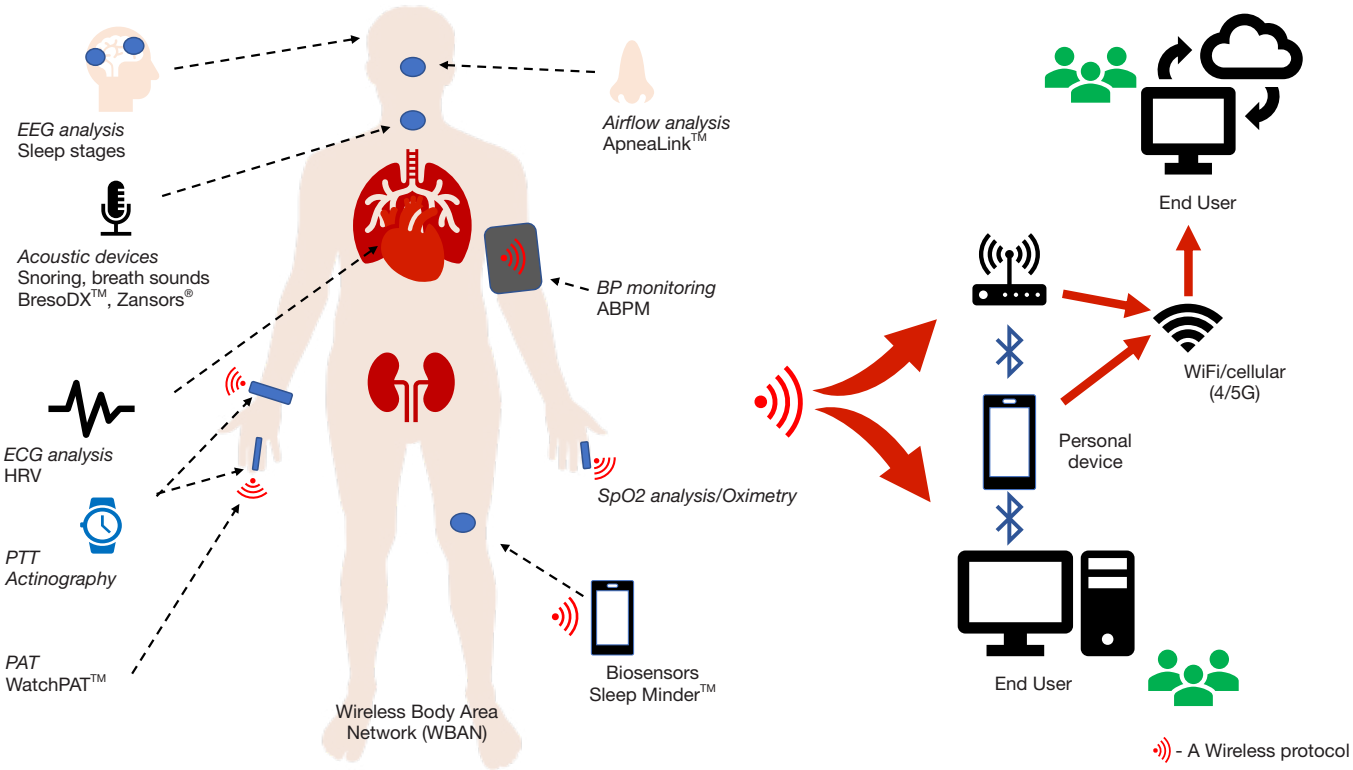

Figure 2 Potential physiological signals for the diagnosis and monitoring of OSA. Signals can be fed wirelessly, for example, using Bluetooth to a router or Smartphone and then uploaded to a secured database, whereby end users (i.e., physician) may access and review the data. OSA, obstructive sleep apnoea; EEG, electroencephalogram; ECG, electrocardiogram; HRV, heart rate variability; PTT, pulse transit time; PAT, peripheral arterial tone; BP, blood pressure; ABPM, ambulatory blood pressure monitor

Novel approaches to evaluating oxygen saturation metrics

Overnight oximetry (ONO), typically using a pulse oximeter has long being proposed as an accessible, uncomplicated and reasonably reliable technique for OSA diagnosis, especially in severe cases (35,36). In OSA, recording of the arterial oxygen saturation (SpO_2) requires a high sampling rate (>0.5 Hz) for an overnight period to ensure adequate detection of intermittent oxygen desaturations. In clinical practice, several relevant data can be obtained from the recordings, including the oxygen desaturation index (ODI) [number of desaturations per hour which drop 3% (ODI3) or 4% (ODI4) below baseline], the cumulative time with a saturation below a predetermined level, usually 90% (T90), and signal variability, which may be referred to as the delta index (8,37). In OSA, the common "saw tooth" pattern of transient oxygen desaturation is seen, especially in severe cases, which gives an instant visual picture of the disease that is unique to OSA. Simple indices fail to capture all of the important and potentially diagnostic pathophysiological characteristics (36) and novel strategies for analysis of oximetry have concentrated on the use of automation (38-40) to maximise the diagnostic potential of these data.

