Sleep Apnoea Detection with Smart Internet of Things Technology

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Candidate Declaration

I hereby declare that:

1. I have not been enrolled for another award of the University, or other academic or professional organisation, whilst undertaking my research degree.

2. None of the material contained in the thesis has been used in any other submission for an academic award.

3. I am aware of and understand the University's policy on plagiarism and certify that this thesis is my own work. The use of all published or other sources of material consulted have been properly and fully acknowledged.

4. The work undertaken towards the thesis has been conducted in accordance with the SHU Principles of Integrity in Research and the SHU Research Ethics Policy.

5. The word count of the thesis is 39,970.

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Abstract

Sleep apnoea (SA) is a hazardous condition characterized by interrupted breathing during sleep. This prevalent medical issue affects individuals of all ages, potentially leading to severe complications when untreated including, cardiovascular problems, diabetes, and daytime fatigue etc. Unfortunately, SA often remains undiagnosed due to the costly and inconvenient diagnostic procedures associated with it. It stands as a significant global health concern, impacting nearly one billion people worldwide, with a prevalence of 17 to 23% in women and 34 to 50% in men. SA is recognized as a risk factor for cardiovascular disorders (CVD) and carries substantial individual, societal, and economic burdens. The economic costs of SA diagnosis and treatment services run into billions of dollars annually.

The reference standard for diagnosing SA is polysomnography (PSG), conducted in a laboratory setting by trained professionals. However, this process is time-consuming, susceptible to human error, and demands technical expertise for both execution and interpretation. The inconvenience of in-lab PSG has spurred the need for new, simplified methods. This thesis posits that Computer-Aided Diagnosis (CAD) systems can enhance diagnostic efficacy. To explore this hypothesis, the thesis introduces innovative real-time detection techniques for Obstructive Sleep Apnoea (OSA) and the development of a high-performance OSA detection system. This system, offering continuous OSA detection, addresses the practical challenges associated with traditional diagnostic approaches. The integration of Internet of Things (IoT) and advanced Artificial Intelligence (AI) technologies, with a focus on the Lifetouch sensor, represents a novel approach to improve the accuracy of OSA detection. This innovative strategy aims to overcome barriers to timely and reliable diagnosis and monitoring of sleep disorders.

To thoroughly assess the algorithm, a clinical study enrolled 15 patients with a history of OSA. Simultaneously, standard PSG monitoring and diagnosis were conducted, serving as the benchmark for comparison. This dual approach ensured a robust evaluation of the DL algorithm's performance against established PSG methods, providing a comprehensive understanding of its capabilities in OSA detection. The trial results highlight the potential of the proposed technology model, showing a high level of patient acceptance and satisfaction with Lifetouch wearables. However, the identification of only two OSA cases among the 15 patients studied was lower than anticipated. These findings emphasize the need for improved detection methods, as addressed by the novel techniques introduced in this thesis. The results presented here also highlight the efficacy of the developed methods, showcasing their ability to deliver quick, reliable, and standardized analyses an essential step forward in overcoming the limitations of conventional diagnostic approaches.

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Completing a research project and thesis is a challenging endeavour, and I am grateful for the support and guidance I received. I express sincere gratitude to all those who have helped me during my research journey.

Firstly, I am grateful to Allah for His blessings and guidance throughout this period, enabling me to complete my thesis. The successful completion of this project would not have been achievable without the tremendous assistance of my director of study, Dr Ningrong Lei. I extend my heartfelt appreciation for her unwavering support, expertise, and invaluable insights. I extend my thanks to my co-authors, Dr Oliver Faust, Dr Hajar Razaghi and Professor Alex Shenfield, for their valuable input and collaboration. I am thankful to my close friends Dr Murtadha Kareem for his support and encouragement.

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List of Abbreviations

Abbreviations	Full-Form
1D-CNN	1-D Convolutional Neural Network
AASM	American Academy of Sleep Medicine
Acc	Accuracy
AHI	Apnoea-Hypopnea Index
AI	Artificial Intelligence
ANFIS	Adaptive Neuro-Fuzzy Inference System
ANN	Artificial Neural Network
ASV	Adaptive Servo-Ventilation
AUC	Area Under Curve
BiPAP	Bilevel Positive Airway Pressure
BP	Blood Pressure
BPM	Beats Per Minute
CAD	Computer-Aided Diagnosis
CASADS	Computer Aided Sleep Apnoea Detection System
CNN	Convolutional Neural Network
COPD	Chronic Obstructive Pulmonary Disease
CPAP	Continuous Positive Airway Pressure
CSA	Central Sleep Apnoea
CVD	Cardiovascular Disorders
DL	Deep Learning
DNN	Deep Neural Networks
DT	Decision Tree
ECG	Electrocardiogram
EDR	Electrocardiogram-Derived Respiration

EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
FN	False Negative
FNT	False Negative Rate
FP	False Positive
GCP	Good Clinical Practice
GERD	Gastroesophageal Reflux Disease
GPT	Generative Pretrained Transformer
GPU	Graphics Processing Unit
GRU	Gated Recurrent Unit
HCRW	Health And Care Research Wales
HMM	Hidden Markov Model
HPG	Home Polygraphy
HR	Heart Rate
HRA	Health Research Authority
HRP	Home Respiratory Polygraphy
HRV	Heart Rate Variability
IMF	Intrinsic Mode Functions
IoT	Internet of Things
KNN	K-Nearest Neighborhood
LDA	Linear Discriminant Analysis
LOOCV	Leave-One-Person-Out Cross-Validation
LR	Linear Regression
LR	Logistic Regression
LSTM	Long Short-Term Memory

MGH	Massachusetts General Hospital
ML	Machine Learning
MMA	Maxillomandibular Advancement
MT	Myofunctional Therapy
NHTSA	National Highway Traffic Safety Administration
NN	Neural Networks
NREM	Non-Rapid Eye Movement
OA	Oral Appliances
OSA	Obstructive Sleep Apnoea
PAP	Positive Airway Pressure
PG	Polygraphy
PLMS	Periodic Limb Movements
PPG	Photoplethysmogram
PPIE	Patient and Public Involvement and Engagement
PSE	Patient Status Engine
PSG	Polysomnography
QDA	Quadratic Discriminant Analysis
R&K	Rechtschafen and Kales
REC	Research Ethics Committee
REM	Rapid Eye Movement
RF	Random Forest
RIP	Respiratory Inductance Plethysmography
RLS	Restless Leg Syndrome
RM	Remote Monitoring
RNN	Recurrent Neural Network
RNN	Residual Neural Network

ROC	Receiver Operating Characteristic
SA	Sleep Apnoea
SAS	Sleep Apnoea Syndrome
SHU	Sheffield Hallam University
SOP	Standard Operating Procedures
Spo2	Oxygen Saturation
SVM	Support Vector Machines
SWS	Slow Wave Sleep
TN	Ture Negative
TNR	Ture Negative Rate
TP	Ture Positive
TQWT	Tunable-Q Factor Wavelet Transform
UPPP	Ubulopalatopharyngoplas
WHO	World Health Organization

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Publications and Conference Abstracts During Candidature

During my PhD journey, I collaborated with researchers in my field, publishing several articles and conference abstracts. These publications allowed me to share my research findings, receive feedback from experts, and gain experience in collaborative research. In the following section, I will present a comprehensive list of the accepted publications and conference abstracts from my PhD, highlighting the contributions of my co-authors and myself to the academic community.

Peer-reviewed journal articles

I. **Barika, R**., Elphick, H., Lei, N., Razaghi, H., & Faust, O. (2022). Environmental Benefits of Sleep Apnoea Detection in the Home Environment. *Processes*, 10(9), 1739. This article can be found in Appendix 11.

II. Faust, O., **Barika, R**., Shenfield, A., Ciaccio, E. J., & Acharya, U. R. (2021). Accurate detection of sleep apnea with long short-term memory network based on RR interval signals. *Knowledge-Based Systems*, 212, 106591. This article can be found in Appendix 12.

III. Faust, O., Razaghi, H., **Barika, R**., Ciaccio, E. J., & Acharya, U. R. (2019). A review of automated sleep stage scoring based on physiological signals for the new millennia. *Computer methods and programs in biomedicine*, 176, 81-91. This article can be found in Appendix 13.

Book chapter

IV. **Barika, R**., & Faust, O. (2021). A review of automated sleep stage scoring. This book chapter can be found in Appendix 14.

Conference Articles

V. **Barika, R**., Shenfield, A., Razaghi, H., & Faust, O. (2021). A smart sleep apnea detection service. In 17th International Conference on Condition Monitoring and Asset Management, CM 2021. The British Institute of NDT.

VI. **Ragab Barika**, Heather Elphick, Alex Shenfield, Hajar Razaghi, Oliver Faust (2021): Wireless physiological measurements to simplify real time identification of pediatric SA. Organizer: North East Postgraduate Conference (NEPG), 12 November 2021.

Poster presentations

VII. **Ragab Barika** (2021). Accurate detection of Sleep Apnoea with long short-term memory network based on RR interval signals: Materials Engineering Research Institute, Sheffield Hallam University, Howard Street, Sheffield, S1 1WB, UK.

VIII. **Ragab Barika** (2020). Real Time Sleep Apnoea Detection Service: Materials Engineering Research Institute, Sheffield Hallam University, Howard Street, Sheffield, S1 1WB, UK.

IX. **Ragab Barika** (2019). A smart Sleep Apnoea detection service: Materials Engineering Research Institute, Sheffield Hallam University, Howard Street, Sheffield, S1 1WB, UK.

Chapter 1 Introduction

Chapter 1 provides an overview of the thesis. Section 1.1 introduces an overview of Sleep Apnoea (SA), while Section 1.2 discusses the current diagnostic challenges. role of artificial intelligence (AI) in healthcare is present in section 1.3. The motivation behind our research is presented in Section 1.4. Section 1.5 presents the research problem, followed by an outline of our aims and objectives in Section 1.6. Section 1.7 presents the research questions. The major contributions of this thesis are listed in Section 1.8, and the structure of the thesis is explained in Section 1.9.

1.1 Overview

SA is a serious sleep disorder characterized by recurrent interruptions in breathing during sleep, resulting in inadequate oxygenation of the body and various health problems such as hypertension, cardiovascular disease, stroke, and diabetes (Elmoaqet et al., 2020). SA is the repeated temporary closure of the upper airways during sleep Figure 1.1. SA manifests in obstructive (OSA) or central (CSA) forms. OSA is the predominant type, a life-threatening, underdiagnosed condition, characterized by symptoms such as fatigue, daytime sleepiness, cardiac arrhythmia, and systemic hypertension. SA can also lead to excessive daytime sleepiness, reduced quality of life, and increased risk of accidents and injuries (Dhruba et al., 2021). Cognitive impairment and dementia have also been associated with SA (Michael Pearson and Oliver Faust, 2019), highlighting the need for early detection and treatment to prevent or minimize these health problems.

1.2 Current Diagnostic Challenges

PSG is widely acknowledged as the gold standard method for diagnosing SA[1], typically conducted in a supervised sleep laboratory (Berry et al., 2012). However, recent advancements have introduced alternative contact and non-contact methods for unattended home-based OSA diagnosis. PSG involves a sleep study conducted in a lab, where the patient spends the night connected to over 15 channels that collect sleep data, expensive, and time-consuming, which can be inconvenient and uncomfortable. The waiting times for patients to undergo a PSG can be prolonged and may vary across different healthcare centres. A trained sleep technician manually annotates this data, utilizing various channels for different types of information, such as electroencephalogram (EEG) and Electrooculogram (EOG) for sleep stages, Electromyogram (EMG) for wake periods, arousals, or movements, Electrocardiogram (ECG) for potential emergencies, and airflow, oxygen desaturation, and respiratory effort signals for categorizing apnoea events (Almazaydeh et al., 2012; Imtiaz, 2021). Conducting these studies in home or

[1] https://www.nhs.uk/conditions/narcolepsy/diagnosis/

unattended settings would be a more practical, cost-effective, and time-efficient approach. PSG's main outcome, the Apnea Hypopnea Index (AHI), is a standard measure of OSA severity, calculated by dividing the total apnoea and/or hypopnea events by total sleep time. The AHI quantifies the severity of the OSA condition based on guidelines from the American Academy of Sleep Medicine (AASM) (Syeda Quratulain Ali et al., 2019).

The growing awareness of SA and its consequences has led to an increased demand for PSG studies at sleep laboratories. However, the existing sleep laboratory facilities are insufficient to meet this demand. Moreover, PSG is limited in its applicability for large-scale population screening, particularly in unattended or home-based settings. Consequently, there is a substantial need for a simplified SA screening device that is cost-effective, user-friendly, and reliable. The need for alternative approaches arises from the limitations of PSG, emphasizing the significance of developing machine learning (ML) -based methods. These approaches aim to provide more accessible, cost-effective, and potentially home-based solutions for SA diagnosis, addressing the challenges posed by PSG's resource-intensive nature.

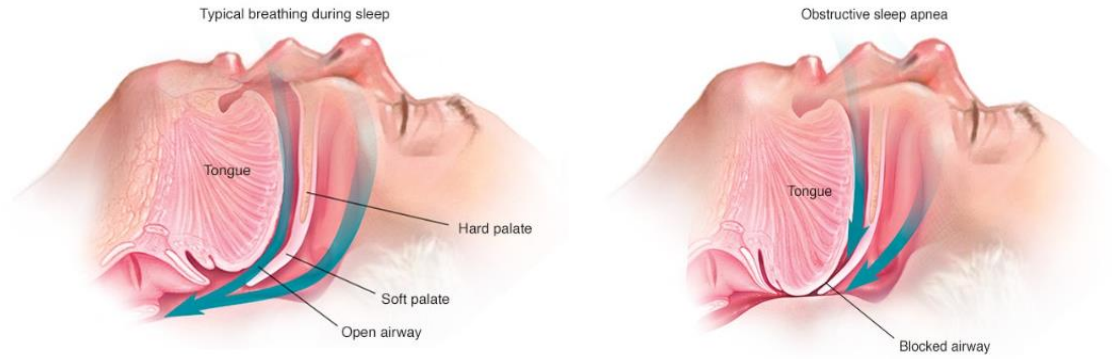

Figure 1.1 Obstructive sleep apnoea occurs when the patient's airway becomes obstructed.[2]

1.3 Role of Artificial Intelligence (AI) in healthcare

The healthcare sector grapples with significant challenges related to various diseases, elevating it to a critical global concern. Research and technological advancements in healthcare aim to enhance life quality through improved diagnostic and treatment methods, with AI standing out as a transformative force in the field. AI's widespread adoption is fuelled by its demonstrated successes, exemplified by innovations like ChatGPT, (Holzinger et al., 2023). In recent times, various AI techniques have been implemented to assist healthcare professionals in diagnosing, monitoring, and treating various human disorders. ChatGPT stands out as a widely used AI-based chatbot that utilizes the GPT (Generative Pretrained Transformer) parser to generate responses resembling human interactions, based on the text input provided by the user (Cheong et al., 2023; Manik Sharma & Sharma, 2023)

[2] https://www.mayoclinic.org/

ChatGPT, an advanced AI system created by OpenAI, holds significant promise in offering valuable assistance within the healthcare domain. Its capability to facilitate virtual consultations with healthcare professionals for health data analysis has the potential to bring about a transformative impact on the healthcare sector. The integration of ChatGPT technology in healthcare has the power to redefine the manner in which patients access care and receive support (Manik Sharma & Sharma, 2023).

The AI introduces unprecedented potential solutions, contributing to essential sustainability development goals. these encompass food security, health and well-being, clean water, clean energy, responsible consumption and production, climate action, life below water, and the sustainable management of terrestrial ecosystems (Holzinger et al., 2023). AI's pervasive influence extends to the life sciences, incorporating ML, big data analytics, knowledge discovery, biomedical ontologies, natural language processing, and decision support tools. AI, with its ability to compute, analyse, reason, learn, and discover meaning, is evolving rapidly, encompassing both 'narrow AI' for focused tasks and 'broad AI' for diverse functions. The broad spectrum of AI applications, including language processing, image recognition, big data analytics, and robotics, holds the potential to revolutionize healthcare by enhancing diagnostics, facilitating new treatments, and extending healthcare accessibility. These technological advancements are not limited to healthcare, as AI applications in various sectors present opportunities to benefit society at large (Federspiel et al., 2023).

1.3.1 Artificial Intelligence's Impact on Healthcare

AI plays a pivotal role in managing critical situations (S. Ali et al., 2023) and offers reliable diagnostic capabilities for a wide range of diseases in healthcare organizations (S. Patil, 2022). It has the potential to enhance healthcare services by assessing disease risks, providing continuous patient care, and reducing complications associated with illnesses (Shaik et al., 2023). The evolution of AI, incorporating narrow and broad AI applications, extends beyond healthcare, presenting opportunities to benefit society at large. However, it's essential to consider the impact of AI on human health and well-being (Dave et al., 2020).

1.3.2 Artificial Intelligence in Healthcare Industry Transformation

AI brings about long-term changes in the healthcare industry, aiding organizations in diagnosing patients and tailoring treatments with high accuracy. In radiology, AI supports physicians in clinical decision-making and, in certain cases, can even replace human judgment. AI's reliance on computers enhances efficiency, predictability, and decision-making in medical systems. The transformative potential of AI in healthcare underscores the ongoing evolution of technological

advancements to improve diagnostics, treatments, and accessibility to healthcare services (Panch et al., 2019; Yousef Shaheen, 2021; Yusriadi et al., 2023).

1.4 Research Motivation

The motivation for this research lies in addressing the escalating global health concern of SA, which poses risks of severe health complications and even death if left undetected. Recognizing the potential of computing and AI technologies, this thesis aims to develop automated classification systems to aid physicians in timely SA diagnosis. This pursuit is driven by the need to alleviate healthcare personnel's workload and tackle the issue of underdiagnosis, particularly due to the limitations and costs associated with PSG. By harnessing AI technologies, the research seeks to offer a cost-effective alternative for SA detection, aligning with efforts to address the underdiagnosis problem highlighted by the World Health Organization. Ultimately, the goal is to enhance individuals' quality of life by enabling accurate, accessible SA diagnoses through innovative AI-driven approaches.

1.5 Problem Statement

The research addresses a critical issue in sleep medicine: the substantial limitations of PSG as the predominant diagnostic tool for SA, coupled with the urgent demand for alternative diagnostic methodologies. Despite its widespread use as the gold standard, PSG's efficacy is marred by exorbitant costs, lengthy examination durations, and patient discomfort, necessitating the exploration of more accessible and patient-centric SA diagnostic approaches. Leveraging the transformative potential of IoT devices and advanced AI technologies, the study endeavours to revolutionize SA diagnosis by delving into sophisticated algorithms and conducting comprehensive large-scale data analyses. Through the development of innovative solutions tailored to address entrenched challenges, this research aims to catalyse a paradigm shift in diagnostic practices within sleep medicine, ultimately fostering improved patient care and outcomes.

1.6 Research Aim and Objectives

In response to the identified shortcomings and gaps in current SA diagnosis methods, the primary aim of this thesis is to harness the revolutionary potential of smart technology for SA detection. The research centres on pioneering IoT-based solutions, comprising cutting-edge sensors, wearable devices, and advanced data analytics methodologies. These technological innovations are designed to surmount the constraints inherent in conventional diagnostic modalities such as PSG and elevate the precision of SA detection, thereby advancing the diagnosis and treatment of this pervasive sleep disorder. By harnessing the transformative capabilities of intelligent IoT technology, the research endeavours to make a substantial

contribution to the field of SA diagnosis, ultimately culminating in superior patient outcomes. To realize this overarching aim, the research delineates the following specific objectives:

- To evaluate IoT-based sensors and wearable devices for accurately capturing relevant physiological data during sleep, with a specific focus on SA indicators.
- To design and implement advanced data analytics techniques that enable the detection and monitoring of SA episodes. Additionally, the research explores the feasibility and effectiveness of remote monitoring solutions using smart IoT technology.
- The study aims to conduct comprehensive validation studies, assessing the performance and effectiveness of the developed IoT-based SA detection system. This includes comparing its performance with traditional diagnostic methods such as PSG and evaluating its potential for real-time monitoring and long-term management of SA.

1.7 Research Questions

In alignment with the identified issues in current SA diagnosis methods and the overarching aim of exploring the potential of smart technology, the research questions in this thesis are strategically crafted to focus on the integration of smart IoT technology in SA detection and monitoring. Specifically, the study seeks to address the question: How can smart IoT technology revolutionize the detection of SA? By delving into this pivotal research question, the thesis aims to uncover the multifaceted ways in which IoT devices and connectivity can revolutionize SA detection and facilitate seamless remote monitoring. The study proposes the deployment of innovative IoT-based sensors and wearable devices capable of precisely capturing pertinent physiological data during sleep. Advanced data analytics techniques will be harnessed to meticulously analyse and interpret the amassed data. The ultimate objective is to explore the feasibility, accuracy, and potential advantages of integrating IoT solutions in SA detection, thereby propelling the field of SA diagnosis forward through the transformative capabilities of smart IoT technology.

1.8 Research Contributions

This research seeks to make significant contributions to the evolution of SA diagnosis by integrating IoT and AI technologies to analyse datasets obtained from patients suspected of having SA. The primary goal is to propose novel, automated approaches for SA diagnosis, leveraging the insights derived from comprehensive data analysis. A major contribution of this work is the integration of IoT and advanced AI technologies, with a specific focus on the Lifetouch sensor, to enhance SA detection. This integration aims to bridge any existing gaps between emerging classification techniques and the current methods for SA detection. By merging cutting-edge technologies, the research aspires to advance the accuracy of SA diagnosis, ultimately contributing to the evolution of diagnostic practices in sleep medicine.

1.9 Summary of Chapters

The thesis comprises six chapters, each focusing on different aspects of the research topic. In addition, two manuscripts have been published as part of the thesis. The content covered in each chapter is summarized as follows:

Chapter 1: This chapter is divided into nine sections that provide background information on SA, discuss the role of AI in healthcare, summarize the research motivation, present the research problem statement, describe the aims and objectives, outline the thesis question, and provide an overview of the thesis structure.

Chapter 2: This chapter presents a comprehensive literature review relevant to the research. It covers various topics related to sleep, including sleep disorders, traditional methods for SA detection, risk factors, financial implications, and consequences of untreated SA. Additionally, it explores AI innovations in SA diagnosis, DL, computer-aided SA detection systems, and automated sleep stage scoring. Moreover, it identifies research gaps to provide readers with a clear understanding of the background and context of the study.

Chapter 3: This chapter focuses on the manuscript titled "Environmental Benefits of Sleep Apnoea Detection in the Home Environment" published in *Processes*. It assesses the environmental consequences of SA detection, particularly the exploration of Remote Monitoring (RM) as a solution to enhance resource efficiency and minimize travel-related impacts.

Chapter 4: This chapter offers an overview of the methodology, drawing insights from the work of Faust et al. (2021) on "Accurate detection of sleep apnea with a long short-term memory network based on RR interval signals". Additionally, it provides insights into the utilization of DL in SA detection. Moreover, the chapter summarizes data collection and preprocessing activities, elucidating the process through which research objectives have evolved over time. The LSTM method discussed in this chapter mirrors the one applied for OSA detection in the clinical study.

Chapter 5: This chapter dives into how experiments were set up to detect OSA using DL methods in real medical settings. The researchers zero in on a specific sensor known as Isansys Lifetouch. Here, the chapter details the planning of the study, collected data, analyzed it, got approvals from regulators, and considered ethical issues. Then, it discusses the results of the study, pointing out important discoveries and insights gained from analyzing the data. It gives a thorough summary of what they found, highlighting any trends or patterns they noticed. After that, the chapter moves on to a critical discussion of the results. It talks about what these findings mean, how they fit into existing research, and suggests ideas for future studies in this area.

Chapter 6: This chapter provides a comprehensive summary of the conclusions derived from the preceding chapters of the thesis. It presents the key findings and insights obtained throughout the research, acknowledges the limitations of the current study, and identifies potential areas for future research and development based on the research outcomes.

Chapter 2 Literature Review

This chapter provides a comprehensive literature survey related to SA. Section 2.2 delves into sleep disorders. Section 2.3 focuses on PSG for SA evaluation, while Section 2.4 describes risk factors associated with SA. Section 2.5 covers the financial costs of SA, while Section 2.6 highlights treatment approaches. Sections 2.7 to 2.11 cover, AI innovations in SA diagnosis, DL, computer-aided SA detection, automated sleep stage scoring, and research gap identifications respectively.

2.1 Introduction

Healthy sleep is essential for individuals of all ages as it comprises approximately one-third of a person's life (Yan et al., 2021). Sufficient sleep has been shown to enhance work productivity and overall mood (Koenker et al., 2013). Conversely, inadequate sleep can contribute to various health issues, including cardiovascular disease, endocrine disorders, memory impairment, and decreased attention span. Systematic reviews and meta-analyses have established a correlation between shortened sleep durations and these health problems. Given that cardiovascular disease is a leading global cause of mortality, the identification and detection of sleep disorders have become crucial public health priorities due to their detrimental effects on mental and cardiovascular well-being (Hongyun Dong et al., 2020).

2.2 Sleep Disorders

Sleep disorders have a significant impact on individuals' well-being, affecting their physical, cognitive, and emotional functioning. Achieving restful sleep becomes a challenge for individuals with sleep disorders (Heima et al., 2019; Michael Pearson and Oliver Faust, 2019). The International Classification of Sleep Disorders (ICSD-3) categorizes sleep disorders into seven groups, including insomnia, sleep-related breathing disorders, and circadian rhythm sleep-wake disorders (Ophoff et al., 2018; Sateia, 2014). The prevalence of sleep disorders varies depending on the type and severity of the condition. Insomnia, for example, affects approximately 30% of adults, with up to 10% experiencing chronic insomnia (Urtnasan et al., 2021). In the United States, an estimated 50 to 70 million individuals have challenging-to-identify sleep disorders, and the adverse effects may not manifest immediately but can have long-lasting consequences (Ademola Bello & Alqasemi, 2021; Princy, 2021; C. Sun et al., 2022). Sleep disorders affect approximately 23% of the U.S. population and 20% of the population in Finland (Loh et al., 2020).

Other sleep disorders, such as restless leg syndrome (RLS) and narcolepsy, also impact a significant portion of the population. RLS, causing uncomfortable leg sensations and an urge to move the legs, affects approximately 5-15% of individuals. Narcolepsy, characterized by sudden

uncontrollable sleep episodes, affects about 1 in 2,000 people. Loh et al., (2020) found that the prevalence of sleep difficulties is substantial, with around 16.6% of adults, or about 150 million individuals, experiencing sleep difficulties. This number is projected to increase to 260 million by 2030. Moreover, according to the National Highway Traffic Safety Administration (NHTSA), sleep-related problems have significant consequences beyond individual health. Falling asleep while driving contributes to over 100,000 car accidents annually in the United States. Sleep-related problems account for 20% of traffic accidents in the United Kingdom and 25% of incidents in Germany (Santaji & Desai, 2020).

Sleep disorders often go undiagnosed and untreated, leading to chronic health issues and a decrease in overall quality of life (Watson & Fernandez, 2021). Some individuals may not recognize the symptoms of a sleep disorder, considering them normal. Others may avoid seeking medical attention due to a lack of awareness, available treatments, or the stigma associated with sleep disorders. Untreated sleep disorders have serious consequences for overall health and wellbeing. They impair cognitive performance, reduce workplace productivity, and increase the risk of accidents and injuries. Sleep disorders can also contribute to chronic conditions like diabetes, cardiovascular disease, and depression. Emotional functioning is significantly affected, leading to mood disturbances and reduced quality of life (Elmoaqet et al., 2020; Heima et al., 2019).

To address the consequences of untreated sleep disorders, it is crucial to increase awareness and improve access to diagnostic and treatment options. Healthcare providers play a critical role in identifying and treating sleep disorders by conducting thorough assessments and referring individuals to specialists as needed. Individuals can also take steps to improve their sleep hygiene by maintaining regular sleep schedules, avoiding stimulating activities before bedtime, and creating comfortable sleep environments.

Treatment approaches for sleep disorders vary depending on the type and severity of the condition. Lifestyle modifications, such as improving sleep hygiene or making changes to diet and exercise, can alleviate symptoms. Medical interventions, such as the use of continuous positive airway pressure (CPAP) machines for SA or medications for insomnia, may be necessary in some cases. Behavioural therapies, such as cognitive-behavioural therapy for insomnia (CBT-I), have also proven to be effective (Massie et al., 2023). Sleep disorders have a significant economic impact due to their prevalence and associated symptoms, affecting sectors reliant on alertness and decision-making abilities (Imtiaz, 2021; Perslev et al., 2021). Undiagnosed sleep problems in the United States resulted in an estimated economic burden of $149.6 billion in 2016, with an additional $49.5 billion projected for diagnosing and treating sleep problems in the future (Dietz-Terjung et al., 2021). Lin et al., (2021) found that the impact on healthcare expenses is evident, particularly among older adults who experience sleep

problems and delayed sleep time. These findings underscore the importance of screening, detecting, diagnosing, and monitoring sleep disorders. There is a need for simple and accurate methods of detection or classification to ensure that individuals receive the necessary interventions and support for better sleep health.

2.2.1 Sleep Apnoea

SA is a challenging disorder to diagnose due to its complex nature (Salari et al., 2022). Apnoea is a Greek word that has the meaning "without breathing". Clinically, an apnoea event is defined as a cessation of airflow during sleep lasting 10 seconds or more, whereas a hypopnea event is characterized by an airflow reduction rather than a full cessation (Baillieul et al., 2022; JeyaJothi et al., 2022; Zarei et al., 2022). As a result, the body is unable to enter a deep sleep state, and blood oxygen levels decrease. Brief awakenings may occur to restore normal breathing (Moridian, Shoeibi, Khodatars, & Pachori, 2022; Schütz et al., 2021; Zarei et al., 2022). A patient's SA severity can be expressed by their AHI, which is simply the number of apnoea and hypopnea events per hour of sleep (Syeda Quratulain Ali et al., 2019; Alsubie & BaHammam, 2017). Table 2.1 provides an illustration of the four severity groups used to categorize the severity of OSA.

Table 2.1 The four severity groups of OSA.

AHI < 5	No OSA
5 ≤ AHI < 15	Mild OSA
15 ≤AHI < 30	Moderate OSA
AHI ≥ 30	Severe OSA

SA has a significant global impact and is particularly prevalent in certain populations (Baillieul et al., 2022; Benjafield et al., 2019; Xia & Sawan, 2021). Children aged 2 to 8 years, especially pre-schoolers, are at higher risk, often due to enlarged adenotonsils (Duman & Vural, 2022). The elderly population is particularly susceptible to SA (Mukherjee et al., 2021). However, despite its prevalence, SA is often underdiagnosed and inadequately treated. The challenges in detecting and predicting SA contribute to rising healthcare costs (Baillieul et al., 2022).

The cost burden of SA is substantial, with significant economic implications. In the United States alone, the cost of identifying and treating SA was estimated to be approximately $12.4 billion in 2015 (Benjafield et al., 2019). Frost & Sullivan, (2016) estimated that the undiagnosed SA among US adults resulted in an estimated cost burden of $149.6 billion in the same year, considering factors such as lost productivity, increased comorbidity risks, motor vehicle accidents, and workplace accidents. Diagnosing and treating all adults in the US would incur an additional cost of $49.5 billion but result in savings of $100.1 billion. While global cost

estimates are limited, early recognition and treatment of SA are crucial due to its significant long-term consequences.

SA is not only a respiratory disorder but also a significant risk factor for various health problems, including CVD, stroke, car accidents, and diabetes (Dhruba et al., 2021; Moridian, Shoeibi, Khodatars, & Pachori, 2022). Breathing interruptions during sleep, characteristic of SA, can contribute to oxygen depletion, increased nerve activity, blood pressure fluctuations, and changes in heart rate. This puts individuals with SA at a higher risk of developing CVD and other cardiovascular issues (Kristiansen et al., 2021). Heima et al., (2019); Mashrur et al., (2021) found that the link between SA and health problems is supported by several studies. Increased apnoea episodes in SA have been associated with a higher likelihood of developing CVD, stroke, car accidents, and potentially diabetes. However, identifying the cause of health problems associated with SA can be challenging due to patients' unawareness of their awakenings (Kristiansen et al., 2021). Common symptoms of SA include daytime fatigue, loud snoring, breathing difficulties during sleep, trouble concentrating, restlessness, morning headaches, and dry mouth (Syeda Quratulain Ali et al., 2019; Gandhi et al., 2021; Kristiansen et al., 2018, 2021; Salari et al., 2022; San & Malhotra, 2021; Sweed et al., 2019) These symptoms, detailed Figure 2.1 can significantly impact an individual's quality of life and disturb their bed partner's sleep. Recognizing these signs and seeking timely diagnosis and treatment is crucial to mitigate potential health risks and improve overall well-being. Addressing SA and its associated symptoms can lead to improved sleep quality, reduced daytime tiredness, and a lowered risk of developing cardiovascular and other related health conditions.

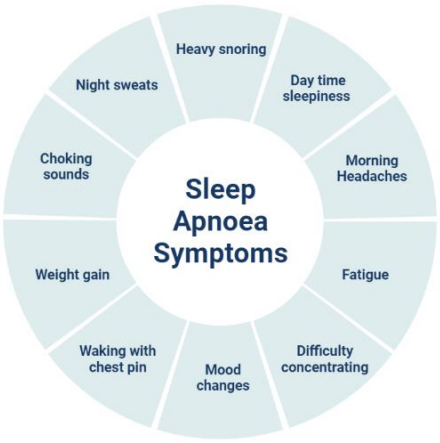

Figure 2.1 Different symptoms of SA.[3]

[3] BioRender (2022). Circular Diagram (Layout 10x1). https://app.biorender.com/biorender-templates/figures/all/t-62c6407f810101923a912315-circular-diagram-layout-10x1

2.2.2 Prevalence of Sleep Apnoea

SA is a common sleep disorder affecting a significant number of individuals worldwide (Faust et al., 2021). According to the WHO, nearly one billion people globally are affected by SA (Baillieul et al., 2022; Benjafield et al., 2019; Mukherjee et al., 2021; Xia & Sawan, 2021). However, most cases go undiagnosed, with an estimated 80% of individuals with SA remaining unidentified. This highlights the need for increased awareness and improved diagnostic tools to address this underdiagnosis (Shieu et al., 2022).

The prevalence of SA has been increasing globally in recent years. Reported rates vary across regions, with Europe and North America having prevalence rates of 9-38%, and China reporting rates of 8.8-24.2% (Duan et al., 2022; Natsky et al., 2021; Senaratna et al., 2017). OSA, a subtype of SA characterized by breathing pauses due to a blocked airway during sleep, has an estimated 5-year incidence of 7-11% in middle-aged adults. Symptoms of SA are experienced by at least 4% of men and 2% of women worldwide, with approximately 34% of men and 17% of women in the general population affected by SA (Tietjens et al., 2019). The reasons for the higher prevalence of SA in men compared to women are not entirely clear, but potential explanations include differences in sex hormones, upper airway shape, craniofacial morphology, pattern of fat deposition, and variations in occupational and environmental exposures (Young et al., 2002).

Evidently, the prevalence of SA varies remarkably across countries and regions, underscoring the urgent need for improved awareness, advanced diagnostic tools, and enhanced treatment accessibility. In the United States, it is estimated that 22 million individuals suffer from SA, with a high proportion of cases going undiagnosed (Ademola Bello & Alqasemi, 2021; Hassan & Haque, 2016). The prevalence rates in Europe range from 4% in Portugal to 24% in Croatia. In Asia, Japan has the highest prevalence, affecting an estimated 7.5 million individuals. In Australia, approximately 9% of adults have moderate to severe SA (Deloitte Access Economics, 2011; Faust, Barika, et al., 2021). Despite the high prevalence of SA, improved awareness, and diagnostic tools, as well as increased access to treatment, are needed to address this significant public health issue.

2.2.3 Physiology of Sleep Apnoea

Section 2.2.3 delves into the Physiology of SA, a condition with various manifestations, such as OSA, CSA, and MSA (Bertuzzi et al., 2022; Elmoaqet et al., 2020). This section unravels the physiological intricacies underlying these distinct types, providing insights into the mechanisms and factors that characterize the different forms of SA. Understanding these physiological aspects is crucial for a comprehensive grasp of the condition and its diverse presentations.

2.2.3.1 Obstructive Sleep Apnoea

OSA is indeed the more common type of SA, affecting a significant portion of the adult population. Despite the frequency of this condition and the serious consequences of leaving it untreated, the OSA remains largely unknown. Studies have estimated the prevalence of OSA to be between 3% and 7% among adults (Baillieul et al., 2022; Elmoaqet et al., 2020; Faust et al., 2016; Foldvary-Schaefer & Waters, 2017; Natsky et al., 2021; Salari et al., 2022; Senaratna et al., 2017). It is more prevalent in men and individuals who are overweight or obese (Jung et al., 2017). The global estimate for the number of OSA patients exceeds 200 million, with 425 million experiencing moderate-to-severe OSA (Elmoaqet et al., 2020).

In specific regions, such as Norway, OSA affects a significant portion of the population, with 22.1% of individuals aged 30-69 experiencing the condition. The frequency of moderate-to-severe OSA in the general population ranges from 6% to 17% (Benjafield et al., 2019; Chung, 2021; Kapoor et al., 2022; Kristiansen et al., 2021; Mashrur et al., 2021). In the United Kingdom, approximately 1.5 million people are affected by OSA, and the condition is associated with hypertension (39%), obesity (34%), depression (19%), gastroesophageal reflux disease (GERD) (18%), diabetes mellitus (15%), hypercholesterolemia (10%), and asthma (4%) (Miller & Cappuccio, 2021). Studies conducted in different countries, such as Russia and Italy, have also highlighted the prevalence of OSA among the population. For example, a survey in Russia found a high prevalence of AHI among citizens aged 30 to 70, and investigations in Italy revealed a significant probability of developing OSA among children aged 6 to 12 (Khokhrina et al., 2020; Paduano et al., 2019; Saldías Peñafiel et al., 2020; Santilli et al., 2021).

OSA prevalence can be even higher in specific high-risk populations. For example, patients undergoing major noncardiac surgery may have OSA rates as high as 68 to 70% (Chan et al., 2019). In the context of diabetes, Feher et al., (2019) conducted a study in the United Kingdom to assess the prevalence of OSA among individuals with type 1 or type 2 diabetes in a primary care setting. The study found an overall OSA prevalence of 0.7% in the examined population. Among individuals with type 2 diabetes, the prevalence was 0.5% in those with normal weight and 9.6% in the obese category. For type 1 diabetes patients, the prevalence was lower at 0.3% for those with normal weight and 4.3% for the obese category. The study revealed that among all the groups examined, obese adults with type 2 diabetes had the highest rate of OSA (9.6%). When comparing the genders, a higher proportion of men than women in the overweight and obese categories were found to have OSA. This difference was particularly notable in the obese category, with a prevalence of 6.5% for men and 2.6% for women. A similar pattern was observed for individuals with type 1 diabetes ((Feher et al., 2019), Figure 2.2 (a) and (b))s, reproduced from (Feher et al., 2019).

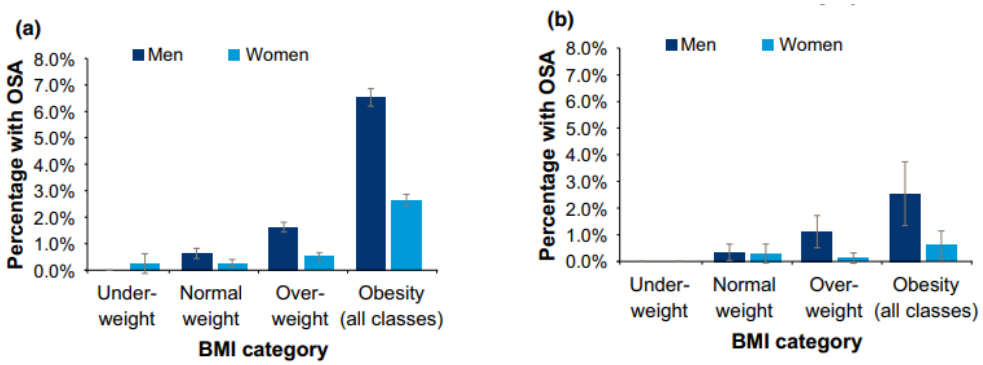

Figure 2.2 OSA prevalence in 1 275 461 adults with (a) Type 2 diabetes and (b) Type 1 diabetes in the UK, according to BMI category and gender.

OSA not only has significant negative health impacts on individuals but also carries substantial economic consequences globally Deloitte Access Economics, (2011). In Australia, OSA is the primary contributor to sleep disorder-related expenses, with total health system costs reaching $408.5 million and indirect financial costs totalling $2.6 billion. In the United States, the economic burden of OSA is estimated to be $149.6 billion annually, encompassing both direct and indirect costs (Khor et al., 2023).

The costs associated with OSA include expenses related to its diagnosis and treatment, as well as the impact on productivity, absenteeism, and increased healthcare utilization. Diagnosis often involves a sleep study, which can be costly and may not always be covered by insurance. Treatment options for OSA include CPAP therapy, oral appliances, and surgery. CPAP therapy is the most common and effective treatment, but it can also be expensive and may not be fully covered by insurance. Oral appliances and surgery are alternative options, but their effectiveness may vary compared to CPAP therapy. It is worth noting that the treatment approach for patients with OSA can vary depending on their symptoms and the country of residence (Benjafield et al., 2019), In general, a diagnosis of OSA is typically made if a patient exhibits symptoms, some of its symptoms and consequences are fatigue, daytime sleepiness, cardiac arrhythmia, and systemic hypertension (Massie et al., 2023; Sateia, 2014)

2.2.3.2 Central Sleep Apnoea

In contrast, CSA is a sleep disorder characterized by disruptions in breathing due to the lack of respiratory effort by the individual (Massie et al., 2023). Unlike OSA, which is caused by airway obstruction, CSA occurs when the brain fails to send proper signals to the respiratory muscles, resulting in temporary pauses in breathing (Ademola Bello & Alqasemi, 2021; Schütz et al., 2021). Compared to OSA, CSA is a less well-known condition and has a genetic component (Culebras, 2021). Whereas the symptoms of CSA are often similar to those of OSA, the choice of therapy depends on the type of SA. In cases where CSA is secondary to another medical condition, addressing the primary condition may help alleviate the symptoms. For

example, improving heart function in patients with heart failure can lead to the resolution of CSA. In cases of idiopathic CSA, positive airway pressure (PAP) therapy, such as CPAP or bilevel positive airway pressure (BiPAP), can be used to assist with breathing during sleep. Supplemental oxygen therapy may also be beneficial in certain cases (Massie et al., 2023). Hence, in order for clinicians to make optimal therapeutic decisions, it is crucial to distinguish between CSA and OSA in patients with SA.

2.2.3.3 Mixed Sleep Apnoea

MSA is a complex sleep disorder that combines features of both OSA and CSA. It is characterized by symptoms similar to both OSA and CSA, such as snoring, daytime sleepiness, and disrupted sleep patterns (Bernardini et al., 2021; Pavsic et al., 2021). MSA can be caused by various underlying medical conditions, including congestive heart failure, obesity, and chronic obstructive pulmonary disease (COPD). The treatment of MSA primarily focuses on addressing the underlying medical condition that leads to the sleep disorder. By managing and treating the underlying condition, the symptoms of MSA can be alleviated. In addition to addressing the underlying cause, PAP therapy may also be employed as a treatment option. PAP therapy includes methods such as CPAP, BiPAP or adaptive servo-ventilation (ASV) to assist with breathing during sleep.

2.3 Polysomnography for Sleep Apnoea Evaluation

This study underscores the pivotal role of PSG as a cornerstone in diagnosing sleep disorders. PSG offers a comprehensive evaluation of sleep, empowering researchers, and clinicians with accurate diagnostic capabilities. This work centres on appraising the reliability of PSG in identifying sleep disorders, delving into its merits and constraints as a research tool, and probing its implications for clinical management. Furthermore, the study addresses the emergence of portable home-based PSG devices, spotlighting their user-friendly convenience and accessibility for sleep monitoring. As an invaluable diagnostic instrument, PSG stands as an essential asset for sleep medicine practitioners in the clinical management of sleep disorders. For instance, diagnosing SA hinges on multiple criteria encompassing symptoms, obstructive respiratory events, and physiological metrics (Feng et al., 2021; Loh et al., 2020; Sateia, 2014). Typically implemented using electrodes or sensors, PSG necessitates the patient to be wired, as depicted in Figure 2.3, possibly presenting an inconvenience.

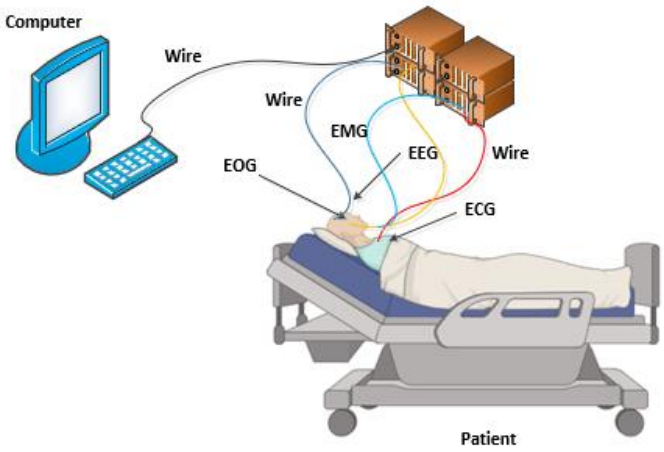

Figure 2.3 A typical PSG setup.[4]

Per the AASM manual, diagnosing SA via PSG involves a substantial decrease of 90% or more in the amplitude of the oronasal thermal sensor signal (Choi et al., 2018). PSG offers an all-encompassing assessment of sleep's physiological and behavioural dimensions, as asserted by Mathias et al., (2018). Nevertheless, the accuracy of PSG in diagnosing sleep disorders can vary, as illuminated by Stuginski-Barbosa et al., (2017). Their research highlighted PSG's reliability in diagnosing conditions like OSA and periodic limb movements (PLMS), yet its accuracy in identifying narcolepsy, insomnia, and other parasomnias is comparatively lower. The accuracy of PSG diagnoses is influenced by factors including sleep specialists' expertise, data quality, and interpretation. Further exploration is necessary to refine our comprehension of PSG's accuracy across diverse sleep disorders.

PSG plays a vital role in diagnosing a spectrum of sleep disorders, encompassing conditions like OSA, insomnia, and RLS. Beyond its diagnostic prowess, PSG enables the exploration of sleep stages such as REM and NREM and stands as a linchpin in unravelling the physiological and pathological underpinnings of sleep. Research driven by PSG has delved into the ramifications of sleep deprivation and fragmentation, spotlighting their impacts on cognitive function, mood, and immune responses. Additionally, studies have unveiled the roles of sleep-in memory consolidation and restorative processes. While PSG is a robust diagnostic tool for sleep-related disorders, it does exhibit limitations. Cost emerges as a significant hurdle, as PSG involves pricy equipment, skilled technicians, and meticulous interpretation (Chen et al., 2015; Faust et al., 2019). Expenses vary substantially, spanning from several thousand dollars to even higher

[4] BioRender (2022). Icon Pack - Patient. https://app.biorender.com/biorender-templates/figures/all/t-63481d37f6cd3a17c56d1193-icon-pack-patient

figures, contingent upon the study's demands and location. This financial barrier can impede access, particularly for uninsured or financially constrained patients.

For instance, Cagle et al., (2023) documented PSG costs ranging from $2581 to $2874, and Mihaera, (2004), reported average costs of around $1100 and $900 in New Zealand. In the USA, annual PSG costs per patient can range from $4,000 to $6,000 (Harvard Medical School, 2010). ECG stands as a prevalent alternative due to its cost-effectiveness, convenience, and non-invasiveness (Mukherjee et al., 2021; C. Sun et al., 2022; Tan et al., 2018). An additional limitation lies in the inconvenience and discomfort associated with overnight stays in sleep laboratories. The unfamiliar setting, electrodes, and sensors can disrupt natural sleep patterns, affecting sleep quality (Barika et al., 2022; Rahul K. Pathinarupothi et al., 2017). The need for multiple wire attachments and channel montages adds further discomfort (Syeda Quratulain Ali et al., 2019; Bsoul et al., 2011; Kalaivani, 2020; Zarei et al., 2022; Zarei & Asl, 2019).

Home-based PSG devices emerge as a convenient alternative, offering the flexibility of conducting sleep studies at home. Despite their benefits, they might not match in-lab PSG's accuracy due to simpler equipment and less comprehensive sensors. Data interpretation requires sleep medicine expertise to ensure accurate diagnosis and treatment decisions. Despite these limitations, home-based PSG devices revolutionize sleep disorder diagnosis and management, expanding accessibility and enabling longitudinal monitoring. They shape the landscape of sleep medicine, enhancing research and providing personalized care for individuals with sleep disorders.

2.4 Risk Factors for Sleep Apnoea

According to the study conducted by (Sin et al., 1999), the risk factors for OSA and CSA exhibit variations, particularly between genders. The research highlights that atrial fibrillation is a risk factor for CSA but not OSA, whereas hypocapnia increases CSA risk in both men and women. Additionally, the study reveals that for men, the most substantial OSA risk factor is an increase in BMI, while for women, advancing age is the primary risk factor. Intriguingly, increasing age is not a risk factor for OSA in men, and BMI increase is not a risk factor for OSA in women. SA as a sleep disorder, disrupts sleep, leading to fatigue and heightened risks of health issues like stroke, hypertension, decreased productivity, and heart attack. It is also associated with an elevated risk of accidents, including motor vehicle accidents, which entail significant financial ramifications. SA development is influenced by various factors, including age, gender, weight, smoking, alcohol use, certain medications, and medical conditions like heart disease, hypertension, and diabetes (Duan et al., 2022; Y. Li et al., 2020; Salzano et al., 2021). The combination of these factors creates a hazardous situation, as the individual may struggle to restore their oxygen levels and faces a risk of suffocation during sleep. Family history of SA and anatomical features such as a narrow airway or large tongue also contribute

(Xiu et al., 2020). Age, gender, and weight stand as significant risk factors for SA (Bachrach et al., 2021; Young et al., 2002), with age over 40 and being male heightening susceptibility (Alonderis et al., 2020) as highlighted in Figure 2.4.

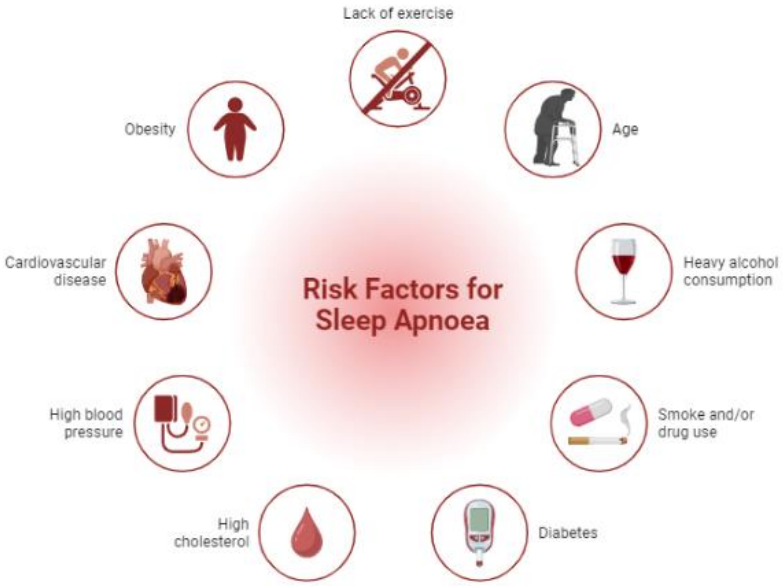

Figure 2.4 The main risk factors for SA[5].

Overweight individuals face increased risks due to airway pressure, making breathing more difficult (Jaiswal et al., 2017). Obesity is a prominent SA risk factor and a global health concern (Bachrach et al., 2021). Weight significantly contributes to SA development, with obesity prevalence steadily rising worldwide. Obesity-related risk factors include a large neck circumference, airway restriction, hypertension, diabetes, and smoking (Baker et al., 2020; Park et al., 2021).

The global count of obese adults continues to escalate, with predictions indicating this trend's continuation. Even minor weight reduction substantially alleviates SA severity (Agha & Agha, 2017). In England, obesity prevalence was 28% among women and 33% among men in 2010, and up to 27% of the population was obese in 2015. Projections based on current trends anticipate that by 2050, 60% of males and 50% of females will be obese, as supported by Figure 2.5 and Figure 2.6. Notably, even modest weight loss can significantly ameliorate SA severity.

[5] Lugano, G. (2022). Risk Factors for Sleep Apnea. https://app.biorender.com/biorender-templates/figures/all/t-63a25cb326f5d6a8ffd76703-risk-factors-for-stroke

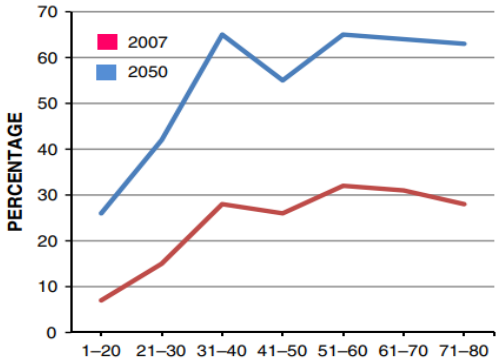

Figure 2.5 Obesity prevalence estimates for men in 2007 and 2050 (Agha & Agha, 2017).

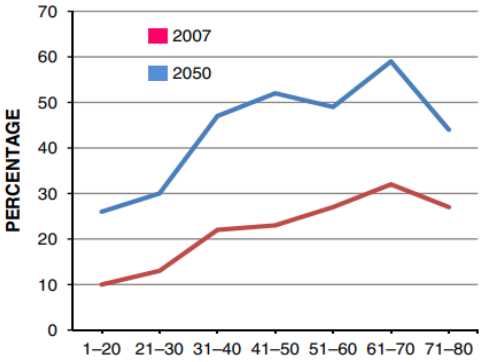

Figure 2.6 Obesity prevalence estimates for women in 2007 and 2050 (Agha & Agha, 2017).

2.5 Sleep Apnoea Financial Costs

Assessing the financial impact of SA on healthcare systems involves a comprehensive evaluation of both direct and indirect costs. Direct costs encompass expenses related to the diagnosis, treatment, and management of SA, such as medical consultations, sleep studies, and specialized equipment like CPAP machines. These costs can vary based on healthcare provider charges, insurance coverage, and the severity of the condition. Indirect costs, on the other hand, reflect the economic consequences of SA on productivity and quality of life. These include factors like accidents, property damage, legal proceedings, and even loss of life, which contribute significantly to the overall economic burden. Quantifying the economic parameters of SA, including cost-effectiveness and cost-benefit ratios, can be complex due to the challenge of assessing the value of healthy individuals compared to those affected by SA. Nevertheless, studies have endeavoured to analyse the economic ramifications of SA and have underscored the substantial financial strain it places on individuals and healthcare systems (Baillieul et al., 2022).

On a broader scale, the impact of SA on healthcare systems is substantial. The increasing global prevalence of SA translates to escalating healthcare expenses as a growing number of individuals necessitate diagnosis, treatment, and ongoing management. Empirical data has revealed staggering figures for the annual costs linked to SA. For instance, in the United States alone, a staggering $65 billion is expended each year on health services for the diagnosis and treatment of SA. The collective indirect costs of sleep disorders, encompassing SA, hover between $50 to $100 billion annually. These figures paint a vivid picture of SA's pronounced economic repercussions on both individuals and society as a whole (Abad & Guilleminault, 2022; Ademola Bello & Alqasemi, 2021; Natsky et al., 2021; Senaratna et al., 2017). A study conducted by Hossain & Shapiro, (2002) delved into societal costs associated with sleep disorders, including medical services and medication. The analysis estimated that in 1995, sleep

disorders incurred a societal cost of $2 billion in France and $13.9 billion in the USA. Hospital visits related to sleep disorders amounted to $700 million annually in each country, with over-the-counter sleep aids constituting an additional annual cost of $84 million.

2.6 Treatment of Sleep Apnoea

SA, a sleep disorder with potential consequences if left untreated, can be effectively managed through various treatment options. Figure 2.7 provides an overview of different strategies for treating SA, including CPAP therapy and surgical interventions aimed at addressing anatomical obstructions. This section will delve into the primary types of treatment used to alleviate SA symptoms and improve overall sleep quality.

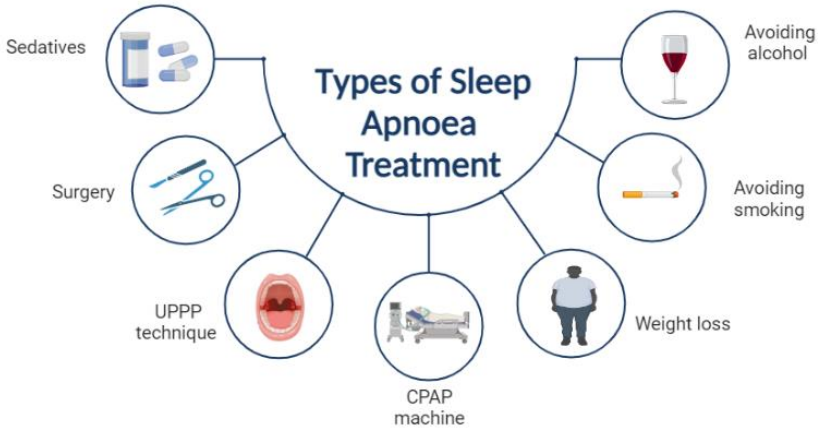

Figure 2.7 Types of SA treatment.[6]

2.6.1 Continuous Positive Airway Pressure

The primary and widely accepted treatment for preventing the collapse of the pharyngeal airway in both children and adults for SA is nasal CPAP (C. Li et al., 2021; National Institute for Health and Care Excellence, 2021). Despite substantial individual variability in response to CPAP therapy duration, research indicates that utilizing CPAP for four or more hours enhances cognitive functioning, subjective sleepiness, and overall quality of life (Tolson et al., 2023). CPAP functions as a pneumatic splint, effectively stabilizing the upper airway, and proves successful with proper adherence. However, achieving consistent adherence poses a considerable challenge, influenced by socio-demographic factors, psychosocial characteristics, disease severity, and treatment-related side effects. Despite enhancements in machine technology and interventions to improve compliance, CPAP non-adherence rates persistently range between 30% and 40% (Brennan & Kirby, 2023). CPAP involves a mask worn during

[6] BioRender (2022). Semicircular Diagram (Layout). https://app.biorender.com/biorender-templates/figures/all/t-61f9812fa30d5d009e189901-semicircular-diagram-layout.

sleep, covering the nose or mouth (M.K. et al., 2020), linked to a machine that delivers pressurized air to prevent airway collapse Figure 2.8.

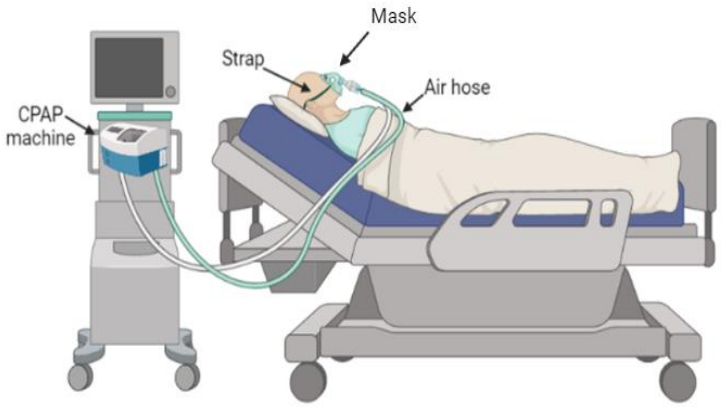

Figure 2.8 Continuous positive airway pressure setup.[7]

However, a notable limitation lies in suboptimal adherence to CPAP therapy, with an estimated 50% of patients failing to meet the recommended usage duration of four hours per night. (Broström et al., 2010; Tolson et al., 2023). Additionally, the noise generated by the CPAP machine can disrupt both the patient and their sleeping partner (Broström et al., 2010). Outcomes are mixed (Brill et al., 2018), necessitating further research. Consistent nightly CPAP use at home is optimal, although not always practical. Regular check-ups are advised to assess adherence, address side effects, and replace components (S. P. Patil et al., 2019). Diagnosis and CPAP wait times vary globally, as illustrated in Table 2.2 (Flemons et al., 2004).

[7] BioRender (2022). Icon Pack - Patient. https://app.biorender.com/biorender-templates/figures/all/t-63481d37f6cd3a17c56d1193-icon-pack-patient

Table 2.2 Waiting time for diagnosis and treatment with CPAP in five countries in 2001.

Country	Population	Waiting Time
United Kingdom	58,800,000	7–60
Belgium	10,000,000	2
Australia	18,970,000	3–16
United States	280,000,000	2–10
Canada	31,400,000	4–36

2.6.2 Bilevel Positive Airway Pressure

In recent years, the use of BiPAP ventilators have demonstrated notable benefits, including enhanced clinical effectiveness, reduced rates of invasive ventilation with endotracheal intubation during acute exacerbations, and shorter hospitalization durations for patients with associated pneumonia and stable-phase acute exacerbations (C. Zhang & Liu, 2023). However, research on the impact of BiPAP on mental disorders in COPD patients with comorbid anxiety and depression remains limited. Illustrated in Figure 2.9, BiPAP shares similarities with CPAP, utilizing a mask connected to a machine delivering pressurized air to the airways. Unlike CPAP, BiPAP provides two distinct levels of air pressure for inhalation and exhalation, offering particular advantages to patients who struggle with exhalation against a constant pressure (Abad & Guilleminault, 2022).

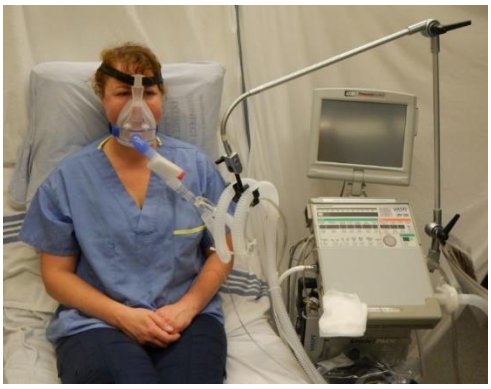

Figure 2.9 BiPAP setup.[8]

2.6.3 Oral Appliances

Oral appliances are specifically designed devices that are worn in the mouth during sleep with the aim of keeping the airway open. They are commonly recommended for individuals with

[8] https://userfiles.steadyhealth.com/images/ic/bipap.jpg

mild to moderate SA and can be an alternative option for patients who find it challenging to tolerate the pressure of CPAP therapy (Abad & Guilleminault, 2022; Aurora et al., 2010).

2.6.4 Surgery

Surgery is sometimes considered as a treatment option for individuals with severe SA who have not experienced improvement with other methods. There are different surgical procedures available, including Uvulopalatopharyngoplasty (UPPP) and Maxillomandibular advancement (MMA). UPPP involves the removal of excess tissue from the throat, while MMA involves moving the jaw forward to widen the airway (Aurora et al., 2010). These surgical interventions aim to address the anatomical factors contributing to SA and can be considered in select cases after a thorough evaluation by a healthcare professional.

2.6.5 Lifestyle Changes

Implementing lifestyle changes can be an effective strategy in managing SA symptoms. Weight loss, avoiding alcohol and sedatives before bedtime, and adopting a side-sleeping position instead of sleeping on the back are all recommended approaches to reduce the severity of SA (Duan et al., 2022; Y. Li et al., 2020). Studies have demonstrated that a 10% reduction in weight can lead to a significant improvement in the AHI, with a corresponding 26% reduction in its severity (C. Li et al., 2021). These lifestyle modifications, when combined with appropriate medical treatment and guidance, can contribute to better management of SA.

2.7 Artificial Intelligence Innovations in Sleep Apnoea Diagnosis

The evolution of technology, particularly in AI, offers a transformative potential for the field of sleep medicine. AI has the capability to efficiently process and analyse extensive volumes of digital health data originating from various inpatient and outpatient sources. This enables the creation of predictive diagnostic and treatment models. AI tools excel in tasks such as data cleansing, disease classification, and detection of specific disease patterns tasks that surpass the capacity of human biological intelligence. With each patient generating more than 80 megabytes of clinical data annually, a figure that continues to rise, the manual review of patient data during limited clinical sessions is increasingly challenging. This surge in data underscores the necessity for advanced technological interventions in diagnosing and managing sleep disorders (Alattar & Govind, 2024).

The AI, which includes various techniques, has emerged as a transformative force in the detection and diagnosis of SA. Algorithms, when applied to diverse datasets including clinical records, PSG data, and even wearable device recordings, enable the identification of patterns indicative of SA. These algorithms can analyse vast amounts of information to recognize subtle variations in breathing patterns, sleep stages, and physiological parameters associated with sleep

disorders. Moreover, advanced algorithms, with their ability to automatically extract intricate features from raw data, have shown promise in enhancing the accuracy and efficiency of SA detection. By training on large datasets, these models can learn complex representations of sleep-related signals, enabling more precise identification of apneic events and aiding in the differentiation between obstructive, central, and mixed forms of SA (Alattar & Govind, 2024; Moridian, et al., 2022).