Application of computer-assisted quantification of the time, number and severity of desaturations aids detection of OSA (39,41). Automation of desaturation events facilitates a better description of events, to include desaturations of >4%, >5% and more, with desaturation duration and depth also calculable (42). Time series variables such as mean SpO_2, variance of SpO_2, minimum SpO_2 and cumulative time with a saturation below a predetermined level can be measured and plotted graphically (43).

Automated signal processing plays an important role in optimizing the use of ONO in the context of OSA diagnosis. Several studies have focused on automated signal processing which look at the time/frequency dynamics of ONO (44), morphological features (45), and analysis

of repetitive apnoeic/hypopnoeic events (39,42). Non-linear analysis, which quantifies information related to the temporal order of values in the oximetry signal, has also been utilized (39,42) in characterizing the changes in ONO. Several devices that encompass these technologies have been developed and most include a sensor that sends data to be examined by Bluetooth to a mobile phone. OSA detecting algorithms compute this data to diagnose OSA. Other devices use smartphones or personal digital assistant (PDA) as the receiver. Algorithm analysis and statistical analysis of time and frequency allow in depth processing to occur with encouraging potential for home testing (46-48). Wireless approaches are also available (48), which may assist in OSA diagnosis and prioritise cases for more detailed study, and may also have a role in treatment follow-up (49).

Oximetry and AHI

ODIs can be directly used as a substitute for the AHI to estimate the number of respiratory events during the night. However, ODIs (>4%) often underestimate the severity of OSA, which can have significant clinical consequences (12,13) and influences treatment decisions (8). Different approaches have been utilised to combat this limitation, including regression analysis (45,50) and machine learning algorithms (51), with average diagnostic accuracy of 96.7% reported. The diagnostic potential of ONO compared to AHI is emphasised by several reports indicating that ODI is a superior predictor of co-morbidity than AHI in OSA patients regarding co-morbid HTN (52) and diabetes mellitus (53).

Oximetry in patients with co-morbidity

Some work has been conducted on the use of portable ONO to diagnose sleep disordered breathing (SDB) in patients with co-morbidities including stoke (54), heart failure (55), morbid obesity (56,57) and COPD (58). In stroke, OSA is associated with impaired recovery and an increased risk of mortality (59). In stroke patients undergoing rehabilitation, >15 events/hour reached 77% sensitivity and 100% specificity in the prediction of an AHI >15 events/h and the authors concluded that ONO could be used as a diagnostic tool for OSA in stroke patients (54). In the setting of congestive cardiac failure, one study found that ONO achieved high sensitivity (97%) but lacked specificity (32%) making it a useful rule out test, but was not diagnostic for OSA in this population (55). In obesity, ONO performs better, with conventional oximetry alone achieving 100% sensitivity and 93% specificity when used alone at home for the diagnosis of severe OSA in patients with morbid obesity (56). ODI4 was shown to be predictive of mild, moderate and severity OSA in a further study of 475 surgical patients (57).

Both OSA and nocturnal hypoxemia are commonly seen in chronic obstructive pulmonary disease (COPD) patients (58,60) and treatment with CPAP as compared to LTOT alone is associated with higher survival rates in patients with OSA-COPD overlap (61). ONO alone in diagnosing patients with the overlap syndrome is limited by low sensitivity (59%) and specificity (60%) (58). However, oximetry when combined with novel technology was able to identify moderate-severe OSA regardless of the presence of COPD (62).

Future direction

Advances in technology and signal processing have expanded the role of ONO but controversy persists. Oximetry alone demonstrates significant variability in diagnostic accuracy, with reported sensitivity ranging from 31–98% and specificity 41–100% (38). Part of this variability may be accounted by the range in sampling frequency and amplitude resolution seen in currently available devices (39) and also without automation, variability in how physicians interpret oximetry tracing (63). Thus, further research is needed to support the use of oximetry at home as a single diagnostic test for OSA, particularly in those patients with comorbidities.

Cardiac based measures

ECG analysis: monitoring of HRV, ECG and respiration

Monitoring of HRV by overnight ECG has long been recognized as a potential diagnostic tool in patients with SDB (64). Under standard conditions, a single lead ECG is recorded during PSG to measure HR and rhythm. Use of dedicated software allows analysis of HRV (65) which can provide insight into autonomic activity and may even distinguish sleep stages (66). Additional information may be obtained from fluctuations in QRS amplitude relating to rib cage movement during respirations. The combination of ECG-derived respiration and sleep apnoea related HRV has the potential to be a reliable predictor of OSA (67) and has potential for screening in the cardiologist's office prior to referral.