The integration of AI techniques into SA detection systems has revolutionized diagnostic approaches by offering non-invasive, cost-effective, and scalable solutions. These technologies facilitate the development of intelligent tools capable of continuous monitoring and real-time analysis of sleep-related parameters, empowering healthcare professionals to identify individuals at risk of SA earlier and intervene promptly. Furthermore, the automation of SA detection processes through AI-driven algorithms streamlines diagnostic workflows, reduces the burden on healthcare providers, and enhances patient access to timely and accurate sleep disorder assessments. As research in this domain continues to advance, the synergy between AI and sleep medicine holds tremendous potential to improve the early detection, management, and treatment outcomes of SA worldwide (Alattar & Govind, 2024; Moridian, et al., 2022).

2.8 Deep Learning

DL is a type of ML that uses large datasets to train a neural network with multiple hidden layers (Faust et al., 2018; Lih et al., 2020; S. Patil, 2022). According to Esteva et al., (2019), it plays a vital role in understanding physiological data and improving the performance of medical systems (Faust et al., 2018). The concealed layers don't directly generate functions to map data for classification. Instead, they furnish valuable information for categorizing a data set into a cluster and extract features and aspects from the input space. DL holds immense potential in healthcare and medicine, particularly due to the growing volume of data generated by medical devices and digital record systems (Esteva et al., 2019). Its application in developing accurate SA detection systems has been a critical area of research in healthcare (Mukherjee et al., 2021).

Researchers have utilized ML and DL techniques to detect apnoea, achieving high accuracy (Cen et al., 2018). For instance, Chang et al., (2020) proposed a 1-D Convolutional Neural Networks (CNN) architecture for OSA detection, achieving an overall accuracy of 87.9%. Mashrur et al., (2021) developed a Scalogram-based CNN for detecting OSA using PhysioNet Apnea ECG signals (Penzel et al., 2000), achieving an accuracy of 94.30%. With the need to record patient data accurately for medical procedures such as SA detection and diagnosis, DL significantly enhances the capabilities of advanced technical aspects. Healthcare professionals and doctors can benefit from learning DL processes with the assistance of AI technology, enabling them to improve their performance while delivering critical treatments to patients (Holzinger et al., 2023).

2.9 Computer Aided Sleep Apnoea Detection System

Computer-aided sleep apnoea detection system (CASADS) uses computer tools to analyse physiological signals like heart rate and breathing patterns during sleep. ML and DL are often used to identify patterns suggesting SA from large datasets. CASAD is a promising tool for diagnosing and managing sleep disorders by offering objective measurements to guide treatment. However, more research is needed to confirm the accuracy, reliability, accessibility, and affordability of these techniques for both patients and healthcare providers (Mousavi et al., 2019). According to Moridian, et al., (2022), the CASADS, which integrates ML and DL approaches for automated SA diagnosis. This research aims to offer valuable support to specialists by enhancing the accuracy of SA detection through ML and DL techniques. By harnessing advanced algorithms rooted in ML and DL, the study aims to empower clinicians to identify and diagnose SA more effectively. This collaborative integration of AI methodologies not only streamlines the diagnostic process but also contributes to refining treatment strategies for patients with sleep disorders.

2.9.1 Sleep Apnoea Detection with Machine Learning, Incorporating Deep Learning

The use of modern technology, such as CAD, can assist in the identification of SA, resulting in faster and more cost-effective diagnosis. Some ML techniques have shown high accuracy in diagnosing SA, but issues such as complexity, memory inefficiency, and the need for human intervention need to be addressed (Syeda Quratulain Ali et al., 2019). Bozkurt et al., (2020) conducted a study using ECG data from ten patients with OSA and ten healthy controls to classify the presence of OSA. They utilized HRV and a digital filter to extract the QRS component at various frequencies and employed the k-Nearest Neighbors (k-NN) algorithm for classification. The study reported a classification accuracy of 82.11% and 85.12% when three and thirteen features were used, respectively. Erdenebayar et al., (2019a) used data from 86 patients, with 69 used for training and 17 for testing, and employed a residual neural network (RNN) algorithm. The study reported the highest accuracy of 99% using this DL approach, indicating its usefulness for automatically detecting SA. F. Chung et al., (2012) improved accuracy to 93.7% for an AHI of 30, despite primarily including surgical patients in their sample. The use of statistical techniques enabled them to achieve diagnostic ability that was most similar to the ML approach. Khandoker et al., (2009) identified 24 variables from the examination of two forms of SA in 83 people using SVM on 125 sets of ECG data. The technique showed a 92.85% accuracy for leave-one-out cross-validation (LOOCV).

Recent studies have focused on utilizing DL methods for the identification and classification of apnoeic events. Long Short-Term Memory (LSTM) networks have demonstrated high accuracy in diagnosing SA, achieving 99% accuracy according to studies by (Faust et al., 2021; Tan et al., 2018). Pathinarupothi et al., (2017) diagnosed SA using a single-sensor approach and

LSTM-RNN with specific network configurations. CNN are effective techniques commonly used in signal processing, image analysis, and computer vision applications (Zarei et al., 2022). Choi et al., (2018) employed CNNs and PSG signals to develop an automatic apnoea detection method. Erdenebayar et al., (2019a) utilized CNN and RNN-based structures to detect apnoeic events using ECG signals. Dey & Chaudhuri, (2018) developed a supervised apnoea detection method based on the CNN architecture and ECG signal.

Various classifiers, including Random Forest (RF), SVM, K-Nearest Neighbors (KNN), Adaboost, Linear Regression (LR), the Hidden Markov Model (HMM), Deep Neural Network (DNN), and Adaptive Neuro-Fuzzy Inference System (ANFIS) have been employed to identify segments of OSA (Sarah Qasim Ali & Hossen, 2018; K. Li et al., 2018; Usha Kumari et al., 2020). Al-Ratrout & Hossen, (2018) achieved 100% accuracy in classifying SA by combining SVM with fivefold wavelet decomposition and dbl filters. Tagluk et al., (2010) introduced a new approach for Sleep Apnoea Syndrome (SAS) classification, combining wavelet transforms and an Artificial Neural Networks (ANNs). Their method involved training the network with different momentum coefficients. Utilizing multi-resolution wavelet transforms, they divided abdominal respiration signals into spectral components, serving as inputs for the neural network. Configured with three outputs, the network classified patients' SAS conditions. Figure 2.10 reproduced from (Tagluk et al., 2010) illustrates their methodology.

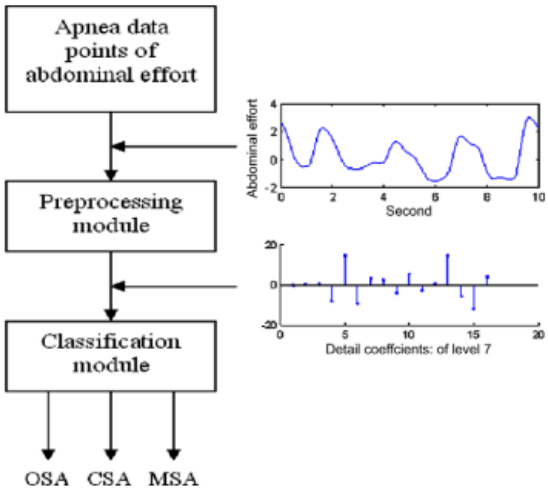

Figure 2.10 Structure of the proposed classification method.

DL-based algorithms have been employed for the categorization of SA by researchers such as (Leino et al., 2021; Mostafa et al., 2017; Rahul Krishnan Pathinarupothi et al., 2017; Yildirim et al., 2019). Cheng et al., (2017) utilized a Recurrent Neural Network (RNN) model with 97.8% accuracy for SA identification. The accuracy of DL algorithms for identifying SA is summarized in Table 2.3. The presented table underscores diverse studies employing distinct classifiers and databases in SA detection, underscoring fluctuations in detection performance.

Prominent gaps involve enhancing specificity in specific models, tackling issues related to respiratory signal detection, and investigating innovative approaches to augment overall accuracy and resilience in real-world contexts. Ng et al., (2008) achieved a sensitivity of 70.29-86.25% by using thoracic and abdominal signals as input features for SA detection. Qin et al., (2021) investigated the relationship between OSA and HRV and found that HRV decreases with the severity of apnoea disease.

Table 2.3 DL networks.

Authors	**Classifiers**	**Database**	**Signals**	**Detection Performance**		
				Acc%	**Sen%**	**Spec%**
J. Zhang et al., 2021	CNN-LSTM	Apnea-ECG	ECG	99.80	96.94	98.97
Wu et al., 2021	1D-CNN	EEG and EOG	EEG, EOG	97.62	94.34	92.33
Faust, et al., 2021	LSTM	Apnea-ECG	ECG	99.80	99.85	99.73
Acharya et al., 2011	CNN	MIT-BIH arrhythmia	ECG	92.50	98.09	93.13
Morales et al., 2017	DBN	Apnea-ECG	ECG	97.64	78.75	95.89
	RNN			85.4	97	87
Acharya et al., 2011	LSTM	Nocturnal ECG	ECG	98	98	98
	GRU			99	99	99
Song et al., 2016	CNN-LSTM	Apnea-ECG	ECG	96.1	96.1	96.2
Pinho et al., 2019	Bi-LSTM	PSG and respiration signals	respiratory signals	-	90.3	83.7

2.9.2 Signals for Sleep Apnoea Detection

The detection of SA relies on the analysis of various physiological signals, including EEG, EOG, EMG, ECG, HR, and SpO2. These signals are essential in the diagnosis and management of SA and can be non-invasively monitored during sleep using a diverse array of sensors and devices. In the following subsections, detailed information regarding these physiological signals will be presented, shedding light on their significance and relevance in SA detection and treatment.

2.9.2.1 Electrocardiogram

This passage explores the utilization of ECG signals in the detection of SA. While ECGs are commonly used to assess CVD, they can also be employed to evaluate SA and other sleep disorders (Behar et al., 2021). ECG signals capture the electrical activity of the heart and are typically recorded by placing bioelectrodes on the body's surface. ECG data extraction entails analysing signals from electrodes on the skin to interpret heart rate, rhythm, and intervals, utilizing algorithms for in-depth insights into cardiac activity, crucial for diagnostic and

monitoring applications in healthcare. However, it's important to note that ECG signals can vary among individuals based on factors such as physical activity and stress levels (Dhruba et al., 2021; Faust et al., 2016).

To detect SA, numerous research studies have utilized ECG signals in combination with other measurements like respiratory airflow and SpO2 due to the limited sensitivity and specificity of ECG alone. These studies have employed various approaches, such as decomposing ECG signals, extracting entropy features, and employing classifiers like support vector machines (SVM) (Banluesombatkul et al., 2019; Bozkurt et al., 2020). Respiratory airflow is measured through methods such as pneumotachography, thermal-based sensors, ultrasonic flowmeters, and capnography, each chosen based on factors like accuracy, patient comfort, and the application context in clinical diagnostics, research, or home monitoring (Ragette et al., 2010). For instance, Hassan & Haque, (2016) employed empirical mode decomposition (EMD) to decompose ECG signals into intrinsic mode functions (IMFs). Nishad et al., (2018) utilized a tunable-Q wavelet transform to decompose ECG signals and extracted entropy features for SA classification using diverse classifiers. Martín-González et al., (2017) proposed a feature extraction technique that classified SA using Linear Discriminant Analysis (LDA), Quadratic Discriminant Analysis (QDA), and Logistic Regression (LR) using HRV information captured from ECG signals. Chen et al., (2015) employed an automatic ECG signal segmentation scheme to obtain segments of varying lengths for classification, with a SVM utilized to screen apnoeic segments. Additionally, Tripathy, (2018) suggests using HRV and electrocardiogram-derived respiration (EDR) signals for SA detection.

In a normal ECG, distinct signal components, including the P, QRS, and T waves, can be visually identified. These waves correspond to specific physiological events during the cardiac cycle (Almazaydeh et al., 2012; Faust, Kareem, et al., 2021). Figure 2.11 provides a schematic representation of a normal ECG, illustrating the different waveforms and their significance (Faal & Almasganj, 2021).

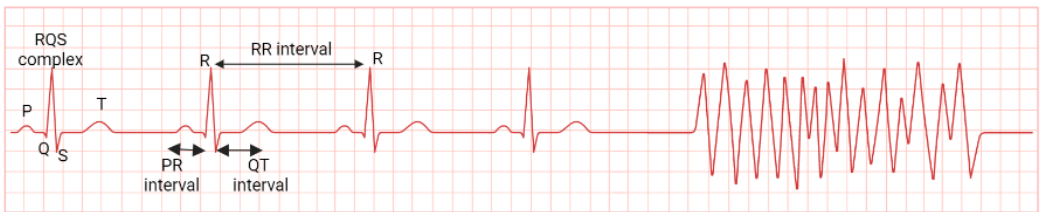

Figure 2.11 ECG signal shows P, Q, R, S, T waves, QRS complex and RR interval.

2.9.2.2 Electrooculogram

The EOG signal is a bio-electric signal generated by eye movement. It is recorded by placing electrodes around the eyes and measures the electrical potential associated with eye movements. Figure 2.12 illustrates the placement of electrodes for recording EOG signals, following the guidelines provided by AASM (Faust et al., 2019). EOG signals have broad applications in clinical settings for diagnostic purposes and in research settings for studying eye movement and visual processing. They provide valuable insights into ocular activity and are instrumental in understanding various eye-related conditions and phenomena.

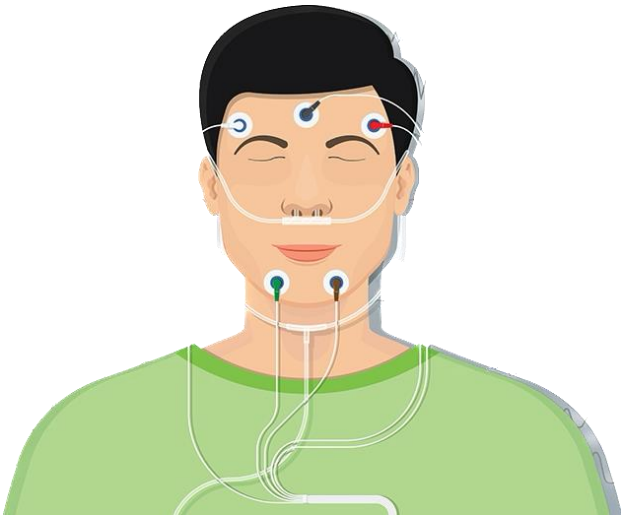

Figure 2.12 EOG electrode is placed above the right eye, while the other electrode is placed above the left eye.[9]

2.9.2.3 Electroencephalogram

The EEG is a measurement of the electrical activity of the brain and plays a crucial role in identifying different sleep stages based on their distinct patterns. Various classification systems have been developed to categorize sleep stages using specific features derived from EEG signals. Signal processing techniques, such as time-domain analysis, spectral analysis, time-frequency analysis, and nonlinear analysis, have been employed to extract relevant sleep-related information from EEG signals. The advent of wearable technologies has made the acquisition of EEG signals more accessible, and the rich information contained within EEG signals has made them an indispensable tool in sleep research. Researchers rely on EEG signals to gain insights into sleep architecture, brain activity during sleep, and the dynamics of sleep-related disorders (Yildirim et al., 2019).

[9] https://cvgclinical.co.za/paediatric-and-adult-sleep-study-clinic/

2.9.2.4 Electromyogram

The EMG signal, also known as the myoelectric signal in biomedicine, is a type of biomedical signal that records the electrical currents produced by muscles during contraction. It provides valuable insights into neuromuscular processes. Muscle activity, whether it involves contraction or relaxation, is controlled by the nervous system. Consequently, the EMG signal is a complex indicator that is regulated by the nervous system and influenced by the anatomical and physiological characteristics of the muscles. By analysing the EMG signal, researchers can gain a deeper understanding of muscle function, motor control, and the coordination of muscle activity. The EMG signal has various applications in clinical and research settings, including the study of muscle disorders, movement analysis, and the assessment of muscle performance and fatigue (Merletti et al., 2009; Reaz et al., 2006).

2.9.2.5 Heart Rate

HR, or heart rate, is a physiological signal that reflects the number of heartbeats per unit of time, typically measured in beats per minute (bpm) (Obi, 2022; Wójcikowski & Pankiewicz, 2020). The normal range for adults usually falls between 60 to 100 bpm, although it can vary depending on factors such as age, gender, and level of physical activity (Dhruba et al., 2021). Abnormal increases in HR can indicate sleeping disorders or SA, which can also influence HR. Conversely, a lack of oxygen in the body can lead to a lower HR (Dhruba et al., 2021).

HR signals consist of consecutive beat-to-beat intervals, which can be extracted from either an ECG or a photoplethysmogram (PPG) signal (Loh et al., 2022). HRV, or heart rate variability, is a significant physiological parameter that quantifies the variations in time intervals between consecutive heartbeats. It is closely associated with heart health and often evaluated in the diagnosis of cardiovascular diseases (Achten & Jeukendrup, 2003; Olmedo-Aguirre et al., 2022). Higher HRV values indicate a healthier cardiac condition and a lower risk of death. SA episodes can affect heart rhythm, and HRV can objectively detect these changes. However, it is important to consider the influence of age and gender on HRV (Faust, O., Yi, L.M. and Hua, L.M., 2013).

2.9.2.6 Oxygen Saturation

Several studies have utilized single biological markers, such as SpO2, for SA detection (Burgos et al., 2010; Ramachandran & Karuppiah, 2020). The AASM Task Force has included blood SpO2 as a measurement to characterize SA and hypopnea episodes (Burgos et al., 2010). In healthy individuals, SpO2 levels typically range between 95% and 100%, indicating well-saturated haemoglobin with oxygen (Moshtaghi-kashanian et al., 2021; Olmedo-Aguirre et al., 2022). However, SA patients often exhibit lower SpO2 values, around 90% (Dhruba et al., 2021). Stone et al., (2016) discovered that SA patients with SpO2 levels below 90% for more than 10% of their sleep had nearly twice the risk of stroke compared to those without such

saturation declines. SpO2 values are categorized as normal and healthy, mild hypoxemia, hypoxic, and severely hypoxic, with oxygen levels below 90% considered dangerous and levels below 80% harmful to vital organs (Elfasakhany et al., 2021; Olmedo-Aguirre et al., 2022). Many studies combine SpO2 and ECG signals to detect apnoeic events, as research has shown that HR and systolic blood pressure rise in response to these episodes (Erdenebayar et al., 2019b). Burgos et al., (2010) utilized SpO2 measurements in their SA detection study.

2.9.2.7 The RR interval

The RR interval, referred to as the interbeat interval, signifies the time between consecutive R-waves during a heartbeat as depicted in Figure 2.11. These R-waves are identified as the highest peaks of specific QRS complexes. QRS complexes correspond to the waveform deflections seen in an ECG trace, representing the ventricular activity of the heart. (Shaffer & Ginsberg, 2017). It is a measure of HRV, which is influenced by the dynamic balance between parasympathetic and sympathetic activity in the autonomic nervous system (Shaffer & Ginsberg, 2017). The healthy heart exhibits complex and non-linear variability, allowing it to adapt to changing environments (Shaffer & Ginsberg, 2017). Almazaydeh et al., (2012) describe the process of generating an RR interval time series for each ECG beat.

$$rr\,(i) = r\,(i + 1) - r\,(i), \quad i = 1\ 1,2, \ldots, n \tag{2.1}$$

In this equation, $r(i)$ represents the time of occurrence of the i-th heartbeat, and $rr(i)$ represents the time interval between the i-th and $(i+1)$-th heartbeat, which is commonly referred to as the RR interval.

2.10 Automated Sleep Stage Scoring

Sleep staging is an essential for diagnosing sleep-related illnesses (Satapathy & Loganathan, 2021). Automated sleep stage scoring aids human and animal sleep analysis since the late 1960s (Grieger et al., 2021). PSG analysis relies on physiological signals like EEG, EOG, ECG, EMG, SpO2, airflow, and respiratory effort, divided into 30-second sleep epochs manually classified by sleep specialists (Krauss et al., 2021; Sokolovsky et al., 2020). These epochs are labeled as wake, light sleep, intermediate sleep, deep sleep, or Rapid Eye Movement (REM) sleep, following AASM recommendations (Yan et al., 2021).

In 1968, Rechtschaffen (R) and Kales (K) proposed a five-stage sleep system, defining standard rules for sleep stage scoring (Hussain et al., 2021; Malafeev et al., 2018). R&K divides sleep cycles into Non-Rapid Eye Movement (NREM) stages 1, 2, 3, 4, and REM. AASM's 2012 revision merged stages S3 and S4 into a single Slow Wave Sleep (SWS) class (Chriskos et al., 2021; Michalek-Zrabkowska et al., 2021; Perslev et al., 2021; Yildirim et al., 2019). A typical sleeper transitions between these stages during the night, with S2 being the most common (Malik et al., 2018). NREM sleep occupies 75%–80% of total sleep time, while REM sleep accounts for 20%–25% (Manish Sharma et al., 2021). ML methods have emerged to categorize

sleep stages with high accuracy, particularly useful for detecting disorders and sleep stages (Santaji & Desai, 2020). Table 2.4 outlines some commonly used ML approaches for sleep stage classification.

Table 2.4 ML approaches that are often used for sleep stage classification.

Category	Techniques	Technique variations
Supervised Learning	Classification	LDA, SVM, hidden Markov model, Bayesian
Supervised Learning	Classification	KNN
Supervised Learning	Classification	Decision tree (DT)
Supervised Learning	Ensemble	Ada-boost, random forest
unsupervised Learning	Clustering	K-means clustering
Supervised Learning	Regression	Techniques specific to regression tasks

2.10.1 Deep Learning Approaches for Automated Sleep Staging

DL can outperform traditional ML in various domains due to its capacity to automatically extract intricate features from raw data, handle large and complex datasets, and model intricate relationships, allowing for more accurate and nuanced predictions. The hierarchical representation learning in DL architectures enables the automatic discovery of hierarchical features, contributing to superior performance across diverse and intricate tasks. These features has motivated researchers to employ DL techniques for automatic sleep stage classification (Eldele et al., 2021). Sleep staging entails the categorization of sleep into various stages and has been addressed through classifiers like CNNs, DNNs, and combinations such as CNN+RNN or DNN+RNN (Faust et al., 2019). Many studies have focused on processing raw PSG data using CNNs and RNNs. Alternatively, successful approaches have utilized precomputed spectrograms along with CNNs and RNNs, capturing the frequency content of signals over time. Between 2010 and 2020, it is worth noting that approximately 75% of research on automated sleep stage classification has employed DL methodologies (Loh et al., 2020).

2.10.1.1 Convolutional Neural Networks

CNNs are ML models inspired by the human visual system. They consist of convolutional, pooling, and fully connected layers that perform a series of operations on input data (Sokolovsky et al., 2020). CNNs have been widely employed for sleep stage classification, leveraging their success in image recognition tasks (Sokolovsky et al., 2020).

Yulita et al., (2018) achieved an 84% accuracy in automatic sleep stage classification by employing a fast-convolutional method for feature extraction. Dong et al., (2018) utilized LSTM to classify sleep stages from EEG signals, achieving an accuracy of 78.94% to 83.60%.

Zhao et al., (2022) utilized the 1D CNN-LSTM method to automatically classify sleep stages using various physiological signals. They achieved an accuracy of 93.47% when using the Fpz-Cz channel EEG signal and 94.15% when combined with the EOG signal. Malik et al., (2018) applied a CNN classifier to a single-lead ECG signal for automatic sleep staging. They also investigated the effects of using a CNN on the instantaneous heart rate (IHR) series as an approach to quantify heart rate fluctuation. H. Sun et al., (2020) developed a set of DNNs to classify sleep stages using ECG and/or respiration signals, utilizing a large-scale dataset of 8682 PSGs acquired at the Massachusetts General Hospital sleep laboratory (MGH).

2.10.1.2 Recurrent Neural Network

RNN, In the 1980s, the RNN was developed with an architecture consisting of input, hidden, and output layers. RNNs use repeating modules in a chain-like structure to serve as memory, retaining important information from previous steps. Unlike feedforward networks, RNNs include a feedback loop, allowing them to process sequences by incorporating the output from the prior step into the current step. This sequential processing capability makes RNNs effective for learning and analysing sequences, as depicted in Figure 2.13 (Abdullah et al., 2022; Le et al., 2019).

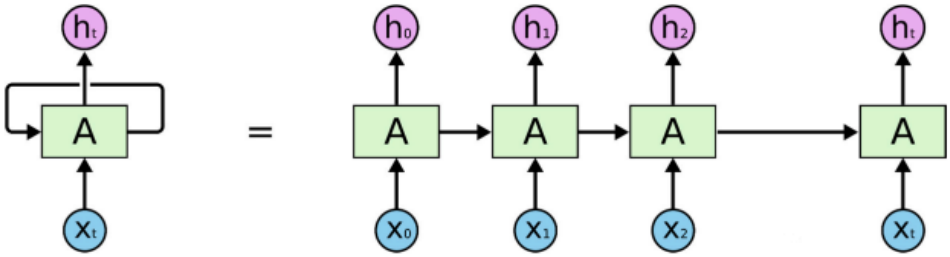

Figure 2.13 depicts a basic RNN expanded into a complete network, featuring one input unit, one output unit, and one recurrent hidden unit, where X_t is the input at time step t and h_t is the output at time step t.

RNNs have emerged as the state-of-the-art approach for various tasks, including natural language processing and speech recognition. In the context of language processing, sequential data can be represented as sequences, such as words (sequences of letters), sentences (sequences of words), and documents (sequences of sentences) (Michielli et al., 2019). Suited for modelling time series data with long-term dependencies, RNNs, as a subset of ANNs, incorporate time delay units and feedback connections. Particularly useful in automatic sleep stage classification, RNNs extensively use DL models trained with subsets of PSG recordings, comprehensive tests capturing various physiological signals during sleep.

Table 2.5 provides an overview of some of the PSG recordings used in previous studies for training DL models in the context of automatic sleep stage classification.

Table 2.5 Summarizes the DL algorithms used for automated sleep stage classification in the Sleep-EDF dataset, utilizing PSG recordings.

Author	Signals	Samples	Approach	Tools/Programming Languages	Accuracy (%)
Zhu et al., 2020	EEG	15,188	attention CNN	–	93.7
Qureshi et al., 2019	EEG	41,900	CNN	–	92.5
Yildirim et al., 2019	EEG	15,188	1D-CNN	Keras	90.8
Hsu et al., 2013	EEG	2880	Elman RNN	–	87.2
Michielli et al., 2019	EEG	10,280	RNN-LSTM	MATLAB	86.7
L. Wei et al., 2018	EEG	–	CNN	–	84.5
Seo et al., 2020	EEG	42,308	CRNN	TensorFlow	84.9
X. Zhang et al., 2020	EEG	–	CNN	PyTorch	83.6
Supratak et al., 2017	EEG	41,950	CNN-BiLSTM	–	82.0
Phan et al., 2019	EEG	–	Multi-task CNN	–	81.9
Tripathy et al., 2018	EEG HRV	7500	Autoencoder	MATLAB	73.7
Biswal et al., 2018	PSG	10,000	RCNN	PyTorch	87.5
Xu et al., 2020	PSG	–	DNN	–	86.1
J. Zhang & Wu, 2018	EEG	–	CUCNN	MATLAB	87.2

2.10.1.3 Long Short-Term Memory

The LSTM, a specialized type of RNN developed by Hochreiter, gained popularity for its unique architecture addressing long-term dependency issues (Nifa et al., 2023). Widely used in sleep stage classification for handling variable-length sequences, LSTM dominates sleep staging studies (Ebrahimi & Alizadeh, 2022; Faust et al., 2018). Studies exploring LSTM's impact on sleep staging depth find a single hidden layer often sufficient for high accuracy in various applications. (Radha et al., 2018; Y. Wei et al., 2019; Yulita et al., 2017).

LSTM algorithms, widely applied in analysing time series data, find utility in domains like natural language processing, speech recognition, and handwriting recognition (Fu et al., 2021; Oh et al., 2018). Their architecture, with gates controlling information flow, enables long-term memory retention. The LSTM structure includes key components like the cell state, representing long-term memory, and input and hidden states. Gates, including forget, input, and output gates, regulate information flow (Nifa et al., 2023; Urtnasan et al., 2020). For more information about the LSTM, please Kindly consult Chapter 4 in 4.2.3.1 for detailed insights.

2.11 Research Gap

The current landscape of SA diagnosis faces formidable challenges attributed to invasive, time-consuming, and costly conventional methods, primarily the PSG conducted in sleep laboratories. PSG's limitations, including inconvenience and discomfort, underscore the need for alternative, non-invasive, and cost-effective diagnostic tools. This research identifies a critical research gap and positions the convergence of IoT and AI technologies as a promising avenue to address this challenge and reshape SA diagnostics. IoT devices such as wearables, smart beds, and smartphones have demonstrated their capability to collect diverse sleep-related data, encompassing heart rate, respiratory patterns, and snoring sounds. Simultaneously, AI algorithms, spanning ML and DL, exhibit potential in constructing predictive models for accurate SA detection. However, despite these advancements, a research gap persists in optimizing the integration of IoT and AI for optimal SA detection.

The identified gap prompts further exploration into the intricacies of IoT-AI integration, specifically focusing on defining effective sensor setups, refining data preprocessing methods, and selecting AI algorithms that ensure reliable SA detection. To address this gap comprehensively, clinical trials become imperative, serving to validate system performance, scalability, and usability in real-world scenarios. Moreover, the thesis emphasizes the necessity for investigating individual variations and comorbidities to enhance diagnostic accuracy. Recognizing the potential of real-time feedback and interventions within IoT-AI systems emerges as a critical area for improvement in SA treatment and management. This research endeavour aims to bridge these identified gaps, laying a robust foundation for the development of advanced SA diagnostic tools. The ultimate goal is to propel sleep medicine forward, offering enhanced diagnostic accuracy and, consequently, improving patient outcomes in the realm of sleep disorders.

Chapter 3 Environmental Benefits of Sleep Apnoea Detection in the Home Environment

The content in this chapter is based on a manuscript titled "Environmental Benefits of Sleep Apnoea Detection in the Home Environment" by Barika et al., (2022). The manuscript's primary objective is to evaluate the environmental consequences associated with the detection of SA, specifically focusing on the potential of Remote Monitoring (RM) as a solution.

This research discusses the environmental impact of SA detection methods and proposes RM as a solution. The document highlights the detrimental effects of SA on mental and cardiovascular health and the need for its detection as a public health priority. Currently, PSG, the gold standard diagnostic procedure, is resource-intensive and negatively affects sleep quality and the environment. The document suggests that RM using mobile communication, cloud computing, and AI could establish SA detection and diagnosis support services in the home environment, leading to improved clinical outcomes and reduced environmental impact. However, the adoption of RM technology faces barriers. The document reviews 113 scientific studies and finds that over half of the proposed RM-based SA detection systems use real-time signal processing, while 30% rely on measurement devices that require travel when the internal buffer is full. The establishment of SA detection services through RM technology could reduce travel, resource sharing, and environmental impact.

3.1 Introduction

SA is a prevalent sleep disorder affecting nearly one billion people globally (Corrigan et al., 2020). In developed countries, at least 20% of adults are estimated to suffer from SA (Banluesombatkul et al., 2019). SA is associated with various comorbidities, including high blood pressure (Kristiansen et al., 2021), CVD (Sweed et al., 2019), type 2 diabetes mellitus, and stroke (DM) (Gurrala et al., 2021; Kristiansen et al., 2021; San & Malhotra, 2021). While SA diagnosis currently relies on the AHI and clinical criteria, this approach has limitations. Overnight monitoring in a sleep lab is resource-intensive and contributes to environmental degradation. To address these challenges, RM technology, which integrates mobile communication, cloud servers, and artificial intelligence, has emerged as a promising and sustainable alternative for SA diagnosis. The widespread adoption of RM for SA detection is expected to improve clinical outcomes by enabling early and real-time SA detection, reducing hospitalizations, and decreasing waiting lists. However, it is crucial to consider the environmental impact associated with RM-based SA detection.

This work examines the potential environmental benefits of utilizing RM based SA detection services in the home environment. The authors argue that RM-based SA detection services can offer lower environmental impact compared to traditional methods of detecting sleep disorders.

This is primarily due to reduced travel for both patients and healthcare specialists, as well as the ability to share resources. The authors conducted a comprehensive review of 113 papers on SA detection systems and found that the key factor influencing the environmental impact of a system is whether the measurement evaluation is conducted online or offline. They discovered that over 50% of the reviewed RM-based SA detection systems employed online processing, while approximately 20% did not report this feature, indicating that at least 30% of the studies did not prioritize minimizing their environmental impact. The authors also observed that environmental considerations were rarely addressed in the reviewed articles, emphasizing the importance of promoting the environmental benefits of RM-based SA detection in the home environment.

3.2 Background

Sleep is characterized by a temporary suspension or altered state of consciousness, particularly during the REM sleep stage (Loh et al., 2020). However, direct measurement of consciousness is challenging, which poses difficulties in detecting sleep disorders. To overcome this, a wide range of physiological signals are typically recorded during a sleep study (Faust et al., 2019). These studies, often in the form of PSG, involve recording sleep-related data for at least one night, and manual analysis of the data can take up to 4 hours per night. With the emergence of RM-based SA detection services that can collect data over multiple nights without limitations, manual analysis by human experts becomes impractical and demanding. Therefore, an essential aspect of all SA detection services should include automated data analysis based on AI models.

3.3 Sleep Apnoea Detection in the Home Environment

In this section, we describe the evaluation process used to assess technologies for detecting SA in the home environment. To identify relevant research articles, we conducted a comprehensive search using Google Scholar, focusing on articles published between 2018 and 2022. This time frame was chosen to capture the latest advancements in AI, which is crucial in the context of SA detection. Using predefined Boolean search terms, we queried the database, specifically targeting the keyword "apnea home." The initial search yielded 179 matches, as indicated in Table 3.1. To ensure the selection of high-quality studies, we applied the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method, following the approach outlined by Faust et al., (2022). The PRISMA flow diagram, presented in Figure 3.1, illustrates the process of filtering and selecting articles. During the screening process, we excluded duplicate entries, review articles, conference papers, non-English publications, and submissions lacking appropriate findings related to automated SA detection. Through this rigorous selection process, a total of 65 papers were excluded, resulting in a final selection of 113 unique research publications for further analysis.

Table 3.1 Boolean search strings.

Title	AND (Full-Text and Metadata)	Database	No. of Studies
“Apnea home”	“Apnea home”	Google Scholar	179

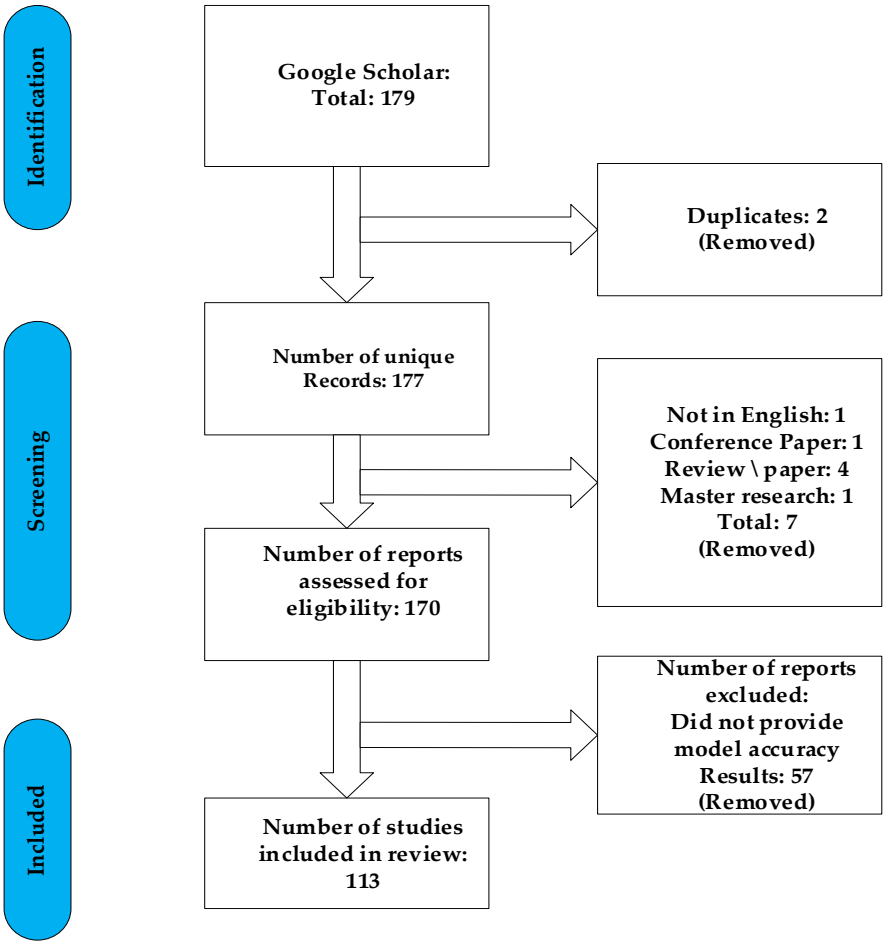

Figure 3.1 Flow chart of the PRISMA model for article selection.

3.4 Results

The article examines 113 studies on SA detection systems in the home setting and provides information on the signals used, detection methods employed, data handling, participant count, and detection performance. The choice of physiological signal used for SA detection significantly impacts the environmental footprint of the system, considering factors such as setup requirements, communication bandwidth, storage capacity, and processing power. Analysing the detection mechanism and participant count can help determine the technology readiness level of these systems.

Table 6.1 presents a summary of the SA detection performance and detection methods used in the 113 studies analysed. While some studies achieved high detection performance as measured by the ACC score, it is important to note that these findings were specific to the "apnea home"

examination and may not represent a general pattern across all studies. Duplicate items, review articles, non-English publications, master's theses, and works unrelated to the criteria were excluded from the analysis. Additionally, some papers meeting the criteria were identified through their abstracts during the search process. The analysis reveals the variety of signals employed in the research, each serving a unique purpose. The signals used in the SA detection studies include PSG, SpO2, home respiratory polygraphy (HRP), home polygraphy (HPG), ECG, seismocardiography (SCG), PPG, polygraphy (PG), respiratory inductance plethysmography (RIP), audio, and HR. Figure 3.2 provides a visual representation of the signals used across the 113 analysed studies. For additional details on these SA detection studies, Table 6.1 in Appendix 10 can be referred to. Figure 3.3 shows the SA detection methods used in the research, with the percentages in the pie charts indicating the number of studies that reported each technique.

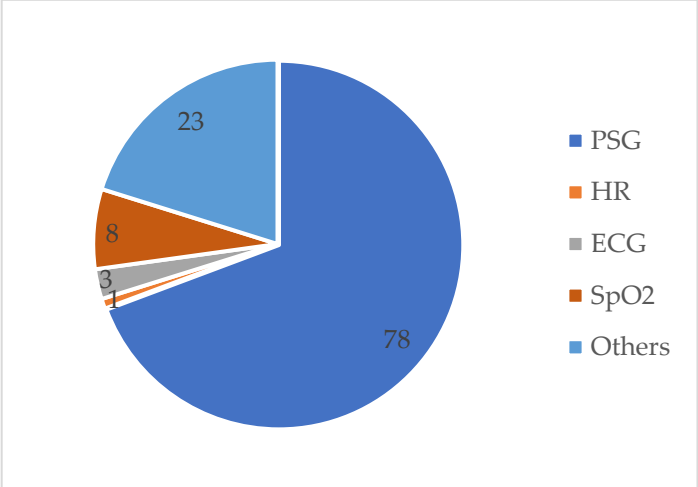

Figure 3.2 PGS, HR, ECG, SpO2, and others are the signals used to detect SA.

Among the 113 research articles analysed, PSG signals were the most explored method, with 78 articles utilizing this signal. ECG signals were used in only three studies, while HR signals were used in eight studies. SpO2 was employed in just one study. Figure 3.2 presents a pie chart illustrating the distribution of signal usage in the research articles. In terms of additional signals, 23 research articles utilized signals other than PSG, ECG, HR, and SpO2. ML and DL techniques were each applied in four studies. Among the 113 studies, sleep doctors were most frequently reported as the method for identifying SA, with 75 studies employing this approach. Figure 3.3 showcases a pie chart displaying the utilization of various SA detection methods. Regarding data management strategies, 48 studies did not report their data handling method, while 30 studies conducted their analysis offline, and 35 studies conducted it online. Figure 3.4 provides an overview of the data management strategies used in the studies.

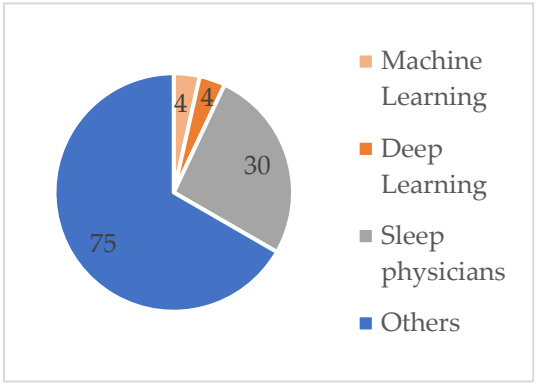

Figure 3.3 SA detection method.

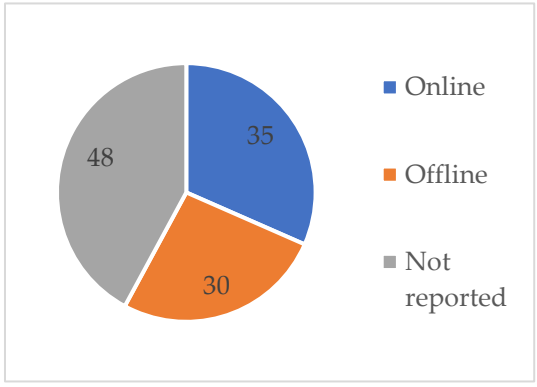

Figure 3.4 Data handling method.

Figure 3.5 presents the number of participants involved in the research, with a total of 101 participants, including 12 who opted out. Figure 3.6 depicts the distribution of accuracy reported in the studies. It also highlights the characteristics of 53 studies that did not report their accuracy and 60 studies that did report their accuracy.

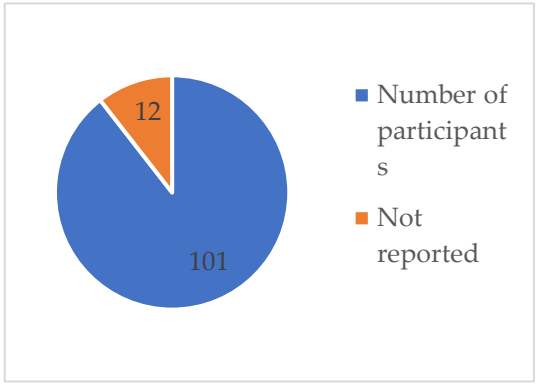

Figure 3.5 Number of participants reported.

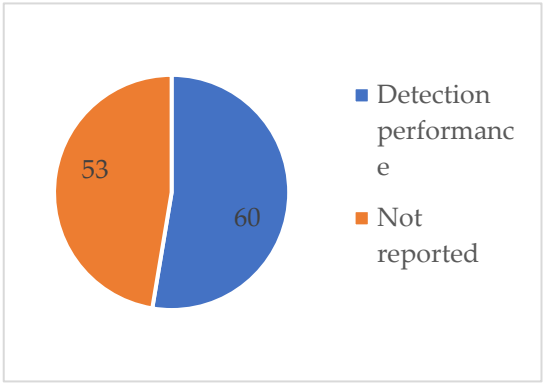

Figure 3.6 SA detection performance stated.

3.5 Discussion

This study focuses on the environmental impact of SA detection and highlights the challenges associated with traditional diagnostic testing conducted in sleep labs. The setup and supervision of data collection in sleep labs require significant resources, including the presence of a professional sleep technologist throughout the night. Furthermore, the analysis of collected data by a sleep physician can be time-consuming, leading to delays in obtaining results. The need for patients to travel to sleep labs also contributes to environmental drawbacks, such as increased carbon emissions and resource scarcity.

RM offers a promising solution to minimize travel and improve access to healthcare services. By employing RM for SA detection within the confines of one's home, automated detection becomes possible, thereby alleviating the requirement for physical travel while concurrently offering real-time monitoring. Advancements in technology, such as covert sensors, cloud computing, and increased internet connectivity, have greatly enhanced the monitoring and

management of human health (Dimitrievski et al., 2021). The IoT paradigm has revolutionized healthcare monitoring, with wearable technologies capable of tracking physical activity and heart rate. The widespread adoption of RM technology and increased internet connectivity further contribute to the expansion of RM in healthcare.

During our review, we examined the application of AI models in computer-aided SA diagnosis, as well as the use of RM systems for SA detection in home settings. Figure 3.1 provides an overview of the research output in AI models, indicating a growing focus on automated SA detection. This suggests an active field with ongoing advancements in tools and techniques for AI-based SA detection. The integration of RM methods further enhances the positive environmental impact. However, we also observed a significant development in DL for SA detection, which introduces uncertainty regarding its environmental impact. DL models typically have higher computational complexity compared to traditional ML models, raising concerns about their environmental footprint (Faust et al., 2018).

Our analysis of SA detection in the home setting revealed that PSG measurements are the primary source of objective data in most systems. However, this approach is not environmentally ideal due to the complex equipment and resources required for PSG signal measurements. For instance, the setup of measuring equipment often necessitates a nurse or sleep technologist to travel to the patient's home. In contrast, individual signals such as HR, ECG, and SpO2 are simpler to measure and require less setup than a complete PSG measurement. Among these individual signals, HR signal acquisition requires the least amount of setup, making it conducive to patient-led data acquisition. In this scenario, patients can install the sensor and ensure that the data is transmitted to a cloud server. The cloud server utilizes a DL model to automatically detect SA. Such a service would have minimal environmental impact since the communication infrastructure and cloud server facilities are shared and require very little additional energy. Considering environmental impact alongside moral considerations, technological feasibility, and financial expenses is crucial when evaluating SA detection systems.

3.6 Conclusions

The prevalence of SA is a significant economic and health concern, particularly in developed countries. To assess the environmental benefits of RM-based SA detection, the authors conducted a study examining SA detection systems in the home environment and evaluating the supporting technologies. The study emphasized the importance of physiological signals and their analysis in SA detection, with AI-based methods emerging as a promising technology. However, only a small number of studies 8 out of 113 utilized AI methods for SA identification, indicating the need for further advancement in this area.

The study highlighted the progress in SA detection and diagnosis assistance services using RM technology, which can be implemented without causing significant harm to the environment by leveraging existing infrastructure. While recognizing the important role of sleep labs in research and diagnosis of sleep disorders, the authors argued that RM enables early detection of SA with comparable or slightly increased resource utilization. As a result, the need for constructing new specialized sleep labs from an environmental perspective is reduced, as the existing infrastructure can be utilized, or the requirements significantly minimized. In summary, the integration of RM-based SA detection offers the potential for improved patient outcomes while minimizing the environmental impact associated with building new sleep labs.

Chapter 4 Methodology

4.1 Introduction and Background Integration

The methodology chapter draws heavily from Faust et al.,'s (2021) manuscript on "Accurate detection of SA with long short-term memory network based on RR interval signals," implementing a similar approach in a clinical study. It details the use of advanced techniques, notably the LSTM network, for precise detection of SA, emphasizing meticulous data collection, preprocessing, and validation phases to demonstrate reliability and effectiveness. The clinical study mirrors Faust et al.'s methodology, employing bidirectional LSTM models and comprehensive performance evaluation metrics like Receiver Operating Characteristic (ROC) analysis to achieve promising SA detection results. Illustrated in Figure 4.1 is a customized system configuration, showcasing each processing step as a block with arrows indicating data flow. Additionally, the chapter addresses identified weaknesses and gaps, presenting a clear methodology that outlines the evolution of initial ideas into concrete objectives and goals, alongside a summary of data collection and preprocessing activities, elucidating the refinement of research objectives over time. The LSTM method discussed aligns with that applied in a clinical study involving 15 patients, detailed in Chapter 5, with a summary of study activities, locations, and participating NHS organizations provided in Table 4.6 for reference.

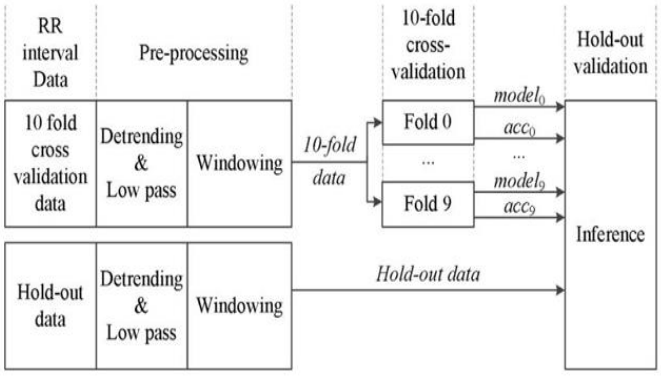

Figure 4.1 Block diagram for training and validating the DL model.

4.2 Collection and Preprocessing

This section delineates the types of data acquired for this research project, serving as the foundation for answering research questions and achieving stated objectives. The study's methodology primarily entails collecting data from secondary sources such as books, articles, journals, and online references. It outlines the key components employed in constructing the system, including details about the sleep datasets for model training/testing and experimental outcomes achieved using the bidirectional LSTM model. While the model had an existing

foundation, minor adjustments were implemented for enhanced performance. The primary data source was the Apnoea-ECG Database, sourced from various sleep studies (Goldberger et al., 2000; Penzel et al., 2000). The subsequent sections delve deeper into specific processing steps and data, offering a comprehensive insight into the study's methodology. This enables readers to understand the study's approach in detail.

4.2.1 RR Interval Data and Dataset Details

An RR interval is characterized as the duration between two successive R peaks, as depicted in Figure 2.11. These R peaks, in turn, signify the maximum amplitude within a given QRS complex. The QRS complex is defined as the deflections in an ECG tracing that indicate the ventricular activity of the heart. In this research, we employed a dataset comprising 35 records, each identified by labels like a01 through a20, b01 through b05, and c01 through c10. In this naming convention, the structure is clear: a letter signifies a specific category, while a numeric identifier distinguishes individual instances within that category. For example, "a01" represents an instance in class A, with the identifier 01, while "b02" indicates an instance in class B, with the identifier 02.

It's important to note that "a01" and "b02" serve as patient IDs. Therefore, in compliance with medical regulations, patient data must undergo anonymization processes. This ensures that sensitive patient information remains confidential and protected, adhering to strict privacy standards within the healthcare industry. This systematic approach aids in organizing and referencing data points efficiently during analysis and model training. Recording lengths slightly varied from just under 7 hours to 8 hours. The subjects, both men and women aged 27 to 63, had weights spanning 53 kg to 135 kg, corresponding to BMI values of 20.3 to 42.1. Table 4.1 offers signal details for both 10-fold cross-validation and hold-out validation. For model training, the 35 annotated ECG recordings of apnoea signals were categorized into two sets: a 10-fold data set and a hold-out data set. The latter included five records (a11, a15, a17, b01, and c07), while the remaining records were part of the 10-fold data set. Figure 4.2 exemplifies RR intervals within the first 1000 seconds of a01.

Table 4.1 Displays beat counts and signal names for both 10-fold cross-validation and hold-out validation data from the Physionet Apnea-ECG Database.

10-fold cross-validation No. beats=935462						**Hold-out-validation** No. beats=169959	
Name	Beats	Name	Beats	Name	Beats	Name	Beats
a01	29639	a12	33829	b05	26937	a11	32953
a02	34931	a13	39723	c01	27643	a15	33948

10-fold cross-validation						Hold-out-validation	
No. beats=935462						No. beats=169959	
a03	33966	a14	28212	c02	32137	a17	36131
a04	30902	a16	34948	c03	23758	b01	35081
a05	28740	a18	29970	c04	28089	c07	31846
a06	27199	a19	38738	c05	27957		
a07	37462	a20	34246	c06	28062		
a08	41102	b02	34877	c08	30360		
a09	31318	b03	28918	c09	31179		
a10	32263	b04	24379	c10	23978		

Additionally, Figure 4.3 displays the Power Spectral Density (PSD) of RAW RR interval data showcased in Figure 4.2. These visuals and information comprehensively acquaint readers with the dataset, aiding in understanding its distinct characteristics for training and validation purposes.

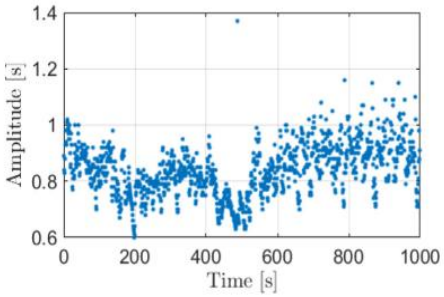

Figure 4.2 RAW RR interval data from record a01.

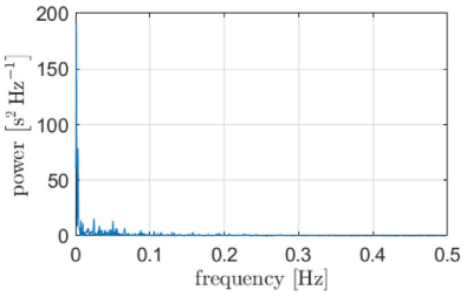

Figure 4.3 PSD of the RAW RR interval data.

4.2.2 Pre-Processing Steps

During this phase, the necessary data underwent processing to extract essential features, which were then input into the training model. Preprocessing RR interval signals for the 10-fold and hold-out data sets involved a two-step procedure. First, low-pass and high-pass filtering techniques were applied. RR interval signals underwent high-pass filtering through detrending, eliminating low-frequency components and noise, thereby enhancing signal clarity and quality. The second step involved windowing, segmenting RR interval data into fixed-length windows. The following sections elaborate on and visually represent the steps involved in processing the datasets.

4.2.2.1 Detrending and Low-Pass Filtering

In this study, we employed a specialized filter introduced by Fisher et al., (2012), to process the RR interval signal. This filter utilizes a third-order Gaussian process of the Ornstein-Uhlenbeck type, operating directly on the RR interval data. The filter's application aims to augment signal quality by reducing noise and unwanted variations. Figure 4.4 visually presents the filtered rendition of the raw RR interval signal from Figure 4.2. The filtered signal, a result of the (Fisher et al., 2012) filter, showcases enhanced smoothness and diminished noise in comparison to the raw signal.

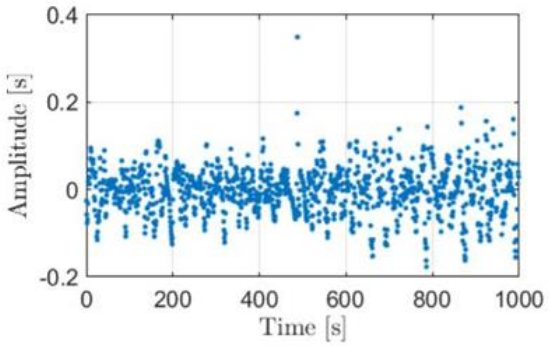

Figure 4.4 Detrended and low pass filtered RR interval data.

4.2.2.2 Windowing and Class Labelling

To segment the data for the classification algorithm, we implemented a sliding window approach with a window size of 100 RR intervals. The choice of a window size of 100 RR intervals was made to effectively segment the data for the classification algorithm. The window moves incrementally by one RR interval at a time. Essentially, this windowing technique constructs individual data blocks comprising 100 RR intervals for each beat in the database. This strategy enhances temporal resolution, ensuring an ample amount of data for effective training and testing of the DL algorithm. Class labels for windows were determined using a set threshold. Windows were categorized as apnoea (positive) if a minimum of 25 RR intervals within the window were identified as apnoea. Conversely, windows with fewer than 25 apnoea-identified RR intervals were labelled as non-apnoea (negative). Apnoea/non-apnoea annotations for individual RR intervals were sourced from the Apnoea-ECG Database.

4.2.3 10-Fold Cross-Validation

To ensure a robust evaluation of the DL model's performance, the study adopted a 10-fold cross-validation method. This choice aimed to minimize the impact of sample selection on overall results and provide a more comprehensive assessment of the model's efficacy by dividing the dataset into ten subsets for iterative training and testing. The labelled data was divided into ten folds, as depicted in Table 4.1. Among these, one-fold, Part 0, was designated

for network testing, while the remaining nine parts were used for training. This process iterated across all ten parts, enabling each part to function as a testing set once to evaluate the performance of the model. By adopting this strategy, every data point was involved in both training and testing sets, ensuring a more exhaustive evaluation.

Table 4.2 Summary of studies on algorithmic SA detection based on RR interval signals from records in the apnoea-ECG database.

Author	Classifier	Validation method	No. features	Acc. in %	Sen. in %	Spe. in %
Mendez et al., 2007	K-NN	Leave-One-Out	52	85.7	81.4	88.4
Surrel et al., 2018	SVM	10-fold	88	88.4	73.3	87.6
Bsoul et al., 2011	SVM	Variable-folds	111	88.49	96.77	83.62
Song et al., 2016	SVM+LR	10-fold	32	86.2	80.0	89.9
Hassan, 2016	Adaboost	10-fold	18	87.33	81.99	90.72
Janbakhshi & Shamsollahi 2018	Assemble	Cross-validation	85	90.90	89.60	91.80
De Chazal et al., 2003	LD/QD	Many-fold	52	92.5	91.4	93.1
Z. Dong et al., 2018	Threshold	Single fold	6	90.10	88.29	90.50
Wang et al., 2019	Residual network	10-fold	0	94.39	93.04	94.95
		Hold-out		80.60	–	–
Proposed method	LSTM	10-fold	0	99.80	99.85	99.73
		Hold-out		81.30	59.90	91.75

The data configuration for the 10-fold cross-validation is depicted on the left side of Figure 4.5’s flowchart. The right side of the flowchart showcases fold processing based on epochs. The model fitting strategy encompassed 40 epochs in total. During each epoch, the LSTM network underwent training on training data from each fold. Subsequently, the trained model was evaluated using corresponding testing data to gauge its performance. The primary metric for evaluating the model was the accuracy of the LSTM network's predictions. Upon completing all folds and assessing the LSTM network's performance for each, the "Select best model" block identified the optimum model based on prediction quality. This selection process involved considering accuracy to determine the K best models.

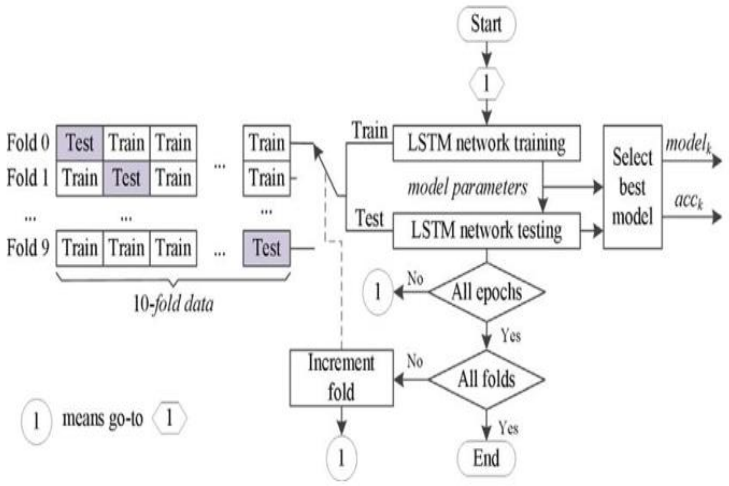

Figure 4.5 Flow chart for 10-fold cross-validation, where $model_k$ indicates the best LSTM model for fold *k*, similarly acc_k is the best accuracy for fold *k*.

4.2.3.1 Architecture and Bidirectional Model

Figure 4.6, illustrates the functional layout of the LSTM method, offering insights into the LSTM cell's inner mechanisms and the RNN loop's unrolling. The LSTM cell employs mathematical functions like the hyperbolic tangent function Tanh(...) and sigmoid activation function σ(...) for computations.

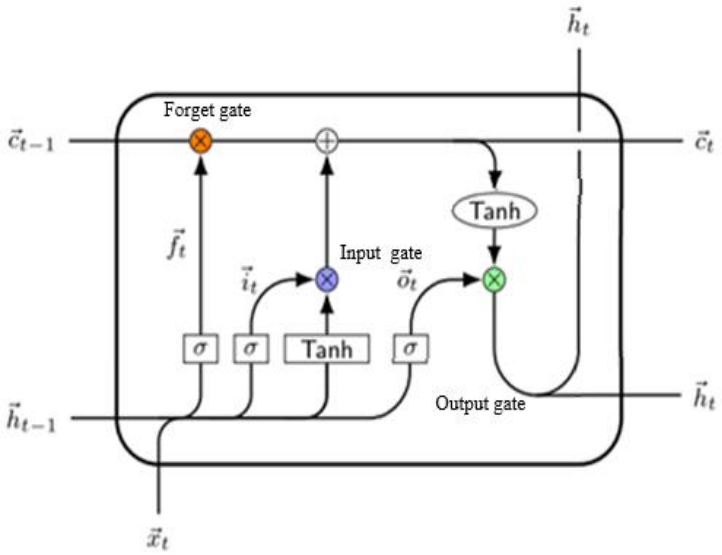

Figure 4.6 Structure of the LSTM memory cell.

The LSTM structure includes key components like the cell state, representing long-term memory, and input and hidden states. Gates, including forget, input, and output gates, regulate information flow. These gates perform specific functions: the input gate determines which data

from the current input should be stored in the memory cell, highlighted in blue. The forget gate determines which data from the previous cell state should be retained or discarded, highlighted in orange, and the output gate determines which data from the memory cell should be passed to the next hidden state, highlighted in green.

In the testing phase, the trained LSTM model classifies a 100 RR interval block to determine SA presence. The model employs learned weights and biases from the training phase for this classification. The utilized architecture, as presented in Table 4.3 features a bidirectional LSTM model (Graves & Schmidhuber, 2005). In this architecture, the RR input sequence undergoes forward processing using one LSTM model (i.e. samples x_0, ..., x_n) and backward processing using another LSTM model (i.e. samples x_n, ..., x_0). The performance evaluation methods for the LSTM model will be discussed in the next section, shedding light on how accuracy and effectiveness were gauged.

Table 4.3 Bidirectional LSTM architecture.

Layer	Type	Output shape	Number of parameters
1	Input	100, 1	0
2a	LSTM (forward)	200, 400	161600
2b	LSTM (backward)	200, 400	161600
3	Global 1D max pooling	400	0
4	Fully connected Rectified Linear Unit (ReLU)	50	20050
5	Dropout	50	0
6	Fully connected (Sigmoid)	1	51

The bidirectional LSTM model adopted in this study facilitates the capture of temporal dependencies in both preceding and subsequent timesteps, augmenting the model's contextual understanding, as illustrates in Figure 4.7. In the network, the outputs of the forward and backward LSTM models are combined through concatenation, forming a consolidated representation of the input data. This concatenated output is then subjected to one-dimensional global max pooling, providing a concise representation. To address overfitting and enhance generalization, recurrent dropout with a probability of 0.1 is applied to both LSTM cell inputs and hidden states. Additionally, standard dropout with the same probability is implemented between the final fully connected layer and the output layer. These dropout techniques serve as regularization mechanisms, preventing the model from relying too heavily on specific features or memorizing the training data (Semeniuta et al., 2016). Placing dropout after every hidden layer might excessively constrain the network's learning capacity, leading to diminished performance or slow convergence. It's typically more effective to carefully select specific layers

or portions of the network where dropout is applied, based on the complexity of the problem and the available data.

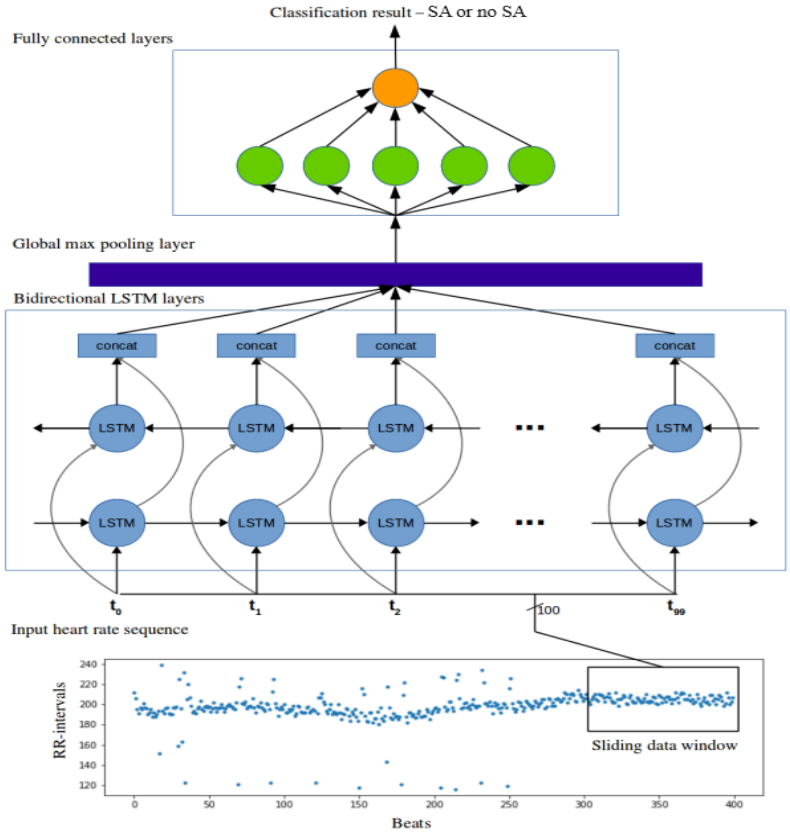

Figure 4.7 Bidirectional LSTM architecture used for SA classification.