PTT

The PTT is derived from the ECG and the photoplethysmographic arterial pressure wave measured by a finger probe, which

has been shown to reflect inspiratory effort (68). PTT measures the time required for the arterial pulse wave to travel between two points in the arterial tree: from the moment when the pulse leaves the aortic valve (R-wave on ECG) to the time when it reaches the vessels in the finger as identified by pulse oximetry. Pulse wave speed depends on the vessel stiffness, which is influenced by BP levels. PTT fluctuates with changes in arterial wall stiffness and has the potential to identify apnoea and arousals (68).

Peripheral arterial tonometry (PAT) (the pulse wave as a measure)

PAT allows a closer look at the pulse wave and is one of the more robust diagnostic tools available. Amplitude of the wave is modulated by sympathetic tone, and arousals can be estimated by drops in pulse amplitude. Sleep stages may also be estimated by pulse rate analysis (69). The WatchPAT™ device (Itamar Medical, Ltd) uses a proprietary algorithm that combines PAT, oximetry, HR monitoring, and actigraphy to provide an estimate of TST and to calculate a respiratory disturbance index (70). It has been validated in a number of studies (69-71) and the overall agreement between sleep indexes calculated by in-lab PSG and those calculated using PAT devices have a reasonable correlation (r=0.889) (72), making it an attractive and reasonably reliable diagnostic tool for OSA.

BP monitoring as a potential diagnostic tool

OSA is a known independent risk factor for daytime HTN with apnoeic episodes during sleep also recognized to result in acute BP elevation (5,73). Meta-analysis suggests that OSA increases the likelihood of non-dipping blood pressure (NDBP) by approximately 1.5 times (74), suggesting ambulatory BP monitoring may serve as a surrogate marker of OSA, An increased frequency of reverse systolic dippers (73.5%), which is also independently associated with OSA is also seen (75). A recent report from this department has indicated a high predictive value for moderate to severe OSA in unselected patients recruited from a HTN clinic who demonstrated a non-dipping pattern of nocturnal BP (76).

However, standard ambulatory BP measurement with a pneumatic cuff may cause arousals during sleep and cannot track the rapid BP changes that are observed in OSA (77,78). Continuous BP measurement can be conducted by finger photoplethysmography, whereby a miniature cuff fits on the finger and provides a continuous signal. This provides beat-by-neat pressure curves, allowing assessment of BP variability which can be increased in OSA (79). A novel smart-watch, CareUp™ (Farasha Labs, Paris, France) has been developed for estimating BP in real time (80). This watch has been validated in 44 subjects, representing a promising tool for home monitoring of BP and may serve as a screening tool to identify patients with OSA, whilst also identifying and monitoring BP variability which could help improve the management of OSA and reduce cardiovascular risk in these patients (77). Cardiac-based signals potentially useful in the diagnosis and monitoring of OSA are summarised in *Table 1*.

Biomarkers in OSA and associated comorbidities

Markers of inflammation or oxidative stress, metabolic markers, novel exhaled breath analysis have potential as novel biomarkers in OSA. Chronic hypoxic stress may increase circulating levels of biochemical mediators of inflammation such as C-reactive protein (CRP), tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8) which could have potential as markers of disease severity and likelihood of associated comorbidity (81,82). However, no studies have identified an ideal biomarker. Furthermore, certain co-morbidities such as non-dipping nocturnal BP have potential as a biomarker in OSA (76).

Exhaled breath analysis is an innovative and non-invasive approach that allows collection of a wide range of substances that provide information on pathophysiological and metabolic processes in a wide range of disorders. In sleep disorders, exhaled breath analysis has allowed insight in to the metabolomics of OSA and its consequences. Most studies focus on markers of inflammation and oxidative stress (IL-6, TNF-α) which can correlate with measures of OSA severity. Further research into this area may facilitate earlier diagnosis and assist therapeutic monitoring (83).

Acoustic and airflow devices

Acoustic devices

Despite snoring being a common finding in OSA, on its own, snoring is probably of limited value in the assessment of OSA, due to its weak relationship with AHI (84). However, breath sounds are capable of being recorded and may offer an alternative home measure of AHI. BresoDX™ (BresoTec Inc., Toronto, Ontario, Canada) is a portable device consisting of an open lightweight face frame, embedded electronic module and a microphone. Breath sounds are stored continuously for up to 8 hours and

Table 1 Application of technology to measure cardiovascular signals in the diagnosis of OSA

Parameter	Sensor	Signals	Comments	Applications
ECG	ECG leads attached to chest	HRV	Use of automated software to analysis HRV (64)	Screening prior to referral
		QRS amplitude	Analysis of QRS amplitude relates to rib cage movement and respiration—can be used in conjunction with HRV analysis (66)	
PTT	ECG leads	Pulse wave speed	Measures time needed for arterial pulse wave to travel between two points	Identify SDB
	Pulse oximetry (photoplethysmographic arterial pressure wave)		Shorter times equate to increased sympathetic tone (increase BP). Can identify apnoea's and arousals (67)	Use in wearable technology
PAT	Pulse oximetry	Pulse wave	Measures arterial pulse volume changes in the finger as a result of vasomotion (vasoconstriction and vasodilatation)	Home diagnosis of OSA
	Finger probe	Pulse rate analysis	Automated algorithms to detect apnoea's (68-71)	WatchPAT™ (69)
BP	Finger photoplethysmography	BP variability	BP variability seen in OSA (78)	Screening tool
	BP cuff			Monitoring CareUp™ (78)

ECG, electrocardiogram; HRV, heart rate variability; PTT, pulse transit time; SDB, sleep disordered breathing; PAT, peripheral arterial tonometry; OSA, obstructive sleep apnoea; BP, blood pressure.

can be transferred to a central server for acoustic analysis (85,86). In this context, an intermittent pattern of snoring is likely to be the most useful predictive pattern for OSA. AHI determination using BresoDX™ in one study of 135 subjects showed good correlation to PSG with a diagnostic accuracy ranging between 88.9% and 93.3% at AHI cut-offs of 5–15 (87).

More recently *Z*ansors® has developed a small, wireless wearable patch that measures sleep breathing patterns using an inbuilt microphone and an accelerometer to record movement. In a pilot study the device demonstrated 75% sensitivity and 71% specificity for detecting sleep apnoea events compared to gold standard PSG. Further results are awaited, but highlights the potential for an acoustic sensor to have improved diagnostic performance when used with other signals (88).

Airflow devices

Home single-channel nasal pressure (HNP) devices such as ApneaLink™ (Resmed, Sydney, Australia) (89) have been proposed as a cheaper alternative to PSG for OSA diagnosis. ApneaLink™ is a portable, battery powered, single-channel nasal pressure device that measures airflow through a nasal cannula. Sophisticated algorithms calculate the AHI (90). When compared to PSG, home ApneaLink™ recordings have a 73.1% sensitivity and 91% specificity for detecting an AHI >15 in at risk populations (89), with similar results reported in other studies (90,91). These results suggest a promising role for devices that measure one or two signals only, with appropriate pre-selection of patients, but further study is needed to fully validate their role.

Actigraphy

Immobility is a predictable and distinctive feature of sleep compared to wakefulness. Actigraphy involves the collection of data representing body movement (often an accelerometer built into a wristwatch) over time. Actigraphs can display daily sleep-wake cycles, which may be useful in the diagnosis and evaluation of several clinical sleep disorders. In 1995, the AASM concluded that actigraphy was useful as a research tool in sleep (92) and since, advancements in technology have allowed for cheaper and smaller devices that can unobtrusively measure sleep in large-scale, real life settings (see section "Use of technology to improve adherence in OSA"). In 2007, actigraphy was accepted by the American Academy of Sleep Medicine (AASM) as an alternative to PSG to allow prolonged monitoring of sleep (93).

Previous reviews (94-96) have noted that actigraphy can provide useful information about sleep in the natural sleep environment, measures of basic sleep indices and/or

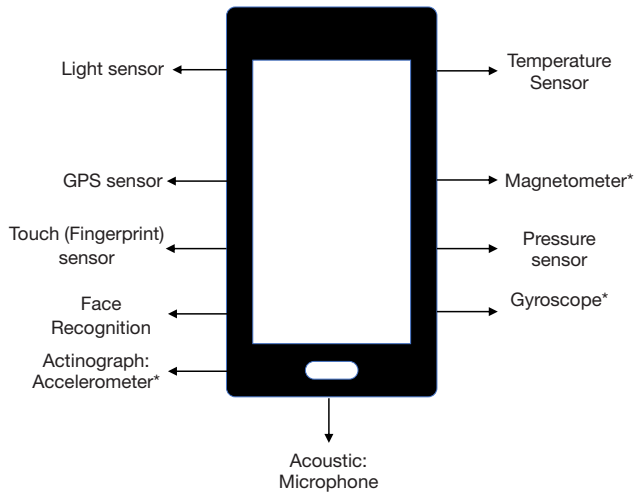

Figure 3 Signals potentially available with smartphone technology that may be relevant to evaluating sleep disordered breathing.

inform when extended monitoring is clinically indicated. However, actigraphy is not able to accurately detect sleep stage and has low specificity (97). When compared to PSG, actigraphy tends to overestimate TST and underestimate wake time (98). Actigraphy is limited by an indirect signal, namely motion, and estimations of sleep patterns are only inferential. However, with technological improvements, the role of actigraphy is likely to evolve as a screening tool and become part of more complex systems to evaluate OSA.

Wireless systems: biosensors in OSA

Sleep can be monitored wirelessly. The first device was constructed in Finland in the 1980s using pressure sensitive foils in the bed of the sleeping patient, which recorded sleep, HR and respiration (99). These have evolved substantially with the introduction of digital technology for signal processing and signal acquisition, and by the inclusion of oximetry.