In establishing connectivity between the "one" and "another" LSTM model, it is inferred that two distinct LSTM networks have employed one dedicated to processing the input sequence in the forward direction and the other in the backward direction. These bidirectional LSTMs collectively operate to capture information from both temporal directions, enhancing the model's ability to comprehend sequential dependencies. The decision to omit dropout layers following each hidden layer is posited as a strategic measure to mitigate excessive regularization. The deliberate exclusion of dropout layers at each intermediate stage aims to circumvent potential information loss, especially in the context of deep neural networks, where such layers could impede the model's capacity to discern intricate patterns and representations from the dataset. Consequently, the adopted methodology, involving judicious application of dropout after the LSTM cells and preceding the output layer, is deemed instrumental in striking an optimal balance between regularization and efficacious learning.

4.2.3.2 Training Strategy and Optimization

During model training, an Adam optimizer with a learning rate of 1e-3 is employed. The choice of the Adam optimizer with a learning rate of 1e-3 is justified for its adaptive optimization

capabilities. The Adam optimizer adjusts learning rates individually for each parameter, ensuring efficient updates during model training. This adaptability is particularly beneficial for handling varying gradients and achieving convergence effectively. The selected learning rate of 1e-3 strikes a balance between the need for accuracy in parameter updates and preventing convergence issues. It allows for a moderate adjustment at each iteration, avoiding overshooting or slow convergence. In terms of the batch size, 1024 is chosen to optimize graphics processing unit (GPU) memory utilization and training speed. While larger batch sizes can potentially expedite training, they may also demand more memory resources. The chosen batch size represents a practical compromise, ensuring efficient use of available resources without compromising training performance (Kingma & Ba, 2015). The models are developed and implemented using the Keras and TensorFlow frameworks. Keras offers a high-level API for network construction and training, while TensorFlow acts as the underlying computational framework, efficiently executing on GPUs and other hardware devices (Abadi et al., 2016).

4.2.4 Hold-out Testing and Optimization

In the validation phase, the optimal models from each fold are assessed using the hold-out data. This evaluation comprises consolidating predictions from each model, with their weights determined by their relative prediction accuracy. The weight factor for each model is calculated by multiplying its accuracy (acc_k) with the total number of model accuracies (*accAcc*). This multiplication captures the collective accuracy of all models and establishes the weight of each model in the aggregation process.

$$accAcc = \sum_{k=0}^{k-1} acc_{\mathrm{k}} \tag{4.1}$$

Equation 4.1 calculates the cumulative accuracy across all folds, with K denoting the total number of folds. The best model parameters garnered from these folds are utilized to compute the inference value. The weighted prediction outcome is derived by dividing the model's accuracy (acc_k) by the sum of all accuracies (*accAcc*).

$$inference = \sum_{k=0}^{k-1} \frac{predict(Hold\ out\ data, model_{\mathrm{k}}) \times acc_{\mathrm{k}}}{accAcc} \tag{4.2}$$

The function predict(data, model) employs the LSTM algorithm to make estimations for specific data using the model parameters. During hold-out validation testing, *the inference* outcomes are juxtaposed with the labels of the data blocks. The subsequent section delves into a discussion of these comparison results.

4.2.5 Performance Evaluation

In the evaluation of performance measures, this study employs both the confusion matrix and the ROC curve. The confusion matrix, also known as an error matrix, provides a tabular representation commonly used to assess the performance of a classification model when tested against a dataset with known true values. Simultaneously, the ROC Curve serves as a graphical representation that effectively summarizes the classifier's performance across a range of thresholds. This curve is created by plotting the true positive rate (TPR) against the false positive rate (FPR), on the y-axis and x-axis, respectively, while considering different thresholds for class assignment. It is noteworthy that the ROC curve is a widely recognized methodology for evaluating the diagnostic accuracy of tests in modern medicine. Its utility extends to demonstrating how effectively a diagnostic model can distinguish between the presence and absence of a disease, making it particularly adept at handling datasets with imbalances in class distribution.

This section showcases the outcomes of the proposed SA detection method, encompassing the findings from both hold-out and 10-fold cross-validation tests. Each test is accompanied by a confusion matrix that illustrates the counts of correctly identified normal RR intervals (TN), wrongly identified apnoea intervals (FP), wrongly identified normal intervals (FN), and accurately identified apnoea intervals (TP). These matrices offer a comprehensive overview of the classifier's performance. The classifiers' performance metrics are evaluated through accuracy, sensitivity, and specificity. Accuracy gauges the classifier's capacity to accurately differentiate between apnoea and normal events. It is calculated by dividing the number of correct predictions by the total number of predictions. To align the outcomes with true labels, a threshold of 0.5 determined by ROC analysis is employed. The evaluation of the proposed classification model involved an assessment of their performance. Table 4.3 provides a summary of the model parameters. The structure of the confusion matrix is as follows:

- True Negative (TN): Count of correctly identified normal intervals.
- False Positive (FP): Count of incorrectly identified apnoea intervals.
- False Negative (FN): Count of incorrectly identified normal intervals.
- True Positive (TP): Count of correctly identified apnoea intervals.

$$\mathrm{C} = \begin{vmatrix} TN & FP \\ FN & TP \end{vmatrix} \tag{4.3}$$

Typically, C is used to represent this confusion matrix to assess the performance of a model in terms of its true and false classifications. The assessment of performance involved measuring the following metrics to evaluate and analyse the effectiveness of the system:

$$\text{Accuracy} = (TP + TN)/(TP + TN + FP + FN) \tag{4.4}$$

$$\text{Sensitivity} = TP/(TP + FN) \quad 4.5$$

$$\text{Specificity} = TN/(TN + FP) \quad 4.6$$

In summary, the proposed SA detection method underwent evaluation using sensitivity and specificity metrics across various threshold levels. Sensitivity, representing the TPR, and specificity, representing the FPR, were computed to gauge the classifier's performance. The threshold value plays a crucial role in distinguishing between positive and negative outcomes.

4.2.6 Outcome Visualization

To analyse the outcomes comprehensively, we plotted the TPR against the FPR using a ROC curve. The visualization of the confusion matrix derived from the 10-fold cross-validation, as detailed in Section 4.2.3, is illustrated in Figure 4.8. The close agreement between the predicted and actual labels is evident, with a minimal number of false classifications observed. The chosen operating point maximizes the separation between the ROC curve and the dashed red line (Luck). This operating point corresponds to a threshold of 0.5, which is pivotal in determining the entries of the confusion matrix. Therefore, the closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test. With an Area Under Curve (AUC) of 1.00, the results are nearly perfect, indicating that the 1856 misclassifications reported in the confusion matrix hold little statistical significance. Figure 4.9 provides a visual representation of this result.

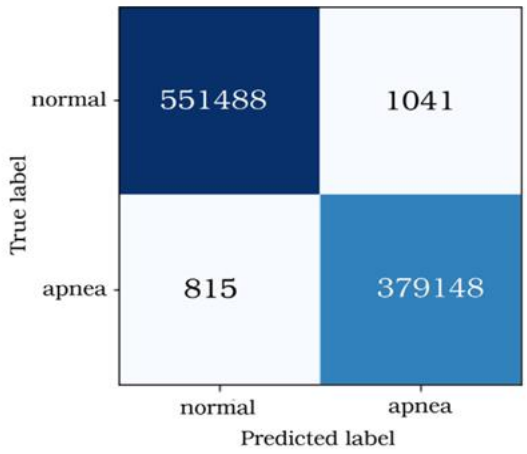

Figure 4.8 Confusion matrix for 10-fold cross-validation.

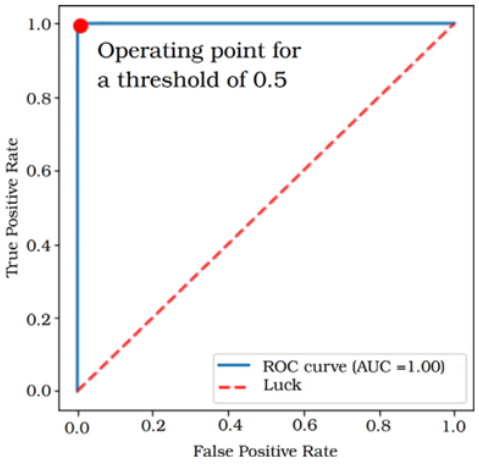

Figure 4.9 ROC for the 10-fold cross-validation test.

The depicted results in these figures were obtained by applying the model to validation sets and combining outcomes from all 10 folds. Table 4.4 displays the average performance across all 10 folds.

Table 4.4 The overall performance results of the LSTM model across the 10-fold cross-validation.

TN	FP	FN	TP	Accuracy	Sensitivity	Specificity	AUC
551488	1041	518	379148	99.80%	99.85%	99.73%	1.00

The outcomes of the hold-out validation approach are depicted in Figure 4.10 and Figure 4.11. Figure 4.10 showcases the accuracy of the test set plotted against the number of epochs, while Figure 4.11 visualizes the model's loss as it varies with the number of epochs. These graphs illustrate the LSTM algorithm's consistent and stable performance across folds, with minimal observable variance within the shaded regions.

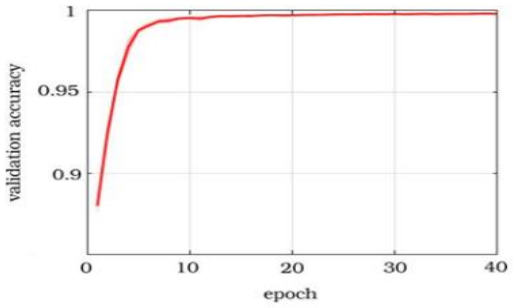

Figure 4.10 Shows mean accuracy over 40 training epochs (solid red line) for 10 folds, with shaded area indicating variance.

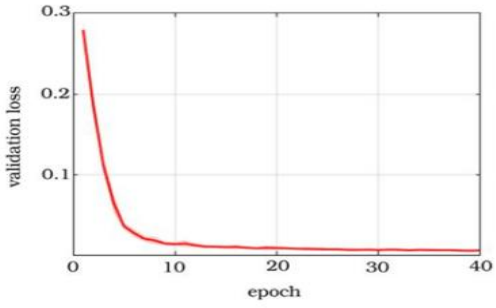

Figure 4.11 Illustrates mean validation loss over 40 epochs, with the solid red line denoting the average and shaded area indicating variance.

After identifying the top 10 LSTM models via 10-fold cross-validation, a hold-out validation procedure was executed, following the methodology outlined in Section 4.2.4. The resulting confusion matrix for the hold-out validation is presented in Figure 4.12, and the classification performance was assessed using the provided metrics. This figure illustrates the evaluation of the SA model for binary classifications. Data points represent the number of heartbeats detected for each class. The diagonal indicates the correctly identified TN's and TP's. However, the cross-diagonal refers to the FP's and FN's. The performance values obtained from the hold-out validation are shown in the last row of Figure 4.12. Additionally, Figure 4.13 presents the corresponding ROC curve, providing further insights into the classifier's performance.

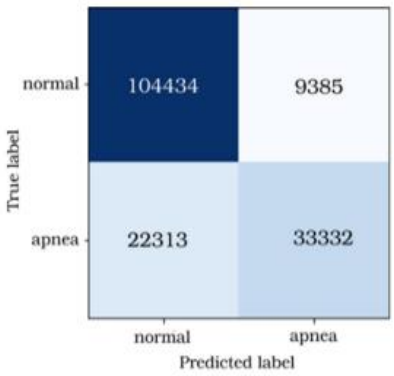

Figure 4.12 Hold-out confusion matrix.

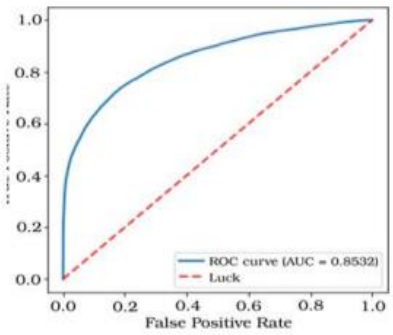

Figure 4.13 ROC for Hold-Out validation.

The outcomes reveal that the suggested LSTM classifier achieves an overall accuracy of 81.30% on a set of entirely new subjects, correctly identifying 59.90% of normal heart rate HR sequences and accurately classifying 91.75% of HR sequences indicating signs of SA. The outcomes from this holdout test set are presented in Table 4.5.

Table 4.5 The overall performance results of the LSTM model across the Hold-Out cross-validation.

TN	FP	FN	TP	Accuracy	Sensitivity	Specificity	AUC
104434	22313	9385	33332	81.30%	91.75%	59.90%	0.8532

In the ROC curve plot, the DL classifier attains an AUC of 0.85%. This indicates that the classifier effectively distinguishes between the presence and absence of SA episodes. The classifier's threshold values range between 0 and 1, where 0 represents TN values and 1.0 corresponds to TP. A ROC curve approaching 1 signifies a higher overall diagnostic accuracy, emphasizing the trade-off between TPR and FPR.

4.3 Setup and Validation of Sleep Apnoea Detection: Methodological Framework

This section outlined the clinical study conducted in collaboration with Sheffield Children's NHS Foundation Trust involved various methodological steps outlined in Table 4.6. These included recruiting patients, obtaining consent, setting up patient accounts on the Patient Status Engine (PSE) for data handling, providing PSG equipment and Lifetouch sensors from Isansys, conducting PSG tests, capturing heart rate using Lifetouch sensors, conducting participant interviews, and performing two-stage data analysis. The study's validation phase compared analysis outcomes, ensuring the accuracy and reliability of the methodology in detecting SA.

Table 4.6 Participating NHS organisation information.

Collaborating NHS Organization	Location
Sheffield Children's NHS Foundation Trust	Sheffield Children's NHS Foundation Trust
Study Activity	
1. Recruiting patients 2. Obtaining consent from patients 3. Setting up an account for each participant on the PSE from Isansys, used for data handling 4. Providing patients with PSG equipment and Lifetouch sensors from Isansys 5. Using Lifetouch sensors to capture heart rate 6. Conducting the PSG test 7. Conducting interviews with participants using a questionnaire 8. Two-stage data analysis: Stage-1 involves analysing PSG measurements by an experienced cardiologist. In Stage-2, heart rate recordings are analysed using DL systems developed by researchers from Sheffield Hallam University 9. Validation phase: Comparing analysis outcomes	

Figure 4.14, shows a timeline of the proposed validation study of the SA monitoring service. The timeline unfolded as follows:

1- Sign up. Patients registered at the sleep centre or sleep clinic.

2- Sensor placement. An Isansys Lifetouch sensor was connected to the subjects' body as depicted in Figure 5.1.

3- Physiological signal acquisition. The embedded Lifetouch sensor constantly measured the heart rate while the subject slept in the sleep lab. The signal was communicated via low power Bluetooth to a tablet computer at the bedside. That tablet computer relayed the data to a cloud application known as the patient status engine.

In addition to the Isansys measurement setup, the patient also wore the `normal' PSG measurement harness. This allowed us to measure both PSG and heart rate signals.

4- Sensor returns. After wearing the Lifetouch and PSG sensors for one night, the sensors were returned to a technical staff member.

5- Data upload. The PSG data was handled like for a normal sleep study. The data from the Isansys sensor was checked.

6- AI based SA detection. The heart rate data was fed to a DL algorithm which analysed the signal. The result of this analysis was an estimated SA probability over time.

7- Data analysis. An experienced human expert analysed the PSG recordings. The analysis results indicated time and duration of SA. These results were treated as the ground truth when it came to validating the SA detection algorithm. The validation was done by comparing the results from the human expert with the machine results.

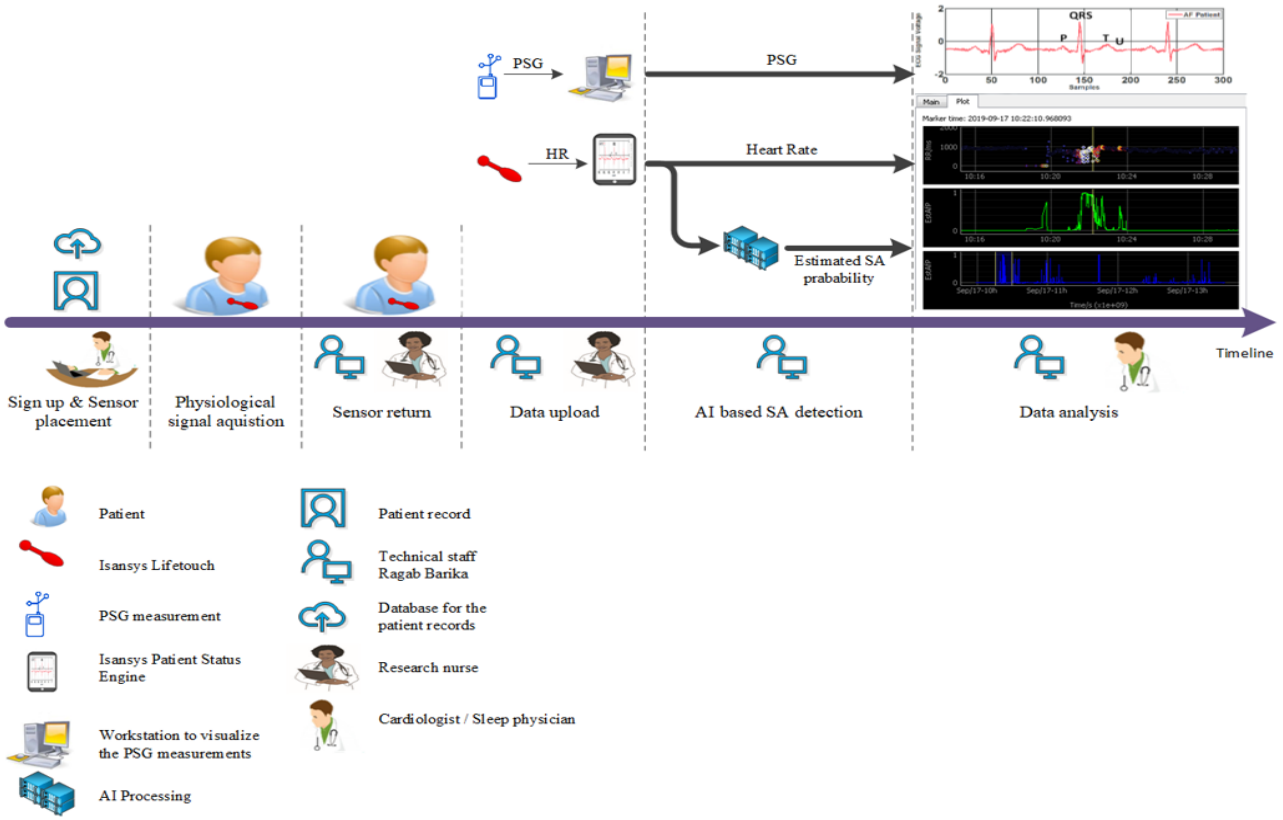

Figure 4.14 A timeline for SA monitoring service validation.

4.4 Patient Gateway

The Isansys Lifetouch system incorporates the Patient Gateway and the Isansys app to ensure efficient and secure access to the recorded data. Acting as a bridge between the Lifetouch sensor and electronic medical records, the Patient Gateway facilitates seamless integration and data exchange. This integration enables the incorporation of collected data into the patient's medical records, contributing to comprehensive healthcare management. For data access, the Lifetouch sensor pairs with an Android tablet via the Isansys app. This pairing process involves scanning a QR code on the sensor, establishing a secure Bluetooth connection. The tablet then wirelessly receives the sensor's data, which can be viewed through the Patient Gateway interface. This user-friendly approach enables healthcare professionals to conveniently access and analyse RR interval signals and other vital signs data.

Figure 4.15 visually represents the comprehensive PSE setup for continuous monitoring, emphasizing the connection process between the Lifetouch sensor, Patient Gateway, and the Android tablet. This visualization highlights the seamless data flow and underscores the secure transmission within the Isansys Lifetouch system. The integration of the Patient Gateway and Isansys app empowers healthcare professionals with real-time vital signs data. This capability enables close patient monitoring, informed decision-making, and rapid response to any changes in condition. The collaborative system optimizes patient care efficiency, contributing to improved diagnosis, treatment, and overall patient outcomes.

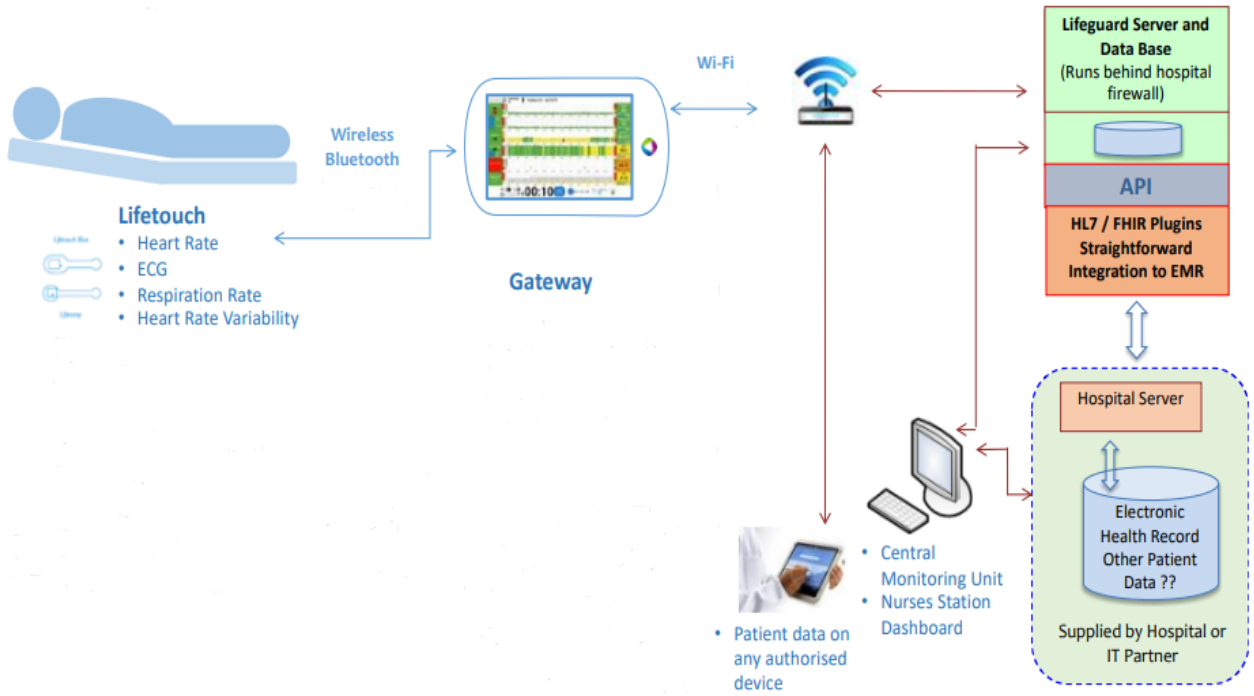

Figure 4.15 Patient gateway.[10]

[10] https://www.isansys.com/en/Patient-Status-Engine

Chapter 5 Detection of Obstructive Sleep Apnoea in Clinical Settings

Chapter 5 serves as a proof of concept for a novel method to detect OSA by integrating DL and IoT technologies. Conducted at Sheffield Children's Hospital NHS Foundation Trust between October 2022 and February 2023. The chapter summarizes the study's objectives, challenges in pediatric OSA diagnosis, materials and methods, pricing details, research design, participant recruitment, screening, statistical analysis, patient and public involvement, ethical considerations, study procedures, and safety assessments.

5.1 Overview of the clinical study

Between October 2022 and February 2023, a proof of principle study was conducted at Sheffield Children's Hospital NHS Foundation Trust to explore the feasibility of detecting OSA using wearable technology and DL. The study aimed to achieve three key objectives:

1. Patient and Public Involvement and Engagement (PPIE): Collect feedback from patients to gain insights into their experiences and perspectives.
2. Wearable sensor usability: Assess the usability of the wearable sensor used for data collection.
3. Accuracy evaluation: Evaluate the OSA detection accuracy of the developed DL algorithm by comparing its predictions with expert evaluations.

We developed a DL algorithm for OSA detection in RR interval signals. To evaluate its performance, we conducted a clinical study with 15 OSA patients. Simultaneously, patients underwent standard PSG monitoring, serving as a benchmark. This parallel approach ensured a robust evaluation of the DL algorithm's accuracy in OSA detection.

5.2 The Problem

Pediatric OSA, impacting 5% of children with airway obstruction and premature infants with central OSA, requires investigation into its prevalence, risk factors, and health effects. Current diagnostics like PSG pose challenges due to cost and reliance on specialized centres (Orr et al., 2017; Stokowski, 2005). There's a need for a user-friendly, accurate, and affordable home-based technology to detect apnoea events, addressing high demand and long wait times. Our research aims to enhance early detection, empower healthcare providers, and improve management of pediatric OSA to reduce negative outcomes.

5.3 Study Aims and Objectives

This study explores integrating the Isansys Lifetouch sensor with a DL algorithm to manage pediatric OSA. It aims to assess the usability and accuracy of this technology compared to the gold-standard PSG for detecting OSA symptoms in 15 pediatric patients. The main goal is to develop a DL algorithm that uses the Isansys Lifetouch sensor to measure RR intervals for

automated pediatric OSA detection. Data collected from the sensor is transmitted to a cloud server for real-time DL analysis to achieve efficient OSA diagnosis. The algorithm's accuracy, sensitivity, and specificity were validated against PSG through a clinical trial at Sheffield Children's Hospital NHS Foundation Trust. Additionally, the study evaluated the comfort and acceptability of the Lifetouch sensor among participants, with parental feedback assessing attachment ease and sensor acceptability for at-home monitoring. Clinical supervision by healthcare experts ensured accurate data collection and successful study implementation.

5.4 Materials and Methods

This section provides a comprehensive overview of the investigation procedures, including data collection, analysis, and study design. It aims to provide a detailed explanation of the practical components involved in the study. The following subsections will outline the key aspects of the research methodology.

5.4.1 Lifetouch Sensor

The Isansys Lifetouch sensor, customized for our pediatric OSA study, is a validated biosensor with extensive patient data in acute care settings. Developed collaboratively, it emphasizes ease of use, reliability, and integration into nursing workflows. Available in various sizes for newborns, infants, and children, this real-time monitoring device ensures uninterrupted monitoring during daily activities. Its continuous monitoring capability enables extensive data collection, providing crucial insights for OSA detection. Equipped with advanced signal processing, it enables real-time analysis, reducing the need for extensive post-processing. The sensor's accuracy in acquiring and analysing RR interval signals makes it valuable for investigating pediatric OSA. Its wireless design and wearability ensure comfort for pediatric patients. The experimental setup, illustrated in Figure 5.1, depicts a child with the Lifetouch sensor and signals on a tablet screen.

Figure 5.1 The Lifetouch sensor is used in conjunction with a tablet that runs the PSE software.[11]

[11] https://www.isansys.com/en/connectivity.

5.4.2 Pricing Details for Lifetouch Sensor Equipment and Services

The pricing specifics for the Lifetouch sensor equipment are outlined in Table 5.1, reflecting the standard pricing offered by the manufacturer. The Lifetouch service is priced at around £25 per day per patient. It's noteworthy that this cost covers not only the sensor itself but also includes the utilization of the PSE Gateway and the Lifeguard Server. This comprehensive package encompasses server infrastructure, security provisions, and connectivity, all calculated on a per patient per day basis.

Table 5.1 Lifetouch equipment cost.

Item	Sizes	Unit cost	Maximum duration of use
Isansys Lifetouch	Medium (175 x 47)	£25	3 to 5 days
	Small (140 x 47)	£25	
	Neonate (70 x 57)	£25	

5.4.3 Research Design and Data Collection

The study was conducted at the sleep house of Sheffield Children's NHS Foundation Trust in Sheffield, UK. This facility specializes in diagnosing sleep disorders and provides an ideal environment for collecting and analysing data for pediatric OSA detection using the Isansys Lifetouch sensor and the developed DL algorithm. The sleep house is fully equipped with advanced tools and resources necessary for conducting comprehensive sleep studies and monitoring various physiological parameters during sleep. A team of highly skilled healthcare professionals, including consultants, physiologists, technicians, nurses, research officers, project managers, and students, all with specialized training in sleep medicine and vast experience working with children, operate within the sleep house.

5.4.4 Sampling

Patients referred to the sleep house at Sheffield Children's Hospital NHS Foundation Trust for suspected OSA were invited to participate in the study. Selection criteria were established in Section 5.5.4 to ensure participants met specific age and suspected OSA requirements. The study aimed to enrol 15 to 20 participants, with 15 meeting the criteria and providing informed consent. Participant recruitment was determined by feasibility and eligible patient availability during the study period.

5.4.5 Participant Recruitment

At Sheffield Children's Hospital, a trained team engaged parents or guardians using Good Clinical Practice (GCP) principles for participant recruitment. They provided comprehensive information and consent forms, allowing ample time for review and questions. Consent was obtained through online meetings or phone calls, ensuring swift issue resolution. Written

consent, with assent from children when applicable, was prioritized to ensure understanding of the study's goals and processes. The process adhered to ethical guidelines, with transparency and collaboration encouraged through scheduled meetings. Utilizing the latest approved consent form Appendix 5 ensured accuracy, with signatures and dates documenting consent for transparency and accountability.

5.5 Participant Screening

The trial, including the six-month follow-up and exit, successfully concluded by March 2023, meeting the study timeline. Sleep onset and end times from PSG reports were used for data analysis, excluding non-sleep periods to align with study objectives. Of the 15 participants following the screening protocol, the average recording time was 7.0 hours, representing the duration of sleep monitoring and data collection per participant. Figure 5.2 visually summarizes participant flow, illustrating numbers at key study stages: screening, enrolment, follow-up, and exit, offering a concise overview of participant progression.

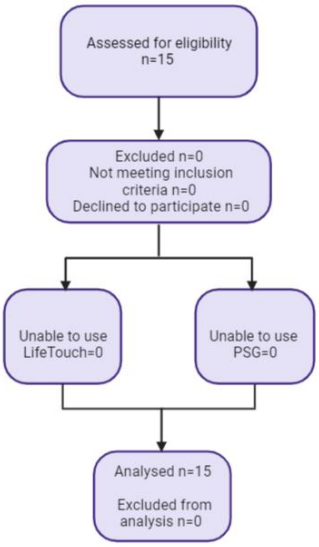

Figure 5.2 Trial screening, enrolment

5.5.1 Subject Characteristics

The study encompassed 15 eligible OSA patients, with a mix of 5 females and 10 males. The participants represented various ethnicities including White-British, Mixed White and black Caribbean, and Black African or Black British. Their ages ranged from 6 months to 16 years, with 50% aged over 5 years. Table 5.2 concisely summarizes patient characteristics, offering an overview of participants' gender, ethnicity, and age distribution.

Table 5.2 Participant information

Research ID	QR Code	Gender	Age	Weight	Ethnicity		Time in bed		Total Sleep (per hour in bed)
					White British	Black -Africa	Start time	End time	
LT001	B1208	F	5.10	Unknown	White British	-	20.16	06.57	6.57
LT002	B1423	M	2.6	Unknown	Unknown	-	20.10	07.55	7.55
LT003	B1247	M	9.8	Unknown	Unknown	-	20.01	07.32	7.32
LT004	B1424	M	2.7	Unknown	Unknown	-	19.59	06.32	8.39
LT005	B1425	M	2.5	Unknown	White British	-	19.20	06.47	9.19
LT006	B1381	M	11.11	Unknown	Unknown	-	20.02	05.53	6.56
LT007	B5687	F	1.11	Unknown	Mixed White and black Caribbean	-	20.33	06.40	4.57
LT008	B1380	M	3.9	Unknown	Black African or Black British	-	20.31	05.32	5.37
LT009	B1427	M	2.1	Unknown	White British	-	19.25	06.55	8.52
LT010	B1445	M	2.7	Unknown	Unknown	-	19.56	04.53	4.04
LT011	B1419	F	3.8	Unknown	Any other mixed background	-	20.59	05.39	6.14
LT012	B1422	F	13.5	Unknown	White British	-	21.01	06.48	7.22

Research ID	QR Code	Gender	Age	Weight	Ethnicity		Time in bed		Total Sleep (per hour in bed)
					White British	Black -Africa	Start time	End time	
LT013	B1451	M	8.6	Unknown	White British	-	20.19	06.50	9.27
LT014	B1454	F	1.4	Unknown	Any other mixed background	-	19.09	06.49	9.31
LT015	B1426	M	9.1	Unknown	White British	-	20.08	06.15	8.16

5.5.2 Statistical Analysis

Following the completion of the sleep study, a qualified clinical physiologist analysed recorded signals using established clinical methods aligned with the AASM's guidelines for diagnosing OSA. The analysis included assessing occurrences of central and obstructive apnoeas, calculating the AHI, and determining the longest central apnoea episode duration, shedding light on the severity and characteristics of OSA episodes. Simultaneously, an AI-based OSA detection algorithm processed heart rate data from the Isansys Lifetouch sensor, generating a diagnostic outcome based on heart rate patterns. Unaware of the clinical team's results, the research team used this analysis to estimate the probability of OSA over time for each participant.