Radio frequency waves, similar to radar technology, can detect very small body movements, as caused by respiration and heartbeat, even through the bed clothes of a sleeping patient, thus allowing the clinician to distinguish sleep and wakefulness, sleep apnoea and normal breathing (100,101). SleepMinder™ (ResMed Sensor Technologies, Dublin, Ireland) is a device that estimates the severity of OSA using a novel method of interpreting the breathing pattern of subjects during sleep (102). The device is non-contact, portable and easy to use. It is based on a multi-channel biomotion sensor and integrated analysis software. The biomotion sensor uses an ultralow power radiofrequency transceiver to measure the biomotion due to breathing and body movement of the subject in bed. Algorithms are used to perform signal analysis, including respiration analysis, sleep quality measurement and sleep apnoea assessment. The device has been shown to correlate well with PSG in the determination of AHI (103) and sleep efficiency (SE) (104) during controlled laboratory settings. More recently, the device was shown to be effective as a screening tool in high risk patients (but demonstrated lower accuracy in mild OSA (105). The device also allowed monitoring over seven nights, which may provide further information on the patient's disorder. Further validation studies are still needed on various populations, but it is a promising and simple home test.

Smartphone technology

PSG, although well studied and the gold standard in diagnosis of OSA, is not a set up that is well suited to ambulatory assessment. In contrast, smartphones are widely available and potentially can track sleep and sleep behaviour in a non-invasive manner. Most smartphones have embedded sensors (*Figure 3*) that can facilitate data acquisition (e.g., accelerometer, microphone), offering novel opportunities to passively monitor patients in their natural environments (106). The majority boast a wide array of computational power which can be fed to a cloud computing database and sophisticated algorithms employed to analyse and score sleep data (107).

The concepts underpinning actigraphy are important as most smartphones rely on sleep assessment methods that involve movement detection, in addition to audio and video recording in some applications. The inbuilt accelerometer act as a modern actigraph to distinguish wake and sleep from the movement detected by the phone's embedded sensors. More novel devices utilise sound recordings (e.g., snoring) to aid detection of SDB. More recently, advances have allowed sensors devices (HR recording, breathing frequency) to be connected to the smartphone device permitting the assessment of more biological signals (106). Given the wide availability, relatively low cost and ease of use, smartphones are considered by many as the best strategy for monitoring sleep outside the traditional PSG set up (108,109), and may have potential as screening tools for SDB (*Table 2*).

Table 2 Advantages and disadvantages of smartphone based technology in OSA

Advantages	Disadvantages
Inbuilt sensors	Not validated
Wireless (reduced risk of connection issues, failures to record and loss of data)	Unable to accurately detect sleep stage
Widely in use	Poor correlation with PSG
Cheap technology (relative to PSG)	Battery life (longer battery life required for continuous monitoring)
New devices: increased computational power allowing use of complex algorithms	Unregulated (at present)
External sensors; oximeters can now be connected wirelessly	Risk of interference from environment (i.e. ambient noise)
Role in compliance/telemedicine	

OSA, obstructive sleep apnoea; PSG, polysomnography.

Applications or "apps" in sleep medicine

Smartphones allow consumers to download third-party applications (apps) through an online mobile store. Mobile apps are the most popular form of consumer technology, running on smart phones or tablets and are common in the area of sleep and sleep hygiene. They can analyse data online and provide real-time feedback to the consumer, functioning through the support of in built sensors (110). The apps monitor sleep tracking, facilitate sleep and dream logging, and may have alarm functions. They allow sleep analysis and are increasing in number (111). Sound recording can also be added to detect snoring (112).

Consumers often use these "apps" to improve or self-monitor sleep. However, robust evidence for their use is lacking (108,113,114) and there is a paucity of clinical validation with traditional sleep technologies (PSG, HSAT, actigraphy) (107,115,116). A review of 51 such "apps" in 2016 (117) found inconsistencies and lack of any scientific publications to back up the accuracy of the apps. Every app reported sleep duration but reporting data on sleep structure (time in light sleep, deep sleep, REM) was unreliable. App's were reliant on inbuilt accelerometers (actigraphy), but each app had its own proprietary algorithm to relate the amount of movement detected to specific sleep stages.

Nonetheless, sleep tracking products remain very popular consumer products and are widely used for sleep tracking (117). One of the top 5 paid apps in 2014 on iTunes was a sleep tracker and alarm clock (106). Data from these apps are currently not regulated for use as medical devices and are used without prescription or clinical guidance. To date, the accuracy of these data when used as healthcare related data remains to be determined (108).

Smartphone vs. PSG

Few studies have compared sleep apps with PSG and most relate to sleep tracking measures. In one study of the sleep app, Sleep Time™ (Azumio, Inc., Palo Alto, CA, USA), no correlation was found with PSG regarding sleep efficiency, light sleep percentage, deep sleep percentage, or sleep latency (SL) (115). Furthermore, the app had poor specificity, similar to previous reports (96,118). Similar poor correlations with PSG are reported for the apps Sleep Cycle™ (Northcube, Goteborg, Sweden) (119), and Motion X 24/7™ (Fullpower technologies, Inc. Santa Cruz, CA, USA) (116), and are not recommended as a diagnostic tool.

A more recent study (120) compared four smartphone apps (Sleep Cycle-Accelerometer™ (Northcube, Goteburg, Sweden), Sleep Cycle-Microphone™ (Northcube, Goteburg, Sweden), Sense™ (Hello, San Francisco, USA), Smart Alarm™ (Plus Sports, USA) with PSG. A combination of sound and movement sensors, either in built or external were used for sleep-wake detection and determining sleep stages. In keeping with previous studies (115,116,119) and a recent systematic review (114), the apps compared poorly to PSG in determining sleep stage and at present are not suitable alternatives to PSG in the diagnosis of SDB. The authors concluded that further validation studies involving accelerometer-based apps are needed.

In contrast, Tal *et al.* (121) evaluated a contact free monitoring system, EarlySense™ (Ltd., Israel) which consists of an under the mattress piezoelectric sensor and a smartphone app, to identify sleep stages in 43 adults compared to in-laboratory PSG. An overall sleep accuracy of 88.5% was found. EarlySense™ also detected snoring and integrated data from multiple signals including HR,

Table 3 Examples of smartphone application based technology in the diagnosis of OSA

Application (reference)	Study aim	Additional sensor(s)	Outcome
Accelerometer based- use principles of actinography to detect movement			
Sleep Time™ (114)	Evaluate the validity of sleep parameters reported by app compared to standard PSG (n=20, adults)	–	No correlation between app and PSG; SE, SL, light sleep percentage, deep sleep percentage
Sleep Cycle™ (118)	Accuracy of an application in recording sleep compared to standard PSG (n=23, paediatric)	–	Poor correlation. Unable to detect sleep stage
MotionX 24/7™ (115)	Comparison of app against PSG and actigraphy (Actiwatch2™) in a clinical paediatric sample (n=78)	–	Poor correlation with PSG, did not accurately measure sleep or wake
Sleep Cycle-acclerometer™, Sleep Cycle-microphone™, Sense™, Smart alarm™ (119)	Reliability of four smartphone applications for sleep wake detection through sound and movement sensors either inbuilt or external to the phone, by comparing their performance with PSG (n=21, adults)	Microphone	Poor correlation. Unable to detect sleep stage
Biomotion sensor based-motion sensor			
EarlySense™ (120): piezoelectric sensor under the mattress at level of patient's chest	Accuracy of contact-free system in recording sleep parameters compared to PSG (n=63, adults)	Microphone Accelerometer, HR, RR	Accuracy 88%. Integration of multiple signals needed
Acoustic based-in built microphone			
SnoreMonitorSleep™, Quit Snoring™, Snore Spectrum™ (111)	Ability to record snoring in the real-life environment	–	Poor reproducibility, difficult to distinguish between noises
Oximetry based-external oximeter sensor/PPG feeds wirelessly to Smartphone			
SleepAp™ (122)	Accuracy of diagnosis of OSA compared to clinician (n=121, adults)	Accelerometer Microphone	92.2% accuracy for diagnosis of moderate-severe OSA
SleepCare™ (123)	Accuracy of screening algorithm in detecting OSA	–	Developed Algorithm demonstrated 85.6% accuracy in diagnosis OSA

OSA, obstructive sleep apnoea; PSG, polysomnography; SE, sleep efficiency; SL, Sleep latency; HR, heart rate; RR, respiratory rate.

RR, and motion detection, suggesting that multiple signals are required to accurately distinguish sleep stages.

Thus, clinicians need to be aware of the limitations of actigraphy as outlined previously, and especially its limitations when used within Smartphone Apps. More research into the measurement validity of these apps and development of enhanced and more sophisticated sleep algorithms are needed, which may in the future improve the diagnostic utility and reliability of these applications.

Examples of smartphone apps that may have a role in screening for sleep disorders and SDB are given in *Table 3*.

Snoring and SDB via smartphone apps

Detection of snoring

Recording sounds during sleep allows physicians to potentially screen patients who are unaware of snoring, which is a risk factor for cardiovascular disease and possibly

points to OSA (124). Nakano *et al.* (125) used a smartphone to monitor and quantify snoring and OSA severity using a built-in microphone and analysed information obtained using a signal processing procedure like that developed for tracheal sound monitoring to detect OSA. Snoring time correlated well with PSG findings. The diagnostic sensitivity and specificity for diagnosing OSA (AHI ≥15) was 0.70 and 0.94, respectively, within laboratory settings.

However, Stippig *et al.* (112) looked at the accuracy of three available apps; SnoreMonitorSleepLab™ (Adactive AB, Sweden), Quit Snoring™ (Pointer Software Systems, Ltd. CA, USA) and Snore Spectrum™ (Zurlin Technologies, Melbourne, Australia) to determine whether this technology could be used in a noisy home environment. The apps demonstrated difficulty distinguishing between snoring sounds and other noises in the bedroom or close by, with both environmental and device variability noted. The authors concluded that the audio recordings were good, but ability to analyse and draw conclusions from the data was limited due to poor reproducibility and poor reliability and cannot replace current screening devices.