5.5.3 Patient and Public Involvement and Engagement for Pediatric Obstructive Sleep Apnoea Monitoring

The thesis incorporates a PPIE initiative focusing on real-time pediatric OSA detection and monitoring. This initiative gathered parental perspectives on the necessity and desirability of such a monitoring device for children under the care of the Respiratory team at Sheffield Children's Hospital. Interviews were conducted via telephone with eight parents representing children aged 1 to 13 years from various regions. Each participating parent received a £20 gift voucher. The interview prompt sheet is available in Appendix 7. Parental insights emphasized the importance of continuous monitoring for accurate OSA diagnosis and expressed enthusiasm for remote data access, potentially eliminating overnight stays at sleep facilities. Parents valued features such as lightweight comfort, ease of use, and inconspicuous design, while also expressing concerns about potential data overload and the need for robust data security.

5.5.4 Participant Eligibility Criteria

Table 5.3 Outline who can join the study, considering factors like age, language proficiency, and medical conditions, while excluding certain situations, such as allergies.

Table 5.3 Inclusion and exclusion criteria applied in this study.

Inclusion Criteria	Exclusion Criteria
• Patients referred to a sleep clinic due to suspected OSA • Age range of 6 months to 16 years • Proficient in understanding spoken and written English • Capable of providing informed consent	• Individuals with communication challenges or non-English-speaking parents/legal guardians/carers • Known allergy to dressings with adhesives • Children anticipated to experience anxiety due to an additional sensor • Clinically deemed too unwell to participate by clinical staff

Inclusion Criteria	Exclusion Criteria
	• Presence of clinical issues, such as skin conditions, in the device placement area • Illiterate or unable to speak English and provide informed consent

5.5.5 System Specifications

The Lifetouch device, customized for this study, prioritizes lightweight and comfortable wearability, particularly during sleep. It integrates a tablet as the Patient Gateway for monitoring, enhancing factors like battery life and portability. Bluetooth technology enables seamless communication, eliminating restrictive cables. Weighing less than 20 grams, it ensures minimal discomfort or sleep disruption, aiming for a user-friendly solution for sleep studies and OSA detection.

5.5.6 Trial Management

The trial at Sheffield Children's Hospital NHS Foundation Trust involved a collaboration between Sheffield Hallam University and the hospital. Dr Oliver Faust and Dr Ningrong Lei from Sheffield Hallam University served as co-investigators, while Professor Heather Elphick led the trial as the chief investigator. Statistical analysis at the sleep house was supervised by Dr Ruth Kingshott, working alongside Professor Heather Elphick. This diverse team of researchers, clinicians, and statisticians aimed to advance understanding and management of pediatric OSA, ultimately aiming to improve patient outcomes through collaborative efforts.

5.5.7 Safety Assessments

The study at Sheffield Children's NHS Foundation Trust adhered to monitoring Standard Operating Procedures (SOPs) established by the Directorate of Research & Innovation. These SOPs ensure regulatory compliance and ethical guidelines are met. Regular monitoring and audits by the Sponsor, Health Research Authority (HRA), and Research Ethics Committee (REC) ensure the study's rigorous and ethical conduct, proper documentation, and adherence to approved protocols.

5.6 Ethical and Privacy Consideration

Upholding ethical standards was central to this study. Informed consent was obtained from all participants, and data handling followed strict privacy protocols to safeguard sensitive health information.

5.6.1 Ethical Approval

The research strategy was collaboratively developed by the researcher and their supervisor. Ethical review resulted in approval from the HRA and Health and Care Research Wales (HCRW) on January 6, 2022 (approval reference number: 21/SC/0366). HRA and HCRW approval indicates ethical acceptability, considering participant rights, safety, and well-being. Ethical considerations encompass participant recruitment, informed consent, data confidentiality, and potential risks and benefits. Appendix 2 contains the approved ethical documentation, detailing the protocols to be followed throughout the study.

5.6.2 Informed Consent

Trained study team members, who had prior experience and knowledge in GCP, obtained informed consent from participants. An invitation letter provided potential participants with comprehensive information about the study's objectives, procedures, and risks. It emphasized voluntary participation and the right to withdraw without consequences. Contact details for the study team were included for clarification. The invitation letter ensured participants were well-informed and empowered them to make informed decisions. Appendix 1 contained the invitation letter for further information on the study's details and informed consent.

5.6.3 Justification of Resources

The Lifetouch sensors utilized in this study were provided free of charge by Isansys, enabling their incorporation into the research project without incurring extra expenses. Sheffield Hallam University supplied all other essential resources for the study, ensuring efficient and effective research conduct.

5.7 Patient Information Sheets

Patients participating in the study received informational sheets in person or via post. These sheets included parent information and age-specific materials tailored to different age groups: under 5, 6-10 years, and 11-16 years. The research team assessed each child and parent to determine if obtaining the child's assent was appropriate. Participants were given sufficient time to review the information without time constraints. Study details were thoroughly explained to ensure clear comprehension of the purpose and procedures, with patients encouraged to seek clarification or ask questions by contacting the research team. This approach aimed to ensure that both participants and parents had all the essential information needed to make an informed decision about participating in the study.

5.8 Study Procedures

The study adhered to rigorous protocols, encompassing participant recruitment, data collection, and analysis. Ethical considerations were paramount in ensuring a secure and confidential research environment.

5.8.1 Interview with Health Care Professionals

Participants were informed that their involvement in this study was entirely optional, allowing them to withdraw at any point, even during the interview or when faced with uncomfortable questions, without needing to provide a specific reason. The study recognized and respected potential concerns or discomfort.

5.8.2 Questionnaire Content

The study questionnaire consisted of two pages, each for different participants. The first page targeted children, aiming to capture their experience and comfort during the study, with parental assistance if needed. The second page contained questions for parents, providing insights into their perspective on their child's experience. Participants also answered three questions related to the Lifetouch sensor to assess comfort and overall experience, using a five-point attitude scale to rate their agreement with statements. Detailed information about the questionnaire's content is available in Appendix 4, outlining the specific questions and response options.

5.8.3 Parent and Child Questionnaire

Participants, including both the child and their parent if applicable, received a questionnaire to gather perspectives on the Lifetouch sensor's acceptability, ease of use, and suitability for home use. Seven questionnaires covered various aspects of the study, ensuring comprehension with simple language and a font size of 14 points for readability. Appendix 4, provides detailed information about the questionnaire, including specific questions and response options.

5.8.4 Medical History

Participants' medical histories were meticulously reviewed to create thorough records of their medical conditions and surgical procedures. These records encompassed data from diverse sources, including sleep studies, apnoea monitors, sleep and breathing histories, and other pertinent medical records. For further details regarding the specific data sources and their utilization in the study, please consult Appendix 9. This appendix offers additional insights into the data collection process and the various types of medical records that informed the analysis.

5.8.5 Clinical Sleep Study Set-Up Procedure

Families of participants aged 6 months to 16 years were contacted and invited to join the study. Upon receiving consent (and approval for legally adult patients), a cardiologist gathered the

patients' medical history through a clinical examination. Subsequently, patients underwent a clinical sleep study at the hospital using standard equipment known as SOMNOscreen plus, which includes various monitoring components. Each patient was assigned a unique ID for efficient organization, with a checklist available in Table 5.2, to aid in tracking and management throughout the study.

5.8.6 Research Study Set-Up Procedure

The research procedure involves positioning a tablet beside the patient's bed and attaching the Lifetouch sensor to the child's chest. In cases involving post-pubescent female patients, assistance may be required due to breast tissue. The researcher ensures successful acquisition of physiological signals before leaving the room. Clinical staff monitor the child closely throughout the night for signs of illness or discomfort, with the option to remove the Lifetouch sensor if necessary. If the sensor is misplaced or removed and cannot be reattached, the child's participation in the study will be terminated. In the morning, all clinical sensors, including the Lifetouch sensor, are removed, and families are interviewed for feedback on their experience. Data, including heart rate measurements and PSG recordings, are uploaded and analysed by technical staff. Heart rate data undergo processing using a DL algorithm to estimate OSA probability over time, while PSG recordings are evaluated by a qualified professional for further diagnosis.

5.8.7 Conducting the Study at Sheffield Children's Hospital NHS Foundation Trust

On the first day of the study at Sheffield Children's Hospital, patients arrive at the designated time for an allergy test to ensure safety. Parents or guardians are briefed on the consent form, addressing any queries before signing to participate. Isansys equipment, including the Lifetouch sensor, is set up with clear usage instructions prioritizing comfort. Throughout the night, the study team monitors patients closely, addressing any concerns promptly. On the second day, equipment is collected, and parents or guardians complete a questionnaire about their child's sleep patterns, with the child also filling out a questionnaire if applicable. Before departure, a sign-out session clarifies any remaining questions, reinforcing understanding of the study procedures. Data collected is analysed and shared with healthcare providers for diagnosis and treatment decisions. For a detailed overview of study activities and locations, refer to Table 5.4.

Table 5.4 Visit schedule.

Day1	
Time (pm)	**Event**
18.00	Patient arrival
18.30	Allergy test

Day1	
Time (pm)	**Event**
18.35	Explain the consent form
18.45	Setting up the Isansys equipment
19.00	Set up for Nocturnal Polysomnogram
Day2	
Time (am)	**Event**
07.00	Take away the medical equipment
07.30	Sign out the Parent and child questionnaire

5.9 Results and discussion

In the realm of global healthcare, OSA stands out as a significant concern, often slipping under the radar due to inherent diagnostic complexities. This thesis boldly ventures into the domain of real-time detection methods, introducing a cutting-edge OSA detection system fortified by advanced technologies such as AI and the IoT. In addition to our study, conducted at Sheffield Children's Hospital NHS Foundation Trust, it's worth noting that patients were concurrently monitored and diagnosed using standard methods. Our research involved a thorough evaluation of a DL algorithm's effectiveness on 15 patients with a history of OSA. The primary aim was to assess its accuracy in comparison to PSG monitoring, a widely recognized standard in sleep disorder diagnostics. Prior to commencement, rigorous enrolment procedures were implemented, encompassing the dissemination of comprehensive study materials and the procurement of informed consent from parents, orchestrated under the guidance of the chief investigator. Additional study details are provided in Appendix 1, offering a deeper understanding of our methodology and approach.

5.9.1 Patient and Clinician Feedback

The PPIE initiative provided a rich source of insights into the perceptions of both patients and clinicians regarding real-time OSA detection. Participants expressed a strong acceptance of the technology's potential to monitor OSA in home environments, highlighting its convenience and comfort. The positive feedback regarding the ease of wearing the sensor underscores its user-friendly design, which is crucial for ensuring patient compliance and long-term usage. Moreover, the unanimous desire for continuous monitoring reflects a growing awareness of the importance of proactive healthcare management, indicating a shift towards personalized and preventive healthcare approaches. This feedback from stakeholders emphasizes the need for

patient-centered technologies and underscores the potential impact of wearable sensor technology on improving healthcare outcomes.

5.9.2 Challenges in Pediatric OSA Detection and Model Adaptation

Despite initial optimism surrounding the DL algorithm trained on adult data, its performance in detecting OSA in children fell short of expectations. This critical finding underscores the necessity for tailored models specifically designed for pediatric populations. While our system did not detect two cases of OSA that were diagnosed by sleep physicians, the study uncovered promising aspects regarding patient acceptance of Lifetouch wearables and the potential of DL algorithms for OSA detection. However, the limited identification of OSA cases among the 15 patients emphasizes the urgent need for continuous refinement and advancement of detection methods to bridge existing diagnostic gaps. The study's exploration of limitations associated with OSA detection using HRV-based models shed light on significant challenges. The utilization of a window size of 100 HRV by the LSTM model proved insufficient for capturing the relatively short duration of apnoea/hypopnea episodes observed in the clinical study. Additionally, the distinct characteristics of pediatric apnoea/hypopnea events compared to those in adults underscored variations in the definition and presentation of OSA in pediatric populations.

These insights underscore critical considerations for future research endeavors. Leveraging the full ECG signal instead of HRV may offer greater efficacy in detecting OSA, particularly in pediatric populations. Furthermore, the failure of the LSTM model to detect OSA highlights the necessity for tailored models trained specifically on pediatric data. While the study encountered challenges, it provides valuable insights into utilizing DL algorithms for OSA detection and the acceptance of wearable technologies among patients. However, the limited identification of OSA cases underscores the ongoing need for refinement and improvement of detection methods, emphasizing the complexity of accurately diagnosing SA.

The methodology employed in the study involved meticulous data collection and analysis procedures, integrating advanced technology such as the Isansys Lifetouch sensor for capturing physiological data during sleep and enabling real-time DL analysis of RR interval signals. Additionally, the study integrated a PPIE initiative, which provided valuable parental perspectives on the necessity and desirability of real-time obstructive OSA monitoring devices for children. Participants emphasized the importance of continuous monitoring for accurate diagnosis and highlighted the potential benefits of remote monitoring in alleviating stress and anxiety for both children and parents.

Furthermore, the economic implications of integrating the Lifetouch sensor technology into clinical practice were carefully considered. Transparent pricing details outlined in Table 5.1 facilitated a comprehensive understanding of the economic impact associated with this integration. Each patient's utilization of the Lifetouch service was priced at approximately £25 per day, covering the sensor, the PSE Gateway, and the Lifeguard Server. This transparent pricing model ensured seamless integration of server infrastructure, security, and connectivity for remote patient monitoring. Moreover, the availability of Lifetouch equipment in varied sizes, all priced at £25 per unit, accommodated diverse patient needs and usage durations, ranging from 3 to 5 days. This pricing strategy prioritized accessibility and affordability while upholding quality and functionality standards, enabling stakeholders to make informed decisions regarding healthcare resource allocation.

In addition to evaluating the accuracy of the DL algorithm, the study assessed the usability and comfort of the wearable sensor. Overall, the findings suggest that DL algorithms integrated with wearable sensor technology hold promise for improving the diagnosis and management of pediatric OSA. However, further research and refinement of these methods are warranted to enhance their accuracy and effectiveness in clinical practice. Furthermore, the study explored the broader implications of DL algorithms and wearable sensor technology beyond diagnostic accuracy. By providing continuous, real-time monitoring in home environments, these technologies offer a more accessible and convenient alternative to traditional diagnostic methods like PSG. Moreover, the integration of IoT-based solutions enables remote monitoring and data analysis, reducing the burden on healthcare facilities and improving patient outcomes.

The collaborative effort between academic researchers and healthcare professionals ensured the successful implementation of the study, from participant recruitment to data analysis. Key personnel played essential roles in overseeing the study's execution and analysis, contributing to its reliability and validity. Future research could enhance accuracy by incorporating additional physiological parameters, and ongoing efforts are needed to refine and expand automated OSA detection systems. Overall, the study's findings serve as a foundation for enhancing the accuracy and practicality of automated OSA detection systems in pediatric settings. Future research and implementation hold promise for advancements in accuracy and applicability, paving the way for improved diagnosis and management of pediatric.

Chapter 6 Conclusion

In this thesis, we conducted a comprehensive exploration into the detection and diagnosis of SA, recognizing its substantial global health impact affecting millions worldwide. By investigating SA's health implications, such as cardiovascular issues and daytime fatigue, we underscored the critical need for improved diagnostic methods. Through an in-depth examination of SA and its diagnostic challenges, we scrutinized the role of AI in healthcare, particularly its application in SA diagnosis. Motivated by the pressing demand for more accessible and precise diagnostic approaches, we identified the research problem and established clear aims and objectives to address this imperative. By formulating pertinent research questions, we guided our investigation towards meaningful insights, aiming to significantly contribute to the field by offering innovative approaches to tackle the diagnostic complexities of SA and thereby improve patient outcomes and healthcare practices.

Our research focuses on leveraging cutting-edge computing and AI technologies to enhance SA detection, motivated by the limitations of traditional diagnostic approaches like PSG. We propose CAD systems that integrate IoT and advanced AI to improve accuracy and accessibility. Through innovative techniques such as real-time detection for OSA and the development of high-performance detection systems, we address the shortcomings of conventional methods. While our clinical study involving 15 patients revealed lower-than-anticipated identification rates, it highlighted the potential of these methods to provide quick, reliable, and standardized analyses.

By evaluating IoT-based sensors, designing advanced data analytics techniques, and conducting comprehensive validation studies, our research significantly contributes to advancing SA diagnosis. The integration of IoT and AI technologies, particularly focusing on the Lifetouch sensor, promises to enhance diagnostic accuracy and management, aiming to transform diagnostic practices in sleep medicine. Collaboration between machine algorithms and human experts ensures safety, reliability, and efficiency in the clinical process, with ongoing research and optimization promising to further improve outcomes for individuals affected by SA worldwide.

Moreover, our study employed advanced techniques, particularly a LSTM network, for accurate SA detection, showcasing promising results with robust validation and optimization strategies, manuscript titled "Accurate detection of SA with long short-term memory network based on RR interval signals" authored by Faust, et al., (2021). We outlined a proposed method for detecting SA using RR interval signals, a key component in assessing HRV. This approach involves preprocessing the signal, filtering it, and segmenting it into blocks for classification using an LSTM network. The collaborative effort between machine algorithms and human expertise enhances the reliability and efficiency of SA diagnosis and treatment monitoring, promising continued advancements in sleep medicine and improved outcomes for patients affected by SA.

6.1 Research Limitations

While this thesis endeavours to provide innovative solutions for the detection and diagnosis of SA, there are several limitations that warrant acknowledgment.

Firstly, the sample size used in the clinical study, consisting of 15 patients with a history of OSA, may not fully represent the diverse spectrum of SA cases. A larger and more varied sample size would enhance the generalizability of the findings and provide a more robust assessment of the proposed technology model's efficacy. Secondly, although the Lifetouch sensor was evaluated as a promising tool for SA detection, its performance may vary in different populations and clinical settings. Further validation studies across different demographic groups and under varied environmental conditions are necessary to ascertain its reliability and effectiveness. Moreover, the proposed method for SA detection using RR interval signals and the LSTM network is based on specific assumptions and parameters. Variations in signal quality, patient characteristics, and other factors may impact the performance of the algorithm, necessitating continuous refinement and optimization.

Additionally, while the collaborative approach between machine algorithms and human experts holds promise for enhancing the reliability and efficiency of SA diagnosis, it also poses challenges in terms of implementation and integration into clinical practice. Addressing these challenges requires careful consideration of workflow dynamics, resource allocation, and training requirements. Furthermore, the focus on leveraging cutting-edge computing and AI technologies may inadvertently exclude certain populations with limited access to or familiarity with these advancements. Ensuring equitable access to diagnostic tools and interventions remains a crucial consideration in addressing the global burden of SA. Lastly, despite the efforts to streamline the clinical process and improve decision support, it's essential to recognize that SA diagnosis and treatment monitoring are multifaceted processes influenced by various factors beyond technological interventions. Factors such as patient compliance, socioeconomic status, and healthcare infrastructure play significant roles and should not be overlooked.

In summary, while this thesis represents a significant advancement in the field of sleep medicine, it is important to acknowledge these limitations and recognize the ongoing need for further research, validation, and refinement to realize the full potential of the proposed technologies and methodologies in addressing the complexities of SA detection and management.

6.2 Future Research

The future research will focus on advancing the field of SA detection and diagnosis by exploring innovative methodologies to overcome current limitations and deepen our understanding of this pressing global health challenge.

The initial phase of the research will concentrate on investigating the potential utility of full ECG signals for SA detection. Recognizing the shortcomings of relying solely on RR interval signals, the study aims to assess the feasibility of integrating complete ECG waveforms to capture additional physiological data. This approach holds promise for enhancing the accuracy of SA diagnosis by providing a more holistic insight into cardiac activity during sleep. Another pivotal aspect of the research will involve characterizing paediatric SA patterns and refining diagnostic criteria tailored specifically to this demographic. Acknowledging the notable differences between paediatric and adult SA, particularly in terms of event duration and diagnostic thresholds, the study will meticulously scrutinize paediatric SA patterns. By fine-tuning diagnostic criteria, the research seeks to better accommodate the unique characteristics of paediatric SA, thereby improving diagnostic accuracy and enhancing patient care within this population.

Methodologically, the research will entail the collection and analysis of extensive datasets comprising both adult and paediatric SA cases. Leveraging advanced signal processing techniques and machine learning algorithms, the study aims to extract relevant features from these datasets to accurately classify SA events. Additionally, a comprehensive literature review and meta-analysis will be conducted to identify gaps and inconsistencies in existing research on paediatric SA and diagnostic criteria. By synthesizing findings from various studies, the research aims to offer comprehensive insights into paediatric SA patterns and the diagnostic challenges encountered in clinical practice.

The subsequent phase of the research will involve the evaluation of full ECG signals for SA detection, presenting findings on both the potential advantages and obstacles associated with this approach. Comparative analyses with established RR interval-based methods will be conducted to assess the efficacy of full ECG signals in enhancing diagnostic precision. Furthermore, the results of the literature review and meta-analysis will be discussed, shedding light on the unique features of paediatric SA and emphasizing the necessity for tailored diagnostic criteria.

In conclusion, this future research thesis aims to make a significant contribution to the refinement of SA detection and diagnosis methodologies. By exploring the potential of full ECG signals and recalibrating diagnostic criteria for paediatric SA, the study endeavours to overcome existing challenges and facilitate the implementation of more precise and effective strategies for managing SA across diverse patient populations. Through meticulous data analysis and comprehensive literature review, the research seeks to advance our understanding of SA and ultimately enhance patient outcomes in clinical practice.

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Appendices

In this appendix section, additional information and supplementary material related to the main content of the document is provided. This includes detailed tables, figures, and graphs, as well as supporting documents such as informed consent forms, survey questionnaires, and other relevant materials.

Appendix 1 Parent/Legal Guardian Information Sheet

PARTICIPANT INFORMATION SHEET

FOR CHILDREN/YOUNG PEOPLE AGED 11 TO 15

Study title: Study to evaluate wireless sensors (Lifetouch) for identification of Paediatric Sleep Apnoea

We are asking if you would join in a research project to find the answer to the question "can the Lifetouch sensor diagnose sleep apnoea as well as the standard Polysomnography?". Before you decide if you want to join in, it's important to understand why the research is being done and what it will involve for you. So please read this leaflet carefully. Talk to your family, friends, doctor or nurse if you want to.

Part 1 – to give you first thoughts about the project

1. Why are we doing this research?

We want to try and find out if a new wearable device, called Lifetouch works just as well as the equipment that we use at the moment for sleep studies, called Polysomnography. If the research finds that Lifetouch is just as good as Polysomnography, then in the future, children might be able to have their sleep studies done using the Lifetouch which would be more comfortable and could be done at home.

2. What is the device that is being tested?

The Lifetouch sensor is a smart-patch that sticks onto your chest. It will remain there monitoring your breathing whilst you sleep.

3. Why have I been invited to take part?

You have been chosen because you may have sleep apnoea and you will be having a Polysomnography.

4. Do I have to take part?

No! It is up to you. We will ask you if you would like to take part and then ask if you would sign a form (this is called and "assent form"). We will give you a copy of this information sheet and your signed form to keep. You are free to stop taking part at

any time during the research without giving a reason. If you decide to stop, this will not affect the care you receive.

5. What will happen to me if I take part?

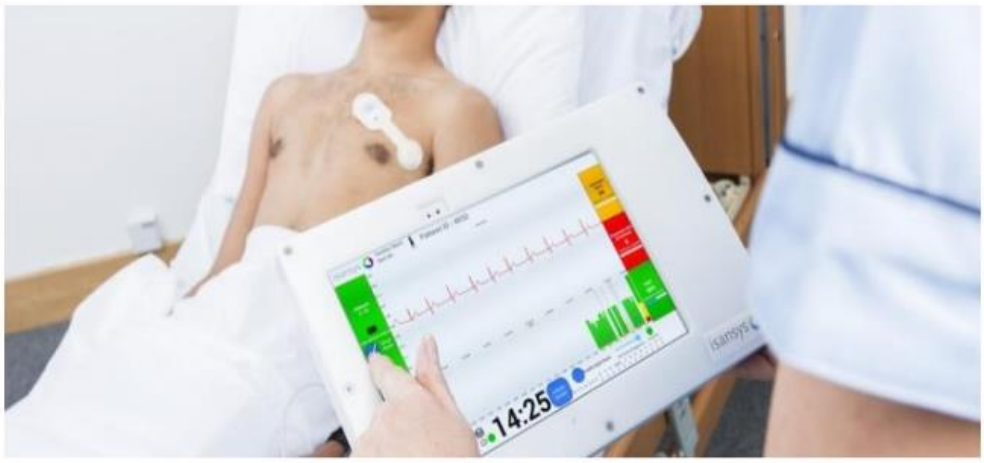
If you agree for your child to take part in this study, you will wear a small sticker on your chest that will monitor your breathing signals overnight. This will be in addition to the equipment for the Polysomnography that your doctor has asked for.

The Lifetouch sensor will be selected to fit you; it comes in various sizes. It will attach to your chest as shown in the photo below. Your parent or carer will be asked to stick it onto you, or you can do that yourself if you prefer. This is so that we can check whether it would be possible to use it at home in the future.

Your doctor will decide whether you have sleep apnoea based on the Polysomnography readings and the research doctors will work out what the diagnosis is from the Lifetouch sensor. Afterwards they will compare the results, to see whether the Lifetouch sensor got it right.

The research only lasts for the one night that you will be in the sleep unit. You do not need to come back to the hospital or have any other tests done.

Below is a picture of a child wearing the Lifetouch sensor, with the signals shown on a tablet.



6. What will I be asked to do?

You will not be asked for anything different other than the normal sleep test. When you wake up from your sleep test, the nurse or researcher will ask you a few questions about how comfortable the Lifetouch sensor was.

7. What are the possible side effects of the device?

There should be no side effects from wearing the Lifetouch sensor overnight. The sensor sticks to your chest and the feeling that you will have after putting it on will be very similar to the feeling of putting on a plaster.

Also, as with any plaster, when you remove it, there might be some redness or very mild irritation of the skin, which for some people can cause slight discomfort for a short period of time.

8. What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help diagnose and treat children and young people with Sleep Apnoea with better diagnosis tools and faster treatment in the future.

9. Contact for further information

Participant Information Sheet Age 11-15
The Lifetouch Study
Version 1.0, Date 16/3/21
Corresponding protocol version 1.0 and date 16/3/21
IRAS ID

TEMPLATE.R&D.37 (5) - INFORMATION SHEET 11-15.docx
Updated by Wendy Swann 06.04.16

*SCH3410

If you would like to know more about research in general, the Clinical Research Facility at this hospital has an **Information for families** section on its website www.sheffieldchildrens.nhs.uk/research-and-innovation.htm or you could contact the hospital Clinical Research Facility:

Dominic Nash
R&D Manager
Sheffield Children's NHS Foundation Trust
Tel: 0114 3053478

If you would like to know more specific information about this research project, please contact the project co-ordinator:

Professor Heather Elphick
Designation: Consultant Paediatrician in Sleep & Respiratory Medicine
Hospital/Department: Dept of Sleep and Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Tel: 0114 271 7400

Thank you for reading so far - if you are still interested, please go to Part 2:

Part 2 - more detail – information you need to know if you want to take part.

10. What happens when the research project stops?
If you withdraw from the study, we will destroy all your signals if you wish.

11. What if there is a problem or something goes wrong?
Tell us if there is a problem and we will try and sort it out straight away. You and your parent or carer can either contact Professor Elphick or the hospital complaints co-ordinator:

Julie Mather
Patient Advice & Liaison Co-ordinator
Sheffield Children's NHS Foundation Trust

Tel: 0114 271 7594

12. Will anyone else know I'm doing this?
We will keep your information in confidence. This means we will only tell those who have a need or right to know. Any information that leaves the hospital will have your name and address removed.

13. Who is organising the research?
This study is organised by Sheffield Children's Hospital and Sheffield Hallam University.

14. Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by <name of> Research Ethics Committee.

It has also been checked by the Research Department at this hospital.

Thank you for reading this – please ask any questions if you need to.

Appendix 2 Health Research Authority Letter of Approval

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Professor Heather Elphick
Consultant in Respiratory and Sleep Medicine
Sheffield Children's NHS Foundation Trust
Sheffield Children's Hospital
Western Bank
S10 2THN/A

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

06 January 2022

Dear Professor Elphick

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Feasibility study to evaluate wireless sensors (Lifetouch) for simplified identification of Paediatric Sleep Apnoea based on RR intervals**
IRAS project ID:	**299944**
Protocol number:	**N/A**
REC reference:	**21/SC/0366**
Sponsor	**Sheffield Hallam University**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **299944**. Please quote this on all correspondence.

Yours sincerely,
Nabeela Gaulton (nee Iqbal)
Approvals Specialist

Email: approvals@hra.nhs.uk

Copy to: *Dr Keith Fildes, Sheffield Hallam University*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Contract/Study Agreement template [mNCA]	2.2	01 January 2021
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance general certificate]		20 September 2021
IRAS Application Form [IRAS_Form_14102021]		14 October 2021
IRAS Checklist XML [Checklist_26112021]		26 November 2021
IRAS Checklist XML [Checklist_04012022]		04 January 2022
Non-validated questionnaire [Questionnaire]	2	04 January 2022
Organisation Information Document [299944 Organisation Information Document]	1	15 December 2021
Other [Response to ethics committee]	1.0	26 November 2021
Participant consent form [Consent]	2	26 November 2021
Participant consent form [Assent]	2	26 November 2021
Participant information sheet (PIS) [PIS 0-5]	2	26 November 2021
Participant information sheet (PIS) [PIS 6-10]	2	26 November 2021
Participant information sheet (PIS) [PIS 11-15]	2	26 November 2021
Participant information sheet (PIS) [PIS Parent]	2	26 November 2021
Research protocol or project proposal [The Lifetouch Study]	1.0	16 March 2021
Schedule of Events or SoECAT [Schedule of events]	1.1	15 September 2021
Summary CV for Chief Investigator (CI) [Research CV]		14 September 2021
Summary CV for student [RB CV]		14 July 2021
Summary CV for supervisor (student research) [OF CV]		19 July 2021

IRAS project ID	299944

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
There is only one participating NHS organisation therefore there is only one site type.	Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study.	An Organisation Information Document has been submitted and the sponsor is intending to use a separate site agreement. The agreement is unmodified.	No application for external funding will be made.	PI would be expected.	No Honorary Research Contracts, Letters of Access or pre-engagement checks are expected for local staff employed by the participating NHS organisations. Where arrangements are not already in place, network staff (or similar) undertaking any of the research activities listed in the IRAS form (except for administration of questionnaires or surveys), would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance. For research team members only administering questionnaires or surveys, a Letter of Access based on standard DBS checks and occupational health clearance would be appropriate.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 3 Authorization Letter of Access for Researcher

CCRF children's clinical research facility
innovative & pioneering treatments for children

Sheffield Children's NHS
NHS Foundation Trust

D Floor Stephenson Wing

Sheffield Children's NHS Foundation Trust

Western Bank, Sheffield S10 2TH

28th January 2022

Dear Ragab Barika

Letter of access for research:
SCH-2617: Feasibility study to evaluate wireless sensors (Lifetouch) for simplified identification of Paediatric Sleep Apnoea based on RR intervals

In accepting this letter, each participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on the **28th January 2022** and ends on **30th August 2024** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from Sheffield Children's NHS Foundation Trust. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving confirmation from the individual organisation(s) of their agreement to conduct the research.

The information supplied about your role in research at the organisation(s) has been reviewed and you do not require an honorary research contract with the organisation(s). We are satisfied that such pre-engagement checks as we consider necessary have been carried out. Evidence of checks should be available on request to the organisation(s).

You are considered to be a legal visitor to the organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation(s) or this organisation to employees and this letter does not give rise to any other relationship between you and the organisation(s), in particular that of an employee.

While undertaking research through the organisation(s) you will remain accountable to your substantive employer but you are required to follow the reasonable instructions of the organisation(s) or those instructions given on their behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by the organisation(s) in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with the organisations policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with the organisation(s) in discharging its/their duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on the organisations premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and each organisation prior to commencing your research role at that organisation.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 2018. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the organisations premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that the organisation(s) do not accept responsibility for damage to or loss of personal property.

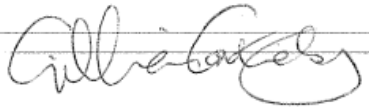
This organisation may revoke this letter and any organisation(s) may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of the organisation(s) or if you are convicted of any criminal offence. You must not undertake regulated activity if you are barred from such work. If you are barred from working with adults or children this letter of access is immediately terminated. Your employer will immediately withdraw you from undertaking this or any other regulated activity and you MUST stop undertaking any regulated activity immediately.

Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

No organisation will indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 2018. Any breach of the Data Protection Act 2018 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in Sheffield Children's NHS Foundation Trust and the R&D office in this organisation.

Yours sincerely



Dr Gillian Gatenby
Associate Director Research and Innovation

cc: HR department of the substantive employer

Appendix 4 Questionnaire Leaflets

Parent and child questionnaire

Study ID: _ _ _ _ _ _ _

For the child to answer (with the parent if needed)

1. Did the Lifesensor feel comfortable when it was on your chest? (Draw a mark on the line)

(Very comfortable) (Not comfortable at all)


I----------I

2. Did it hurt when the Lifesensor was taken off your chest?

(Didn't hurt at all) (Hurt a lot)


I----------I

3. Did you like the Lifesensor better than the other sleep equipment?

(Much better) (Much worse)


I----------I

Parent and child questionnaire

For the parent to answer

1. How comfortable did your child seem wearing the Lifesensor?

On a scale of 1 to 10 (1 being not at all comfortable 10 being extremely comfortable)

1 2 3 4 5 6 7 8 9 10

2. How easy was the Lifesensor to apply to your child's chest?

On a scale of 1 – 10 (1 being very difficult and 10 being very easy)

1 2 3 4 5 6 7 8 9 10

3. If the research shows that the Lifesensor can accurately diagnose sleep apnoea would you prefer this method to the existing diagnostic method if your child had to have another sleep study in the future?

On a scale of 1 – 10 (1 being wouldn't prefer and 10 being would prefer)

1 2 3 4 5 6 7 8 9 10

4. Please write below any specific comments, good or bad feedback about the Lifesensor system

Thank you very much for your time completing this questionnaire

.....
.....

Appendix 5 Parent Consent Form

46703

Trial Consent Form and Information Sheet

Sheffield Children's NHS
NHS Foundation Trust

Participant study number:

PARENT CONSENT FORM

Title of project: Feasibility study to evaluate wireless sensors (Lifetouch) for simplified identification of Paediatric Sleep Apnoea based on RR intervals

Name of researcher: Professor Heather Elphick

Please initial box

1. I confirm that I have read and understand the information sheet dated XX.XX.XX (version X) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of any of my child's medical notes and data collected during the study, may be looked at by researchers and those involved in the running and supervision of the study from Sheffield Children's NHS Foundation Trust or from regulatory authorities, where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
4. I understand that the signals obtained with the different systems used in this project might be used in the future for further research. These signals will not contain any personal information. ☐
5. I agree to my child taking part in the above study. ☐

The Lifetouch Study
Parent/ Guardian Consent form
Version 1.0
Date 16/3/21
Corresponding protocol version 1.0 and date 16/3/21
IRAS ID

*SCH3410

CONSENT FORM PARENT V1
Updated by Wendy Swann 06.04.16

Trial Consent Form and Information Sheet

Sheffield Children's NHS
NHS Foundation Trust

_____	_____	
Name of Parent/ Guardian	Signature	Date
_____	_____	
Name of Child	Relationship to Child	
_____	_____	_____
Name of Person taking consent	Signature	Date

When completed: 1 for participant; 1 (original) for researcher site file; 1 to be kept with hospital notes

*SCH3410

Appendix 6 Assent Form for Children & Young People

Sheffield Children's NHS
NHS Foundation Trust

46703

Trial Consent Form and Information Sheet

ASSENT FORM FOR CHILDREN & YOUNG PEOPLE

(To be completed by the child/young person and their parent/carer)

Title of project: **Feasibility study to evaluate wireless sensors (Lifetouch) for simplified identification of Paediatric Sleep Apnoea based on RR intervals**

Participant study number:

Child (or if unable, parent on their behalf)/young person to circle all they agree with:

Has somebody else explained this project to you?	Yes / No
Do you understand what this project is about?	Yes / No
Have you asked all the questions you wanted?	Yes / No
Have you had your questions answered in a way you understand?	Yes / No
Do you understand it's OK to stop taking part at any time?	Yes / No
Are you happy to take part?	Yes / No

If any answers are 'no' or you don't want to take part, don't sign your name!

If you do want to take part, you can write your name below

Your name _____ Date _____

The person who explained this project to you needs to sign too:

The Lifetouch Study
Assent form
Version 1.0, Date 16/3/21
Corresponding protocol version 1.0 and date 16/3/21
IRAS ID

*SCH3410

ASSENT FORM V1
Updated by Wendy Swann 05.04.16

46703

Trial Consent Form and Information Sheet

Sheffield Children's NHS
NHS Foundation Trust

_____	_____	_____
Name of Researcher	Signature	Date

Thank you for your help.

1 for participant; 1 for researcher site file; 1 to be kept with hospital notes

Appendix 7 A Copy of the Phone Interview Prompt Sheet for PPIE Activity

- What SA detection products or services do you know? What functions or features do you like or dislike, and why?

- Do you think a real-time SA monitoring and detection service is useful? What benefits and shortcomings can you predict?

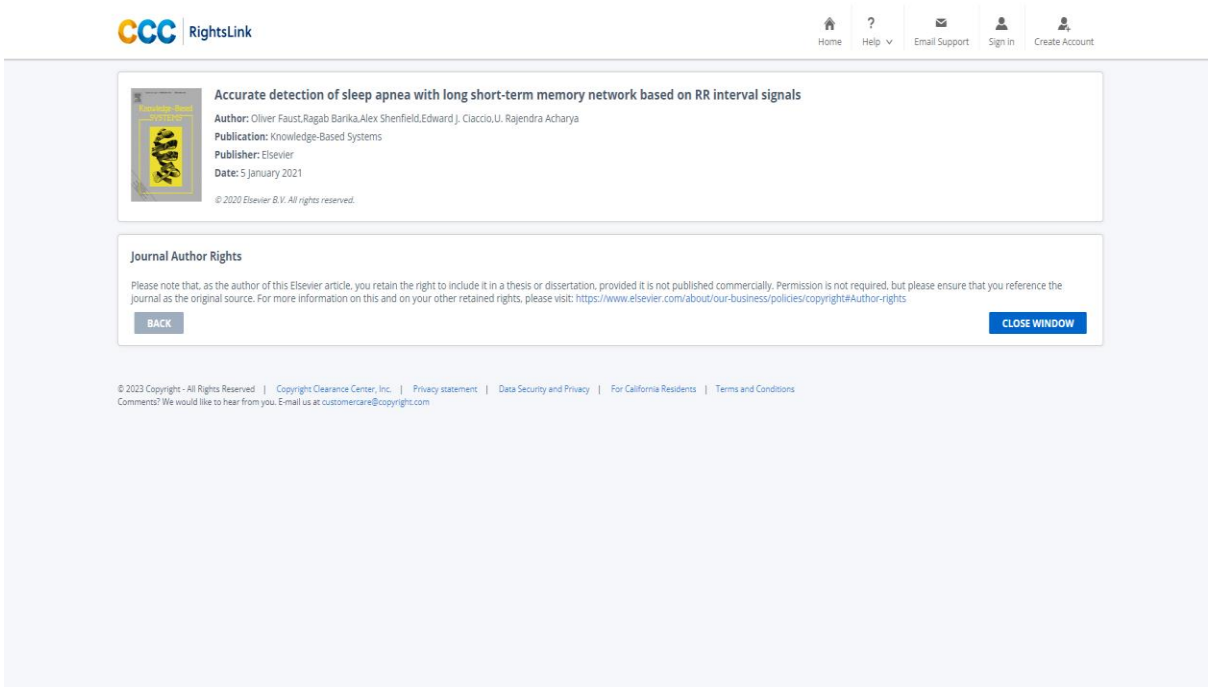
- What features would you like to have as part of the device or service?

- How long should the battery last?

- Would you like educational materials provided with the device or service?

- Do you have any privacy or other ethical concerns with storing and processing your electrocardiogram (ECG) signals?

Appendix 8 Journal Author Rights



Appendix 9 Patient Checklist

The Sleep Unit
Sheffield Children's NHS Foundation Trust

Sheffield Children's NHS
NHS Foundation Trust

SLEEP UNIT ATTENDANCE BOOKLET

SECTION 1 : PATIENT INFORMATION

	Date & Time	**Room**	**Consultant**
	Admitting staff member		
	Person accompanying child: **Full Name:** **Relationship to child:** **Contact Details:**		
	School / Nursery details:		
Like to be known as:			
GP Details:	**Other community / health professionals details:**		
Alerts (medical/safeguarding) *(staff to complete)*:			

SECTION 2 : CLINICAL ASSESSMENT

Height (cm)	**Weight (kg)**	**Allergies (tapes, medicines, food)**		
Moving & Handling Assessment **High / Medium / Low**	**Hoist** **Yes / No**	**Are they up to date with immunisations?**	**Yes / No**	
Are they fit and well for them?		**Current medication : Name / Dose / Frequency**		
Have they been in contact with any infectious illnesses in the past two weeks?				
Do they have any special feeding requirements				

Sleep Admission Document Version 2 18-05-2020

SECTION 3 : MEDICAL HISTORY	
Any relevant comorbidities (e.g. epilepsy, asthma, developmental delay)	
Any previous relevant surgery or investigations (e.g. home oximetry, adenotonsillectomy)	
Emergency care plan? Y/N	

SECTION 4 : SLEEP AND BREATHING HISTORY			
Snores	Yes/No/Occ	Difficulty Settling	Yes/No/Occ
Apnoeas or pauses in breathing	Yes/No/Occ	Restless overnight	Yes/No/Occ
Coughing	Yes/No/Occ	Restless legs; pains in legs	Yes/No/Occ
Mouth Breathing	Yes/No/Occ	Frequent awakenings	Yes/No/Occ
Morning Headaches	Yes/No/Occ	Sleep walking or sleep talking	Yes/No/Occ
Usual bedtime		Excessively sleepy in the daytime	Yes/No/Occ
Usual wake up time		Difficulty concentrating in the daytime	Yes/No/Occ
Other sleep related information (bottle feeds overnight, sleep behaviours to look out for, dummy etc)			

SECTION 5 : APNOEA MONITOR RECORD (please complete if the patient has an apnoea monitor)

Apnoea Monitor Alarm set at ☐ 10 seconds or ☐ 20 seconds

How often does the apnoea monitor alarm go off?

☐ Every night ☐ A few times a week ☐ Once a week
☐ A few times a month ☐ Every few months ☐ Not at all

SECTION 6 : NIV / TRACHEOSTOMY / OXYGEN REQUIREMENT (please complete if on therapy)

CPAP _____cm H20 BIPAP (I)_____/ (E)_____ cm H_20 Rate _____ Ti (s)____

Ventilator Make _____ Mask make and size _____

Tracheostomy Size _____ Suction Catheter Size_____ Neonate/Paediatric/Adult
Make: Bivona / Shiley / Other _____
Cuffed / Uncuffed

Oxygen Requirement _____ l/min Day / Night Nasal Prongs / Mask

SECTION 7 : SLEEP STUDY INFORMATION			
Reason for sleep study			
Sleep Study Type e.g. Full PSG		Special Instructions e.g. off NIV	
Time of set up		Set up completed by	
Consent to video	Yes / No	Consent to teaching	Yes / No
Please tick which sensors were attached			
☐ Nasal pressure	☐ Oronasal thermistor	☐ Respiratory Bands	☐ Body Position
☐ Oximetry	☐ ECG	☐ Transcutaneous CO2	☐ Snore sensor
☐ Leg EMG	☐ Chin EMG	☐ EEG	☐ EOG

SECTION 8 : OXYGEN INITIATION GUIDLINES				
SpO2 Standard Limits		Heart Rate standard limits	SpO2 Limits if different	Heart Rate limits if different
Upper Limit	100%	180 bpm		
Lower Limit	85%	60 bpm		

SECTION 9 : STAFF COMPLETING DOCUMENT		
Date	Name	Job Title

46703

Sheffield Children's NHS
NHS Foundation Trust

Sheffield Children's NHS
Foundation Trust
Western Bank,
Sheffield
S10 2TH

Consent to Clinical Videography and Sound Recording

Affix patient label or complete
SCH Hospital Number……
Surname……
Forename……
D.O.B……
Sex…… Post Code……
NHS Number……

Department:

Video Recorded by:

Date of Video Recording:

I hereby confirm that I give consent for video and sound recordings (the 'material') to be made of me/the above named child. I confirm that the purpose for which the material would be used has been explained to me in terms which I have understood and I agree to the use of the material in such circumstances. I understand that if the material is required for use in any other way than that explained to me then my consent to this will be specifically sought. I understand that my consent may be withdrawn at any time before, during or after the procedure and that this will not affect the level of care I receive.

I understand that the material will form part of my confidential treatment records and has value in clinical assessment and I agree to this use of the material. If my/my child's care is transferred to another health care provider a copy of these records including this material may be transferred also.

Signed: …… **Date:**……

Print Name:…… **Relationship to Patient:**……

I understand the material has value in medical education, and I consent to the material being shown to appropriate professional staff for the purpose of education, staff training and professional development within the department / external teaching (delete as appropriate).
I understand that any material used for external teaching may be uploaded onto the intranet by external sources and that It will not be possible to guarantee these images can be removed at a later date if consent is withdrawn. Images used in publications and teaching are anonymised (ie no names, DOB etc attached to the image)

Signed:…… **Date:**……

Print Name:…… **Relationship to Patient:**……

I confirm that I have explained to the patient/parent/guardian the nature and purpose of this recording in terms which they have understood, and which have been documented in the patient's notes.

Signature:…… **Date:**……

Print Name…… **Designation:**……

Version 2
May 2018
Filed within eDMS under Tab - Photos

SCH533000

Appendix 10 Additional Information on SA Detection Studies.

Table 6.1 Details of the 113 selected studies on SA detection in the home environment.

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Saletu et al., 2018	PSG	Sleep physicians	Online	265	-
Massie et al., 2018	PSG	Sleep physicians	Online	101	-
Rosen et al., 2018	-	Home sleep apnoea test	Online	-	-
S. S. Ng et al., 2019	PSG	Sleep physicians		316	Sensitivity = 78% Specificity = 23% Negative predictive value = 67% positive = 35%
Gu et al., 2020	SpO_2	Sleep physicians	Online	50	Sensitivity = 85% Specificity = 87%% Positive and negative predictive value = 0.88% and 0.83%
Chiner et al., 2020	Home respiratory polygraphy HRP	Sleep physicians	Online	121	Accuracy = 93%
Gutiérrez-Tobal et al., 2019	SpO_2	Machine learning AB-LDA	Offline	230	Accuracy = 78.7%
Zancanella et al., 2022	PSG	EmblettaX100 system	Offline	40	-
Manoni et al., 2020	PSG	MORFEA	Online	-	-
Kole, 2020		Home sleep apnoea testing	-	>800	-
R. Stretch et al., 2019	PSG	Sleep physicians	Online	613	Sensitivity = 0.46, Specificity = 0.95% Positive predictive value = 0.81% negative predictive value = 0.80%
Castillo-Escario et al., 2019a	PSG	MATLAB	Offline	13	Sensitivity = 76%, Positive Predictive Value = 82%
Hunasikatti, 2019	PSG	Sleep physicians	Online	206	-
Romero et al., 2022	PSG	Sleep physicians	Online	103	Sensitivity = 79% Specificity = 80%
Massie et al., 2022	PSG	WatchPAT	Offline	20	-
Kristiansen et al., 2021	PSG	Machine learning	Online	579	Accuracy = 89%

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Nobuaki Tanaka et al., 2021	-	W-PAT	-	776	-
Colelli et al., 2021	HSAT	Sleep physicians	Online	119	-
Ikizoglu et al., 2019	PSG and HPG	Sleep physicians	Online	19	Sensitivity = 100% Specificity = 83%
Aielo et al., 2019	PG	Sleep physicians	Online	300	Accuracy = 95%
Zavanelli et al., 2021	ECG, SCG, and PPG	Sleep physicians	Online	-	Accuracy = 95%
Colaco et al., 2018	PSG	Sleep physicians	Online	43,780	-
(Ekiz et al., 2020)	PSG	Sleep physicians	Online	43,780	-
Maggio et al., 2021	PSG	Embla® Embletta® GOLD portable sleep system	Online	45	Accuracy = 93%
Steffen et al., 2021	PSG and HST	Sleep physicians	Online	131	-
Orr et al., 2018	PSG and HST	MATLAB	Offline	27	Sensitivity = 70% Specificity = 71%
Gutiérrez-Tobal et al., 2021	SpO_2	Least-squares boosting algorithm	Offline	8762	Accuracy = 87.2%
(Fietze et al., 2022)	polygraphy (PG)	Sleep physicians	Online	505	-
Fitzpatrick et al., 2020	PSG	BresoDx® portable monitor	Offline	233	Sensitivity = 85% Specificity = 0.48% Positive and negative predictive values were, 0.81% and 0.54%
Ferrer-Lluis et al., 2019	Pulse oximetry	Apnealink™ Air	Offline	-	-
Huysmans et al., 2021	PSG	Total Sleep Time (TST)	Offline	183	Sensitivity = 78% Specificity = 89%
(Joymangul et al., 2020)	Positive Airway Pressure (PAP) therapy	Python	Online	668	-
Młyńczak et al., 2020	PSG	Audio sensor	Online	30	Accuracy = 86% Sensitivity = 96%, Specificity = 76%

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Van Pee et al., 2022	PSG and PAT HSAT	Sleep physicians	Online	167	-
Castillo-Escario et al., 2019b	audio signals	MATLAB	Offline	3	Accuracy = 95.9%
Navarro-Martínez et al., 2021	pulse oximetry	Epworth sleepiness scale, STOP-BANG questionnaire, and C-reactive protein screening	Online	117	Sensitivity = 80% Specificity = 92%
Patel et al., 2018	PSG	ApneaLink Air devices	Online	106	Sensitivity = 82% Specificity = 92%
Magalang et al., 2019	Nasal pressure	Fifteen HSAT	Offline	-	-
Muñoz-Ferrer et al., 2020	PSG	Sleepwise (SW)	Online	38	Accuracy = 84%
Light et al., 2018	EEG and PSG	Sleep physicians	Online	207	Accuracy = 95%
0Oceja et al., 2021	PSG	HRP	Online	320	-
Di Pumpo et al., 2022	-	WatchPAT	-	-	-
Hoshide et al., 2022	PSG	CPAP therapy	Online	105	Accuracy = 86.9%
Hui et al., 2018	PSG	Respiratory polygraphy	Online	-	Accuracy = 95%
Goldstein et al., 2018	PSG	Sleep physicians		196	Accuracy = 84%
(Jensen et al., 2022)	PSG	NightOwl™	Offline	150	Accuracy = 95%
Simonds, 2022	Body movement, respiratory rate, heart rate, snoring, and breathing pauses	Withings Sleep Analyzer	Online	67,278	Sensitivity = 88% Specificity = 88%
Rajhbeharrysingh et al., 2019	PSG	Machine learning	Online	14	Accuracy = 82.9% Sensitivity = 88.9%, Specificity = 76.5%
F. L. Facco et al., 2019	PSG	Sleep physicians	Online	43	80.0%
Kristiansen et al., 2021	PSG and PG	Sleep physicians	Online	34	Sensitivity = 97.2% Positive prediction value = 94.2%.
C. Li et al., 2021	PSG	Sleep physicians	Online	43,780	-

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Massie et al., 2022	PSG	MATLAB	Offline	261	Sensitivity = 87% Specificity = 89%
Hart et al., 2021	PSG	CPAP	Offline	18	-
da Rosa et al., 2021	PSG	Sleep physicians	Online	94	Accuracy = 80.7%
Ashley et al., 2019	PSG	HRP	Online	430	Accuracy = 95%
Mosquera-Lopez et al., 2018	PSG	Machine learning	Offline	14	Accuracy = 86.96% Sensitivity = 81.82% Specificity = 91.67%.
Lipatov et al., 2019	PSG	HSAT devices	Offline	141	-
Silva et al., 2021	PSG	SPSS software	Offline	427	-
Bonnesen et al., 2018	Audio	Portable device	Online	23	Sensitivity = 75%, Accuracy = 60%
Green et al., 2022	PSG	Online video technician	Online	100	-
Ben Azouz et al., 2018	PSG	Equivital™ EQ02 LifeMonitor	Online	32	-
Honda et al., 2022	Respiration activity	wearable sensor	Offline	-	-
Ghandeharioun, 2021	ECG and SpO_2	Sleep physicians	Online	155	Accuracy = 85%
Labarca et al., 2018	PG	HSAT an Embletta®	Online	198	-
Lee et al., 2021	PSG	HSAT	Offline	154	Sensitivity = 85% Specificity = 95%
Huysmans et al., 2020	ECG and RIP	CNN	Online	81	Kappa score = 0.48
Barriuso et al., 2020	Respiratory polygraphy	HRP	Online	301	-
Mashaqi et al., 2018	PSG	HSAT, RYGB and LSG	Online	10	Accuracy = 94%
Takao et al., 2019	Audio	Autoencoder	Offline	5	Accuracy = 94.7%
Borsini et al., 2021	PG	Apnea Link Plus and Air	Online	3854	Accuracy = 90%
Gu, W., & Leung, 2018	PPG	pulse oximeter	Online	23	Accuracy = 97%
Mieno et al., 2020	PSG	PulSleep LS-140	Offline	58	Sensitivity = 96.4% Specificity = 100%
Arguelles et al., 2019	PSG	HSAT	Online	88	Accuracy = 98%

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
R. Stretch et al., 2019	PSG	k-nearest neighbors algorithm	Offline	415	Sensitivity = 0.43% Specificity = 0.96%
Iqubal & Lam, 2020	PSG	HSAT	Online	88	Sensitivity = 98% Specificity = 76%
N Tanaka et al., 2020	PSG	WP device	Offline	774	-
Kay et al., 2021	PSG	HSAT	Online	1	-
Bollu et al., 2020	PSG	nox-T3 sleep monitor and Nomad HSAT	Online	178	-
Yeh et al., 2020	PSG	Sleep physicians	Offline	-	-
Sterner et al., 2020	-	WatchPAT	-	-	-
Iakoubova et al., 2020	PSG	Sleep physicians	Online	900	-
Arguelles et al., 2018	PSG	Sleep physicians	Online	60	Accuracy = 90%
Gamaldo et al., 2018	PSG	HSAT	Online	147	-
Alakuijala et al., 2019	PG	Sleep physicians	Online	1055	-
He et al., 2020	PSG	WatchPAT	Online	295	-
Pinheiro et al., 2020	PSG	HST	Online	1013	Sensitivity = 95.8% Specificity = 94.3%
Anderer et al., 2020	PSG	Deep Learning	Online	472	Accuracy = 95%.
Zeineddine et al., 2020	PSG	HSAT	Online	33	-
F. Facco et al., 2018	PSG	HST	Online	34	Accuracy = 90.5%
Zhongming et al., 2021	PSG	HSAT	Online	31	-
Carey et al., 2020	PSG	WPHST	Online	62	-
Aydin Guclu et al., 2020	PSG	APAP	Online	43	-
Homan et al., 2021	SpO_2	HSAT	Online	558	Accuracy = 90%
Rudock, R. et al., 2019	PSG	HSAT	Online	-	-
Bliznuks et al., 2022	SpO_2	CPAP	Online	16	-
THOMAS et al., 2021	PSG	HSAT	Online	297	-
Kazaglis, 2018	Audio	Noxturnal T3 device	Offline	2	-
Arguelles et al,, 2019	PSG	HSAT	Online	11	Accuracy = 95%
Fynn et al., 2020	PSG	sleep physicians	Online	246	-

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Wenbo et al., 2019	PSG	ring-type pulse oximeter	Online	32	Accuracy = 95.0%
Gutiérrez-Tobal et al., 2018	SpO_2	SAHS	Online	200	Sensitivity = 83.8% Specificity = 85.5%
R. J. Stretch et al., 2020	PSG	NN approach	Offline	1329	79%
Johnson et al., 2018	-	HSAT	-	-	-
Sever et al., 2018	PSG	Sleep physicians	Online	1	-
Martinot et al., 2020	PSG	Machine learning	Online	192	Accuracy = 84%
Haaland et al., 2018	PSG	Apnealink	Online	1021	-
Do et al., 2022	PSG	HSAT	Online	505	-
Stanchina et al., 2020	PSG	APAP	Online	238	-
Perriol et al., 2018	PSG	CPAP	Offline	66	-
Krause-Sorio et al., 2021	HR and SpO_2	Telephone screening	Offline	5	-
Mahmood et al., 2018	PSG	HST	Offline	454	-
Robinson et al., 2018	PSG	HSAT	Offline	961	Sensitivity = 97.1% Specificity = 100%
Ferreira, 2019	PSG	CPAP	Online	191	-

Appendix 11 Environmental Benefits of Sleep Apnoea Detection in the Home Environment

processes

MDPI

Review

Environmental Benefits of Sleep Apnoea Detection in the Home Environment

Ragab Barika [1], Heather Elphick [2], Ningrong Lei [1], Hajar Razaghi [1] and Oliver Faust [1,*]

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Abstract: Sleep Apnoea (SA) is a common chronic illness that affects nearly 1 billion people around the world, and the number of patients is rising. SA causes a wide range of psychological and physiological ailments that have detrimental effects on a patient's wellbeing. The high prevalence and negative health effects make SA a public health problem. Whilst the current gold standard diagnostic procedure, polysomnography (PSG), is reliable, it is resource-expensive and can have a negative impact on sleep quality, as well as the environment. With this study, we focus on the environmental impact that arises from resource utilisation during SA detection, and we propose remote monitoring (RM) as a potential solution that can improve the resource efficiency and reduce travel. By reusing infrastructure technology, such as mobile communication, cloud computing, and artificial intelligence (AI), RM establishes SA detection and diagnosis support services in the home environment. However, there are considerable barriers to a widespread adoption of this technology. To gain a better understanding of the available technology and its associated strength, as well as weaknesses, we reviewed scientific papers that used various strategies for RM-based SA detection. Our review focused on 113 studies that were conducted between 2018 and 2022 and that were listed in Google Scholar. We found that just over 50% of the proposed RM systems incorporated real time signal processing and around 20% of the studies did not report on this important aspect. From an environmental perspective, this is a significant shortcoming, because 30% of the studies were based on measurement devices that must travel whenever the internal buffer is full. The environmental impact of that travel might constitute an additional need for changing from offline to online SA detection in the home environment.

Keywords: sleep apnoea; artificial intelligence; polysomnography; remote monitoring; computer-aided diagnosis

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1. Introduction

Healthy sleep is necessary for children and adults [1]. Sleep is a vital physiological activity that accounts for around one-third of a person's life [2]. A good night's sleep can help people to be more productive at work and have a more positive attitude in life [3]. Sleep deprivation can lead to cardiovascular disease (CVD), including stroke and coronary heart disease, endocrine problems, amnesia, and inattention, all of which have a negative impact on regular working and living conditions [4]. This was confirmed by systematic reviews and meta-analyses that linked these problems to shorter sleep durations [5]. A report from the World Congress of Cardiology and Cardiovascular Health in 2016 stated that CVDs are the leading cause of death worldwide, with an estimated total of >17 million fatalities [5]. The detrimental effects of sleep disorders on both mental and cardiovascular health make sleep disorder detection a public health priority.

Sleep apnoea (SA) is one of the most common sleep disorders that deteriorates mental and cardiovascular health. It affects nearly 1 billion people around the world [6], and it is difficult to be diagnosed [7,8]. At least 20% of all adults in developed countries suffer

from some form of SA [9]. The disorder is characterised by periods of shallow breathing (hypopneas) or no breathing at all (apnoea) [1,7,10]. In comparison to the general population, patients with untreated SA have a higher mortality rate [8]. The disease is associated with several comorbidities [10,11]. It has a variety of symptoms that might interfere with everyday activities [10], can lead to high blood pressure [12], CVD [8,11], type 2 diabetes mellitus (DM), and stroke [1,12,13]. The prevalence and severity of its symptoms make SA a public health problem. There are three main types of SA events, namely central sleep apnoea (CSA), obstructive sleep apnoea (OSA), and mixed sleep apnoea (MSA) [10]. The most frequent type of SA is OSA, which is caused by an obstruction of the airway during sleep [14–16]. CSA is caused by the brain failing to provide the proper signals to the muscles that govern breathing during sleep [17]. MSA (also known as complex sleep apnoea syndrome) is a combination of OSA and CSA [18]. It is estimated that 80–90% of SA cases are undiagnosed [19]. Therefore, cost-efficient, and sustainable diagnostic pathways are essential for addressing this public health problem. SA diagnosis is based on the Apnoea–Hypopnea Index (AHI), which measures the number of apnoea and/or hypopnea occurrences during one hour of sleep [20,21], as well as clinical criteria such as the daytime sleepiness caused by apnoea-related sleep disturbances. Recently, it has been argued that the AHI is vulnerable to clinical fluctuation and that an alternate metric to determine the OSA severity is needed. The morphology and length of apnoeas are not taken into consideration by the AHI, which is a significant disadvantage. Although the AHI system of severity grading is far from perfect, it has survived because of software that makes computing the AHI easier [22,23]. Overnight monitoring in a sleep lab is a common part of an evaluation. A polysomnography (PSG), often known as a sleep study, is a multi-part examination that measures and records particular physical actions while the patient is sleeping. A skilled sleep specialist analyses the recordings to determine if SA or other sleep disorders are present [24]. However, this approach is resource-intensive because the facility must be built and maintained. Furthermore, patients and sleep physicians must travel to the facility. This travel, together with the efforts of building and maintaining the facility, have a significant environmental impact. That means the current pathways for a SA diagnosis contribute to pollution, contamination, and destruction of the natural environment. Many attempts have been made in recent years to find an alternative device or approach that avoids the limitations of PSG [25]. Replacing central sleep labs with services based on a distributed infrastructure might reduce the environmental impact of SA diagnosis. These services could be established through remote monitoring (RM) technologies that incorporate mobile communication, cloud servers, and artificial intelligence (AI) [26,27]. Initially, SA detection and diagnosis support services based on RM technology were driven by cost pressure and patient comfort [28,29]. Widespread RM deployment and the associated SA diagnosis support systems will assist users in making appropriate and timely therapeutic decisions [30]. This will enhance the clinical outcomes [31], early and real-time SA detection, cost efficiency through fewer hospitalisations, and waiting list reductions [32,33]. It is expected that RM for SA detection will grow significantly in the next decade [34,35]. Given these wide-ranging changes, it is important to consider the environmental impact in RM-based SA detection.

SA detection in the home environment is an emerging technology. We hypothesise that adequate technology choices can lead to positive environmental impacts for the large-scale deployment of patient-led data acquisition. In this review paper, we argue that RM-based SA detection services have a lower environmental impact when compared with the standard sleep disorder detection methods. This advantage comes from reduced travel, for both patients and healthcare specialists, as well as resource sharing. To be specific, a shared communication and processing infrastructure allows us to establish SA detection services that can complement and, in some cases, replace sleep studies in the sleep lab. Having established the general benefits of SA detection services, we have turned our attention to specific systems that enable functionality of the service by reviewing 113 papers on that topic. The reviewed systems used a wide range of signals and methods for SA detection

in the home environment. As a result, these systems had varying levels of practicality. With respect to the environmental impact that arises from deploying specific RM-based SA detection systems, the most important property was whether the measurement evaluation was done online or offline. In general, offline systems require more effort to initiate and maintain the measurements. Moreover, offline measurement durations are limited by device-specific properties such as the available memory within the sensor. Online systems do not have this restriction. Furthermore, it is more difficult to establish resource sharing with offline systems compared to online systems. In this review, we established that just over 50% of the RM-based SA detection systems used online processing, and around 20% did not report that important property. That means at least 30% of the studies do not minimise their environmental impact. Another important finding of this review is the fact that environmental concerns did not feature in the reviewed articles. All the research work was driven by medical needs. Understanding, and indeed promoting, the environmental benefits of resource sharing and less travel through RM-based SA detection in the home environment might lead to more research funding being made available to create practical problem solutions. To the best of our knowledge, this is the first work that has established the environmental benefits of SA detection in the home environment.

The remainder of this manuscript is organised as follows. Section 2 provides some background on the methods used to detect SA in the home environment. Section 3 describes our article search methodology, while Sections 4 and 5 give our discussion and findings, respectively. Section 6 concludes the manuscript.

2. Background

Sleep is characterised by the suspension of consciousness or, during Rapid Eye Movement (REM) sleep, altered consciousness [36]. Unfortunately, there is no direct measurement of consciousness. This makes sleep disorder detection difficult. Therefore, a wide range of physiological signals is captured during a sleep study [37]. Usually, such a sleep study takes the form of a PSG. A PSG is recorded for at least one night, and the manual data analysis for each night can take up to 4 h. RM-based SA detection services are expected to acquire data over several nights—some systems have no restrictions on the amount of data they can acquire. Therefore, the manual analysis of data delivered by RM systems would be too demanding for human experts. Hence, an integral part for all SA detection services should be automated data analysis based on AI models. In the remainder of this section, we discuss the individual topics in detail.