Snoring and SDB

The addition of oximetry should enable better diagnostic utility of smartphones for the diagnosis of OSA and systems have been designed to fit this purpose (126). However, as shown previously, continuous monitoring of oximetry is required and such systems require increased processing power, longer battery life and more detailed algorithms. Al-Mardini *et al.* (122) combined an external oximetry sensor with an in-built accelerometer to detect movement and a microphone to detect respiratory effort with a smartphone application to detect OSA in adults. Testing on a small group (15) demonstrated 100% sensitivity and 85.7% specificity in classifying OSA when compared to PSG, while severity of disease was accurately diagnosed in 87.5%. The authors designed an OSA detection technique that utilised the built-in sensors in the smartphone. The detection platform extracted and analysed physiological signals (SpO_2, movement, respiratory effort) using the smartphones computational power and in-built algorithms.

SleepAp™ was developed for the purpose of screening and monitoring OSA (123). Internal phone sensors and an external pulse oximeter are used to record audio, body position, activity and oxygen saturation during sleep. The clinically validated STOP-BANG questionnaire was also used (127). Specific algorithms used by the app are based on signal processing and machine learning algorithms developed from a larger database. The app classifies the user as either: Non OSA or OSA (mild, moderate, severe) and performed well compared to clinicians with an accuracy of up to 92.2% for those with moderate-severe OSA. Less robust data exists for those with mild OSA, where the app performs less well. Similarly, Nakano *et al.* (125) showed high correlation between smartphone and PSG in terms of total snore time (r=0.93) and AHI (r=0.94) after developing a specific algorithm using a test population of 10 patients.

Daly *et al.* (128) tested SleepCare™ (Sleepcare Technologies Inc., Canada): which comprised a smartphone app, a pulse oximeter, and an online server. The screening algorithms demonstrated 85.6% accuracy in a test database. Strengthened algorithms and use of more than one sensor led to improved detection of OSA and suggests that in order to produce a robust and reliable app, combining more than one sensor and use of objective and subjective sleep assessment maybe a more reliable screening tool. Further work is still needed to validate these systems in the real-world setting.

Wearable technology

Smart watches, fitness trackers and photoplethysmography

Wearable health monitoring technologies such as smart watches and fitness trackers have recently gained popularity (129). These devices are novel in that they are worn on the wrist and can pick up physiological signals directly without additional sensors being attached. The market is growing. In 2016 it was valued at over $13.2 billion and is forecast to reach $34 billion by the end of 2020. Despite the popularity of these device, only limited data are available on how these devices compare to each other and how valid and reliable they are when compared to traditional diagnostic methods (106,130).

The most common sensor technology employed in wearable devices is motion sensing via accelerometery, similar to actigraphy (95). Along with built-in accelerometers, cardiac monitoring is increasingly being used as an additional sensor, through optical and photoplethysmography methods (130). Light sensors on the device record pulse wave signal, with sophisticated algorithms capable of extracting HR and SpO_2 data making these devices ideal for sleep monitoring. However, to date the data suggests these devices have limited accuracy and reliability.

Wearable devices *vs.* PSG

Seventeen studies have examined the accuracy of consumer-

targeted wrist-worn or arm-band accelerometers that include FitBit™ (Fitbit Inc, CA, USA), Jawbone™ (Jawbone Inc, CA, USA), and Sensewear™ (Bodymedia, USA). An early study comparing Fitbit™ with PSG demonstrated that the device overestimated TST by 63 minutes compared to PSG and by 25 minutes compared to actigraphy (131). The more recently developed Fitbit Flex™ (Fitbit, CA, USA) demonstrated more favourable results with an overestimation of sleep duration by 6.5 minutes in good sleepers and by 32.9 minutes in insomniac patients (132). This better performance in good sleepers is expected, given sleep research consistently shows that wrist accelerometry has a high sensitivity for sleep (~90%; i.e., a true sleep epoch is recorded as sleep), while having much lower specificity for sleep (~50%) (130).

Mantua *et al.* (133) compared four devices [Basis Health Tracker™ (Intel Corp, CA, USA), Misfit Shine™ (Misfit Wearables, CA, USA), Fitbit Flex™ (Fitbit Inc, CA, USA) and Withings Pulse O2™ (Withings, Issy-les-Moulineaux, France)] to Actiwatch Spectrum™ (Philips Respironics, OR, USA) and PSG in 40 patients. Their analysis found that the only parameter that was reliably measured for all devices was time to sleep. Another study compared nine devices for accuracy in a 24-h activity measurement. Error rates ranging from 8–16.92% were reported when compared with EEG based sleep duration (134), indicating none were capable of accurately capturing activity data across the entire day.

Combined use of photoplethysmographic methods (HR, SpO2) may improve diagnostic capabilities and determinants of sleep stage. However, the FitBit Charge 2™ (Fitbit Inc. CA, USA) underestimated sleep stage transition dynamics compared with PSG, although performed better in estimating TST and sleep efficiency (135,136). A recent meta- analysis of 22 reports evaluating FitBit™ compared to PSG confirmed that Fitbit™ models overestimate TST and SE (137). Predictably, newer devices that analyze more physiological signals (HR, body movement) performed better but sleep-staging devices were limited by low specificity (137).

Reliability of HR measurement

All wrist worn activity trackers rely on photoplethysmography and use proprietary HR-derived algorithms. Several recent studies investigated the accuracy of wearable devices for measuring HR. Benedetto *et al.* (138) reported that the Fitbit Charge 2™ (Fitbit Inc, CA, USA) underestimates the HR by up to 30 bpm. Another report (139) evaluated the HR accuracy of Apple Watch 3™ (Apple Inc, CA, USA) and Fitbit Charge 2™ compared with ambulatory ECG and reported acceptable HR accuracy (<±10%). However, both slightly underestimated HR and measurements were influenced by wrist movement and higher HR.

Wearable devices *vs.* actigraphy

The accuracy of three consumer wearable devices [Fitbit Flex™, Jawbone Up24™ (Jawbone, CA, USA), Misfit Shine™] was compared to the well validated actigraphy device, Actiwatch-2™ (Philips Respironics, OR, USA). Users wore all devices on the same wrist for seven consecutive 24-hour periods. Overall, both devices were comparable to actigraphy in establishing TST and wake after sleep onset (WASO). Kanady *et al.* (140) compared a consumer grade wearable sleep monitor (Basis B1™ (Basis Science Inc. CA, USA) in the assessment of sleep patterns in normal adults to PSG and research grade actigraphy. The device performed similarly to actigraphy for estimation of TST, but was not accurate for sleep stages and was not a substitute for PSG.

Role in detection of OSA

Wearable sleep trackers are not reliable in the diagnosis of OSA. The ability of two wrist worn sleep trackers; Withings pulse 02™ and Jawbone Up™ and one actigraph (Bodymedia SenseWear Pro Armband™) to measure sleep architecture and sleep quantity in patients diagnosed with OSA assessed during one polysomnographic recording night in a general sleep laboratory was evaluated in 32 patients (141). Both sleep trackers were unable to accurately measure SE, SL or awakenings, could not estimate deep sleep properly and demonstrated poor intra-class correlation, confirming the limited performance of wearable devices in the evaluation of sleep in OSA patients.

Use of technology to improve adherence in OSA

Despite the technological advancements in CPAP devices, including improvements in comfort (humidifiers, pressure ramp features) and more discreet machines over the last 20–30 years, adherence to therapy has not significantly improved and remains a significant stumbling block in the management of OSA patients (142). This data was provided via a systematic review of clinical trials evaluating adherence, but may not be fully reflective of real world practice and in general adherence rates fluctuate widely (50–80%). Traditional intensive support strategies involve

regular nursing visits and detailed education, which is time consuming, costly, labour intensive and produces variable results (143).

However, CPAP devices already objectively record usage data and now with emergence of cloud-based technologies, a unique way of analysing adherence in patients with OSA, in a real-world setting exists. Cistulli *et al.* (144) evaluated 2.62 million patients, using real world data with an observed 90-day adherence rate of 75%, higher than previously reported (142). Still, we can and should do better and new technology also affords development of patient engagement strategies to improve compliance.

Patients may now engage in their own care. Most CPAP machines can display previous nights' usage, and this can facilitate direct feedback to the patient in real time. Cloud-based platforms, similarly, can be used to update physicians on patient's adherence and allow remote monitoring, facilitating better care and be cost efficient (145). Cloud-based technology can also be developed to provide real time feedback to the patient. Malhotra *et al.* (146) compared CPAP adherence among patients who were provided with active patient engagement (APE) technology versus those who received usual care monitoring (UCM). APE was associated with improved adherence (87.3%) compared with UCM patients (70.4%; P<0.001).

Smartphone applications may also improve patient adherence to CPAP. SleepWell24™ (ASU, Arizona, USA) is a multicomponent evidence-based smartphone app that is designed to deliver biofeedback about CPAP use and sleep patterns by combining cloud-based CPAP data and wearable sensor data. It remains to be seen whether this app will be effective in improving adherence and will be evaluated for efficacy compared to UCM in an upcoming RCT (147).

Conclusions

The growing recognition that AHI represents a poor metric to assess the presence of a clinically significant OSA syndrome, together with the move towards ambulatory monitoring of patients for diagnosis and treatment has resulted in an increasing desire to identify biological variables that identify patients with a clinically significant disorder. It is likely that smartphone and wearable technologies will play a significant role in these developments, but currently available technologies have not yet reached that goal. Other strategies such as biomarkers will also likely play a role, especially in the identification of relevant comorbidity. Combinations of signals that can be non-invasively measured in the ambulatory setting are most likely to succeed in replacing conventional testing such as PSG for most patients.

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