2.1. Physiological Signals Used for Sleep Apnoea Detection

Physiological signals reveal how processes, within the human body, unfold over time. Such signals can provide objective evidence for transient disorders where symptoms are not always present. The American Academy of Sleep Medicine (AASM) has recommended the use of both a nasal cannula and a thermistor for the scoring of apnoeas and hypopneas since 2007 [38]. Hence, physiological signals are used for SA detection. As an alternative to the PSG, for the diagnosis of SA, signals can be observed on an oxygen saturation (SpO_2) recording alone if analysed by an experienced physician. The Heart Rate Variability (HRV) and an Electrocardiogram (ECG) can also indicate a suspicion of SA.

2.1.1. Electrocardiogram (ECG)

An ECG is used to diagnose a variety of cardiovascular disorders, including coronary heart disease and cardiac arrhythmias. ECG signals are recordings of the electrical activity of the human heart over time [16]. Several research studies have found that ECGs from different people have some similarities, indicating that using only ECG sensors can achieve a good SA detection accuracy. However, due to the low sensitivity and specificity, this measure is not used alone in clinical practice but is observed alongside measurements such as respiratory airflow and SpO_2 [9,39]. In the absence of heart diseases, ECG signals are highly structured, and individual signal components can be identified through visual

inspection. The ECG trace is made up of several waves that are labelled P, QRS, and T. Each wave corresponds to a different physiological event during the cardiac cycle [7]. The breathing rate is linked to the heart rhythm via the autonomous nervous system [40]. It was observed that, when breathing stops, the heart rhythm slows down [41]. As the time with no breathing increases, the subject becomes tense, and the heart rhythm speeds up again. Morphological variations in the ECG signals reflect these changes. Hence, these signals can be used as an objective measure to detect SA [42].

2.1.2. Heart Rate (HR)

A HR signal is composed from consecutive beat-to-beat intervals of the human heart [43,44]. As such, the HR is the most widely measured physiological signal [45,46]. The beat-to-beat intervals are usually extracted from either an ECG or photoplethysmogram (PPG) signals [47]. HRV is a physiological parameter that measures the variations in the time interval between consecutive heartbeats in milliseconds. It is regularly measured to provide objective evidence that supports a CVD diagnosis, since it is linked to heart health. High HRV values are often connected with a healthy cardiac condition, and so, a lower death probability can be established. SA episodes change the heart rhythm, and these changes will be reported by the HRV directly. It is possible to detect these changes and thereby establish an objective measure for SA. However, gender and age of the patient may have an impact on the HRV [48]. An important environmental benefit of HR measurements arises from the fact that the human heart beats around once every second. The resulting data rate is approximately one sample a second. The very low data rate makes communication resource reuse straightforward. Furthermore, the low data rate implies that the energy requirement for a signal analysis is also low.

2.1.3. Oxygen Saturation of the Blood (SpO_2)

Single biological markers, like SpO_2, have been employed in several studies to detect SA [49,50]. The AASM Task Force has included blood oxygen saturation as one of the measurements that characterises SA and hypopnea episodes [50]. The amount of oxygen that is saturated in haemoglobin is referred to as SpO_2 [43]. A healthy person's oxygen saturation level is usually between 95 and 100% [51]. Oxygen levels of 90–95% are still considered safe for healthy subjects, but dangerous for patients with chronic lung diseases. SpO_2 values can be categorised as flows: normal and healthy arterial level (SpO_2 within 95–100%), mild hypoxemia (SpO_2 within 91–94%), hypoxic (arterial level of SpO_2 is within 85–94%), and severely hypoxic (arterial level of SpO_2 below 85%). It is reported that oxygen levels below 90% are dangerous and that oxygen levels below 80% are harmful to vital organs [43,52]. Most studies use SpO_2 and ECG signals because of their link to apnoeic events. Research has shown that the HR and systolic blood pressure rise in response to apnoeic episodes [53]. Burgos et al. used SpO_2 measurements to detect SA [50].

2.1.4. Polysomnography (PSG)

SA is generally diagnosed and treated in sleep laboratories using PSG, which is associated with significant waiting times for patients and high costs [54,55]. To conduct a sleep study, patients must spend at least one night in the sleep lab with several electrodes attached to their body [56]. These electrodes might disturb a patient's sleep, resulting in measurement data variations [37]. Since it must be performed in a sleep lab with physicians, the diagnosis results may be influenced by the lab environment, as well as the intrusive and inconvenient measurement sensors attached to the patient's body [9]. Many patients have trouble sleeping in such an environment. Due to the presence of numerous leads and monitors, some patients report feeling constrained during in-laboratory PSGs, resulting in them spending more time in the supine position than they would during a typical night at home [7,57,58]. A PSG requires gathering 12 separate signals with a minimum of 22 lead wires linked to the patient's body, making a signal analysis difficult and causing discomfort to the patient [38]. Intrusiveness and restricted availability make PSGs unsuitable for

screening purposes [51]. There is a lack of facilities and a lack of sleep specialists, resulting in extremely long waiting periods for patients [59]. Furthermore, manually analysing and scoring sleep using PSG traces is a time-consuming task [52]. It can take 2–4 h to score all data acquired during a full night's sleep [5].

2.2. Automated Apnoea Detection

AI models can extract objective information from physiological measurements for automated SA detection. These decision support models become essential in long-term monitoring because a manual analysis is impractical for the acquired data volume. For example, an advanced RM-based SA detection service might acquire ECG signals while the patient is sleeping. These signals are communicated in real time to a central cloud server, where they are available for analysis. Such a measurement setup poses no restriction on the amount of data collected, i.e., it is possible to record the ECG every night. A manual analysis would demand that a sleep physician read 6–8 h of ECG every day to monitor one patient. Furthermore, SA detection services in the home environment are scalable, and therefore, a manual analysis would be required for several patients. Hence, automated decision support is essential for any meaningful SA detection service in a home environment. To address that need, scientists created a wide range of AI based SA detection models. These models were based on technologies such as: ECG-Derived Respiration (EDR) [60], Classification and Regression Tree (CART) [61], Statistical Classifier (SC) [62], Convolutional Neural Network (CNN) [63–66], Recurrent Neural Network (RNN) [67], K-nearest Neighbour (KNN) [68], and Support Vector Machine (SVM) [69].

Our background research shows that the tools and techniques are available to establish RM services for SA detection. In the next section, we review systems that establish these services in the home environment. With respect to the discussion of these systems, we are especially interested in the properties that allow us to determine their environmental impact.

3. Sleep Apnoea Detection in the Home Environment

In this section, we outline our approach to review SA detection systems for the home environment. We conducted a comprehensive search across Google Scholar to find all research articles on the topic of automated SA detection in the home environment that were published between 2018 and 2022. We chose this period, because there was a lot of forward-thinking work on AI during that time. The database was queried using predefined Boolean search terms. Table 1 shows that the single search term "apnea home" returned 179 results. These articles were filtered according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) technique [70]. Figure 1 shows the PRISMA flow diagram, which documents the article filtering and refinement process. During the filtering, we eliminated duplicate entries, review articles, conference papers, non-English publications, and manuscripts without ACC results. Overall, the filtering process eliminated 65 papers, and we were left with 113 original research publications.

Table 1. Boolean search strings.

Title	AND (Full-Text and Metadata)	Database	No. of Studies
"Apnea home"	"Apnea home"	Google Scholar	179

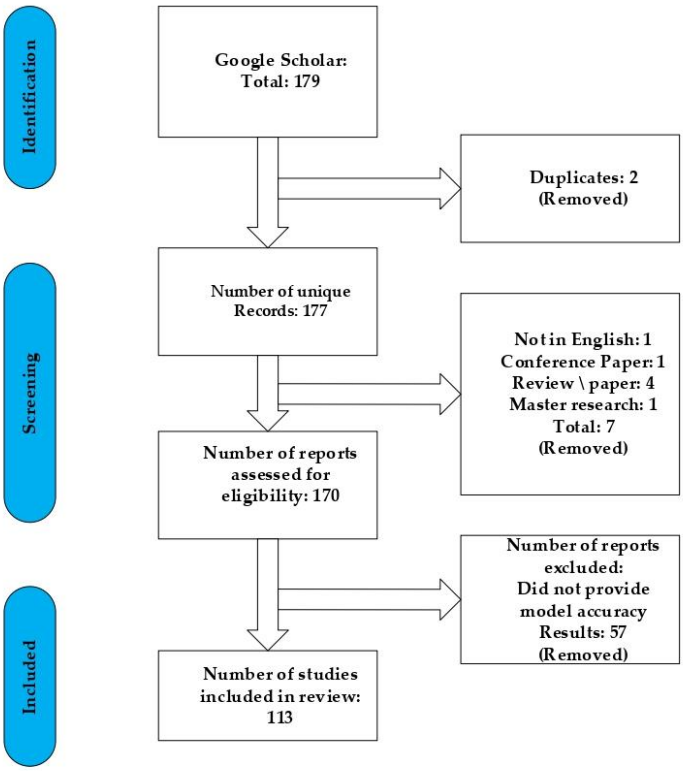

Figure 1. Flow chart of the PRISMA model for article selection.

4. Results

The 113 articles on SA detection systems in the home environment were analysed in terms of the signal used, detection method, data handling, number of participants, and detection performances. The signals used for SA detection have a significant impact on the environmental footprint. Different physiological signals have different requirements in terms of the measurement setup, communication bandwidth, storage capacity, and processing capabilities. As such, knowing the signal will indicate the resources needed to establish an SA detection service for the home environment. Evaluating the detection method together with the number of participants allows us to reason out the technology readiness level. Table A1 in Appendix A provides an analysis result summary.

Table A1 details the detection method used and the SA detection performance for each of the 113 studies under review. The best detection performance, in terms of ACC score, was reached by a few of the investigations. However, these results were based on "apnea home" investigations, hence the findings may not reflect a widespread trend. We excluded duplicate items, review articles, non-English publications, Master's dissertations, and works irrelevant to our criteria. Furthermore, during this investigation, we discovered other papers that were relevant to our criteria, although these articles only had an abstract. In this case, we had to remove these articles from our work. As seen in Table A1, several signals have been employed in a range of different studies. Each signal has different purposes. The signals that were used in this article are PSG, SpO2, home respiratory polygraphy (HRP), home polygraphy (HPG), ECG, seismocardiography (SCG), PPG, polygraphy (PG), respiratory inductance plethysmography (RIP), audio, and HR. Figure 2 shows the signals

used by the 113 evaluated studies. Table A1 in Appendix A provides further details on these SA detection studies. Figure 3 shows the approaches used in this work to detect SA. The numbers in the pie charts represent the amount of research articles that reported each method. The pie chart in Figure 2 reveals that PSG signals are the most-studied method among the examined publications, with 78 total research articles using this method. There were eight studies using HR signals and three studies using ECG. SpO2 was only utilised in one study. Twenty-three research articles employed other signals, as shown in the pie chart in Figure 3. Machine learning and deep learning were utilised four times each, as seen in Figure 3. Sleep physicians were the most reported to detect SA in a total of 30 studies; 75 studies used other methods. Figure 4 depicts the data management approaches, which included 35 online studies, 30 offline research, and 48 unreported studies. Figure 5; Figure 6 show the number of participants and the accuracy distribution. It can be observed that 101 people participated in this study, with 12 not participating. Furthermore, Figure 6 depicts the specifics of 60 studies that reported their accuracy and 53 studies that did not report their accuracy.

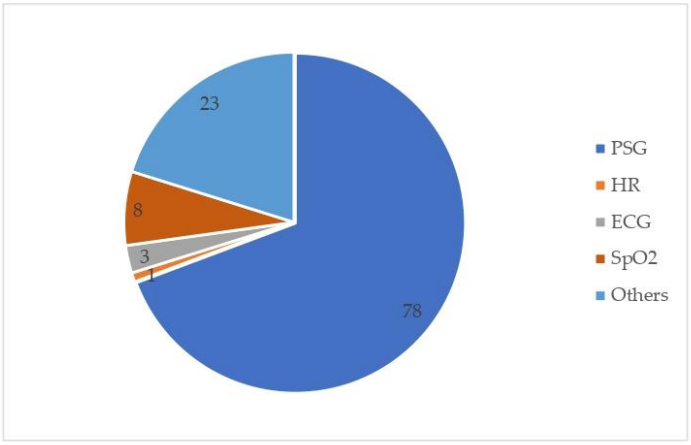

Figure 2. PGS, HR, ECG, SpO2, and others are the signals used to detect SA.

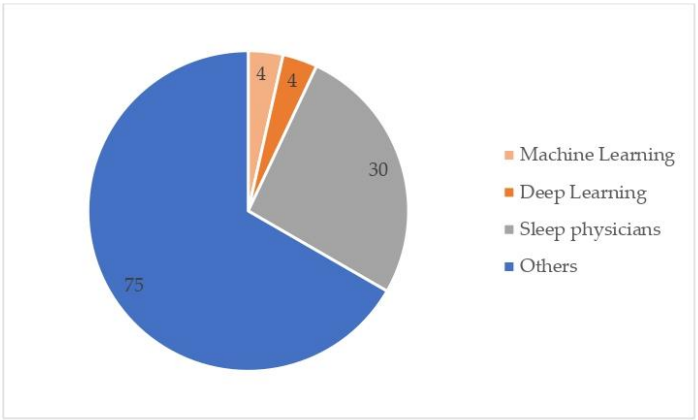

Figure 3. SA detection method.

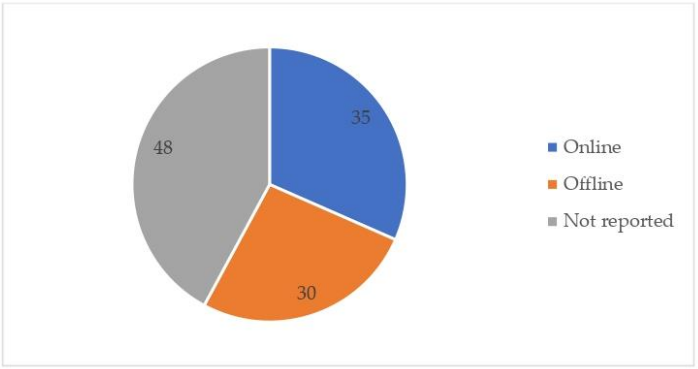

Figure 4. Data handling method.

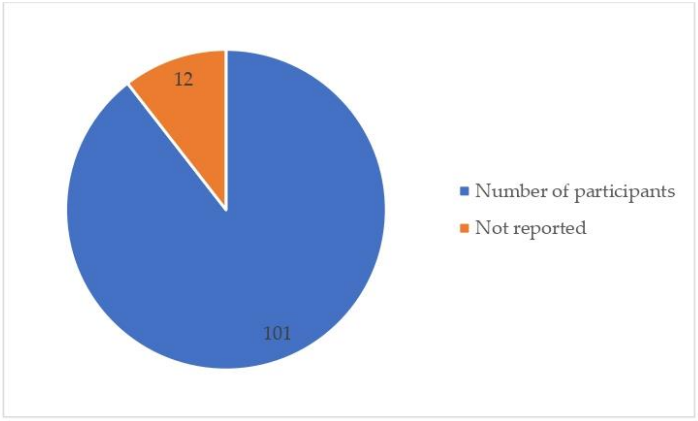

Figure 5. Number of participants reported.

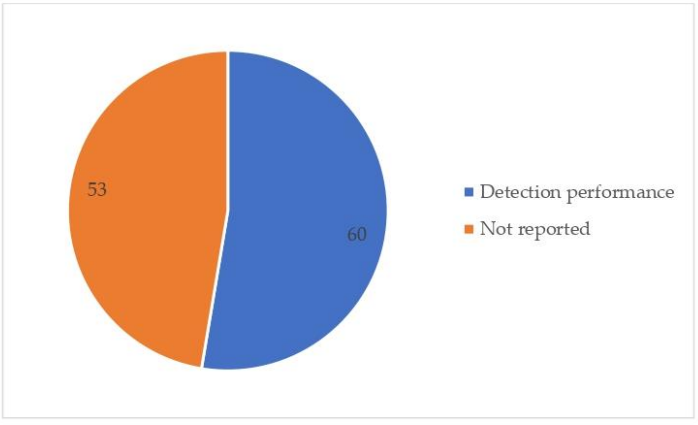

Figure 6. SA detection performance stated.

5. Discussion

The environmental impact of specific actions has become a major societal concern, affecting both business and organisational competitiveness. This has sparked an interest in objective research on this topic, which is based on collecting and analysing data. The term "environmental impact" refers to a change in a situation's outcome. The result of an action or event that affects the social, environmental, or economic well-being is referred to as an outcome [71]. The environmental impact of an activity is significant, and it demands immediate attention to mitigate the negative consequences on global health. The reduced use of equipment may be the most appropriate and effective strategy to minimise an environmental impact. Healthcare is a resource intensive activity and therefore it is important to discuss the environmental impact.

In this study we focused on the environmental impact of SA detection. It has been well established that SA is a significant health and economic issue, particularly in developed countries [72]. As such, SA is the most prevalent sleep condition for which diagnostic testing is performed at sleep labs. This testing takes the form of a PSG, which requires a comprehensive monitoring system to record a range of physiological signals during sleep. The PSG results could take a few weeks to arrive [73]. This type of investigation is very resource-intensive because a certified sleep technologist must set up and monitor the data acquisition equipment for the duration of the measurement, which is usually a whole night. Subsequently, the data must be analysed by a sleep physician, which takes up to four hours. This results in a resource shortage, which causes longer travel distances for patients [74]. From an environmental perspective, this travel is a significant drawback of the PSG. Another detrimental effect on the environment comes from the fact that a dedicated sleep lab needs to be built and subsequently maintained.

RM may be the most effective strategy to limit travel outside of the home environment and lower the risk of diseases like SA. Apart from reducing travel, RM-based SA detection services for the home environment can benefit healthcare providers through automating the SA detection process. The possibility of reducing healthcare costs is one of the most compelling reasons for introducing RM, followed by the desire to improve healthcare access. The savings from RM are not consistently reported in the research literature. Jiménez-Marrero et al. [75] put forward that RM-based SA detection offers significant cost savings. In contrast, Lew et al. [76] found only minor cost savings when they studies admission expenses. To be specific, for some patient categories, the cost only decreased from USD 10,835 to USD 10,678. These findings led to the conclusion that cost savings were a modest EUR 188 per person per year [77]. Other studies found that RM-based SA detection services have the same or even higher costs [29]. Many economic assessments of RM reflect only direct healthcare costs and do not include the overall programme costs like equipment amortisation or service costs. Other factors may also have an impact on the results. For example, RM-based hypertension and congestive heart failure detection is less expensive than the distant monitoring of respiratory illnesses [29].

In recent times, RM and inconspicuous sensors, cloud computing, and enhanced internet connectivity have all improved the technology for monitoring, aiding, and enhancing human health. For instance, the Internet of Things (IoT) paradigm's presence and quick growth has had an impact on how individuals track their health [78]. Moreover, most of today's wearable devices can track the HR and physical activity. More appliances are equipped with an internet connection, and RM is becoming more prevalent. Unobtrusive sensor data can provide a more thorough picture of the health and lifestyle habits of care recipients. As a result, technology has a direct impact on the ability of elderly and disabled individuals to detect their health at home and live more independent lives [79]. From the environmental perspective, the pervasive use of RM technology is a step in the right direction, because it allows us to administer more care with the same or marginally increased resource requirements [80]. A SA detection service in the home environment might become one of many servicers offered by a healthcare platform. The core modules of such a platform

facilitate data acquisition, communication, and storage. Specific modules will customise the platform to offer unique services, such as SA or atrial fibrillation detection [26].

During our review, we looked at the AI models that can be used for a computer-aided SA diagnosis. In a second phase, we looked at RM systems for SA detection in the home environment. For AI models, the overarching trend was that the research output focused on automated SA detection is growing, as shown in Figure 1. That means it is an active field, and we can expect a continuous improvement of the materials and methods for AI-based SA detection. Coupled with the RM techniques, this is certainly beneficial for the environment. However, we came across another trend when reviewing AI-based SA detection, namely the emergence of deep learning. The environmental impact of this trend is not clear. The computational complexity of deep learning models is significantly higher when compared to classical machine learning [81]. Therefore, it takes more energy to design the model. However, the trade-off here is to replace manual design work, in the form of feature engineering for classical machine learning, with automated feature extraction, which happens when we train deep learning algorithms. It seems unlikely that the increased energy requirement for designing deep learning models will be a serious barrier for this technology, especially when we consider the alternative being human labour that is focused on feature engineering.

The review on SA detection in the home environment revealed that most systems rely on PSG measurements to gain objective information. From an environmental perspective, this is not ideal, because PSG signal measurements require a complex measurement setup, which is resource intensive. For example, it might be necessary that a sleep technician or a nurse travel to the home environment of the patient to establish the measurement setup. Compared to the measurement setup of a PSG, individual signals, such as HR, ECG, and SpO2, are more straightforward. HR signal acquisition requires the least measurement setup, which might enable patient-led data acquisition. For example, a patient attaches the sensor and ensures that the data is relayed to a cloud server that runs a deep learning model for automated SA detection. Such a service would have very little environmental impact because both communication infrastructure and cloud server facilities are shared, which causes minimal additional energy expenditure. During service deployment, only the sensor constitutes additional hardware that needs to be produced and maintained. Even the sensor hardware could be shared amongst multiple services. This sensor sharing idea is based on the fact that HRV is a good predictor of human health. Hence, HR measurements can be used to detect and monitor a wide range of diseases, including, but not limited to, heart arrythmias, diabetes, and epilepsy [70]. The resource sharing could be facilitated by a healthcare platform that offers SA detection as one of many services. From an environmental perspective, both infrastructure and sensor reuse are strong arguments that the benefits of the platform approach outweigh the additional burden on the environment.

According to Rosenberg et al. [82], the utilisation of technology, such as RM, in the home environment for the support and care of people with SA is crucial. They reflect the costs that burden citizens with SA, as well as the anxiety that comes with the long waiting times for sleep lab-based diagnoses. According to the research, RM is the most desirable feature for SA detection in the home environment. The implementation of such technology has the potential to improve patient care while also reducing the demand for both resources and medical services. This might reduce the financial strain on healthcare systems. Moreover, the environmental benefits of using RM in SA detection are becoming more widely recognised. It is an unattended instrument that does not require the presence of a laboratory attendant. Individuals can use the monitor at home if they follow the technician's recommendations. Although the sensitivity of SA detection services in the home environment is currently lower than that of PSG, it saves time and money for patients while also providing convenience and comfort.

Looking beyond the current economic costs and system capability reveals future trends that might offer opportunities for businesses and healthcare providers. Smartphones and tablets are equipped with an increasing number of sensors that collect a large amount of

personal data in various formats and for various purposes [83]. For a manual analysis, this constitutes a problem because of the limited availability of sufficiently qualified human labour. However, technology improvements are not limited to the communication infrastructure; it is also projected that AI models for data analysis will continue to improve. Understanding of the algorithms and the availability of a cost-efficient parallel processing infrastructure are the two main drivers for that progress. Hence, as our ability grows to measure physiological signals in the home environment, the progress in AI technology will ensure that the data can be utilised. One use of such data is SA diagnosis support. Technology improvements are general trends that lead to gradual changes. As a result, we predict that there will be a broad acceptance of using more and more data-driven healthcare. It is likely that ethical issues are addressable with technological solutions, such as data encryption to address privacy concerns. Considering the environmental impact of actions like establishing a service platform for patient RM might open an independent line of argument to justify future decisions. To be specific, the environmental impact should be considered alongside ethical concerns, technological feasibility, and economic costs.

5.1. Limitations

There are certain limitations to this paper. First, it is possible that the literature search missed some important papers. Second, not all facets of SA disorders were covered. Third, several of the topics covered lacked high-quality data. Fourth, there was a lack of low cost and readily available RM-based SA detection services that could be used in the home environment. Fifth, patient RM requires internet access, which may not be available in some areas.

During the review, we learned that the environmental impact is hard to quantify, because there are a vast number of factors, even when environmental pollution is considered on its own. Therefore, the best support we have for promoting RM-based SA detection services is that increasing the use of this technology would benefit public health with a moderate environmental impact. Some readers might be dissatisfied with this statement because it appears vague. The statement becomes more concrete when we consider the alternative, which would be to build and maintain more sleep labs. Clearly, more sleep labs would have detrimental effects on the environment.

5.2. Future Work

SA is a life-threatening condition that affects people all around the world. The rapid rise in the number of SA sufferers each year is putting governments under a lot of financial strain. Several SA treatments have been proposed to alleviate or cure the condition. However, there is a scarcity of research comparing these treatments. As a result, a comprehensive guideline for selecting an appropriate treatment for people with various degrees of SA is required. Future research should incorporate the following to create a thorough evidence-based comparison to advise patients and doctors:

With the expanding use of RM around the world and the growing number of people who use it, RM is becoming increasingly important in terms of enhancing patient care, safety, and comfort. For the patients and the healthcare team, RM is an essential technology based on shared resources. Resource sharing and computational decision support result in the fact that upscaling the technology use has a low environmental impact. Therefore, in the future, we should see widespread deployment of this technology.

To reduce sensor waste, it is critical for companies to develop alternative instruments that can be used by patients at home and that can be useful for reducing the workload of both medical staff and patients coping with disease to reduce environmental waste. RM is one tool that can help in this situation.

To enhance healthcare, there is a focus on individuals who suffer from chronic diseases such as SA. Improved decision support algorithms and an appropriate healthcare network can aid the patient with their illness, and the algorithms could also help the doctor to predict, diagnose, and treat a problem. Algorithms could explain and anticipate how

patients interact with their healthcare providers to make health decisions. In addition, algorithms are critical for detecting risk changes on a continuous basis. AI models could choose a sequence of self-performed actions for the patient to manage that risk, such as to increase physical activity or improve the adherence to a prescribed medication regime [84].

6. Conclusions

SA is a major health and economic problem, especially in developed countries. Therefore, physical problem solutions that address or indeed attempt to address SA detection have an impact on the environment. To establish the environmental benefits of RM-based SA detection, we studied the enabling technologies, and we reviewed systems that detect SA in the home environment. During these activities, we learned that physiological signals and their analysis play a central role in SA detection. The most dynamic enabling technology is AI-based SA detection. We found that the research in this field is expanding with the emergence of novel deep learning approaches. However, this continued interest and, indeed, the associated research outputs have not percolated through to practical systems for SA detection in the home environment. Only 8 out of 113 studies used AI techniques for SA detection. Hence, there is room for improvement, especially when we consider the second important review finding, namely the apparent lack of online decision support.

SA detection and diagnosis support services based on RM technology constitute progress. In this paper, we argue that this progress can be achieved without a significant environmental impact. To be specific, these services can be established by reusing existing infrastructure. However, we also recognise that sleep labs will continue to play a vital role in the future for diagnosing sleep disorders that are not yet detectable through remote monitoring and for research purposes. Hence, RM will allow us to diagnose more SA earlier, and this will improve the outcomes for patients with the same or marginally more resources. SA detection and diagnosis support services can be established by reusing the available infrastructure. From an environmental perspective, the infrastructure is already built, and there is no, or at least a significantly reduced, need to construct new dedicated sleep labs. Another important advantage is the geographical and temporal decoupling of patient and physician. This decoupling is not only convenient for all parties involved, but it also reduces the administrative efforts required to synchronise and manage patients and healthcare professionals. Geographical decoupling leads to less mandatory traveling, which is an environmental advantage of RM-based SA detection and diagnosis support services when compared with traditional sleep studies.

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Abbreviations

The following abbreviations are used in this manuscript:

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
AASM	American Academy of Sleep Medicine
AHI	Apnoea-hypopnea index
AI	Artificial Intelligence
CART	Classification and Regression Tree
CNN	Convolutional Neural Network
CSA	Central sleep apnoea

CVD	Cardiovascular Disease
ECG	Electrocardiogram
EDR	ECG derived respiration
GDP	Gross Domestic Product
HPG	Home polygraphy
HR	Heart Rate
HRP	Home Respiratory Polygraphy
HRV	Heart Rate Variability
IoT	Internet of Things
IT	Information Technology
KNN	K-Nearest Neighbour
MSA	Mixed sleep apnoea
OSA	Obstructive sleep apnoea
PG	Polygraphy
PPG	Photoplethysmogram
PSG	Polysomnography
RIP	Respiratory inductance plethysmography
RM	Remote Monitoring
RNN	Recurrent Neural Network
SA	Sleep Apnoea
SC	Statistical Classifier
SCG	Seismocardiography
SVM	Support Vector Machine

Appendix A

Table A1. Details of the 113 selected studies on SA detection in the home environment.

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Saletu et al., 2018 [85]	PSG	Sleep physicians	Online	265	-
Massie et al., 2018 [86]	PSG	Sleep physicians	Online	101	-
Rosen et al., 2018 [87]	-	Home sleep apnoea test	Online	-	-
Ng et al., 2019 [88]	PSG	Sleep physicians		316	Sensitivity = 78% Specificity = 23% Negative predictive value = 67% positive = 35%
Gu et al., 2020 [89]	SpO_2	Sleep physicians	Online	50	Sensitivity = 85% Specificity = 87%% Positive and negative predictive value = 0.88% and 0.83%
Chiner et al., 2020 [90]	Home respiratory polygraphy HRP	Sleep physicians	Online	121	Accuracy = 93%
Gutiérrez-Tobal et al., 2019 [91]	SpO_2	Machine learning AB-LDA	Offline	230	Accuracy = 78.7%
Zancanella et al., 2022 [92]	PSG	EmblettaX100 system	Offline	40	-
Manoni et al., 2020 [93]	PSG	MORFEA	Online	-	-

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Kole 2020 [94]		Home sleep apnoea testing	-	>800	-
R. Stretch et al., 2019 [95]	PSG	Sleep physicians	Online	613	Sensitivity = 0.46, Specificity = 0.95% Positive predictive value = 0.81% negative predictive value = 0.80%
Castillo-Escario et al., 2019b [96]	PSG	MATLAB	Offline	13	Sensitivity = 76%, Positive Predictive Value = 82%
Hunasikatti 2019 [97]	PSG	Sleep physicians	Online	206	-
Romero et al., 2022 [98]	PSG	Sleep physicians	Online	103	Sensitivity = 79% Specificity = 80%
Massie, Van Pee, & Bergmann 2022 [99]	PSG	WatchPAT	Offline	20	-
Kristiansen, Nikolaidis, et al., 2021 [12]	PSG	Machine learning	Online	579	Accuracy = 89%
Nobuaki Tanaka et al., 2021 [100]	-	W-PAT	-	776	-
Colelli et al., 2021a [101]	HSAT	Sleep physicians	Online	119	-
Ikizoglu et al., 2019 [102]	PSG and HPG	Sleep physicians	Online	19	Sensitivity = 100% Specificity = 83%
Aielo et al., 2019 [103]	PG	Sleep physicians	Online	300	Accuracy = 95%
Zavanelli et al., 2021 [104]	ECG, SCG, and PPG	Sleep physicians	Online	-	Accuracy = 95%
Colaco et al., 2018 [105]	PSG	Sleep physicians	Online	43,780	-
Ekiz et al., [106]	PSG	Sleep physicians	Online	43,780	-
Maggio et al., 2021 [107]	PSG	Embla® Embletta® GOLD portable sleep system	Online	45	Accuracy = 93%
Steffen et al., 2021 [108]	PSG and HST	Sleep physicians	Online	131	-
Orr et al., 2018 [109]	PSG and HST	MATLAB	Offline	27	Sensitivity = 70% Specificity = 71%
Gutiérrez-Tobal et al., 2021 [110]	SpO_2	Least-squares boosting algorithm	Offline	8762	Accuracy = 87.2%
Fietze et al., 2022 [54]	polygraphy (PG)	Sleep physicians	Online	505	-

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Fitzpatrick et al., 2020 [111]	PSG	BresoDx® portable monitor	Offline	233	Sensitivity = 85% Specificity = 0.48% Positive and negative predictive values were, 0.81% and 0.54%
Ferrer-Lluis et al., 2019 [112]	Pulse oximetry	Apnealink™ Air	Offline	-	-
Huysmans et al., 2021 [113]	PSG	Total Sleep Time (TST)	Offline	183	Sensitivity = 78% Specificity = 89%
Joymangul et al., 2020 [114]	Positive Airway Pressure (PAP) therapy	Python	Online	668	-
Młyńczak et al., 2020 [115]	PSG	Audio sensor	Online	30	Accuracy = 86% Sensitivity = 96%, Specificity = 76%
Van Pee et al., 2022 [116]	PSG and PAT HSAT	Sleep physicians	Online	167	-
Castillo-Escario et al., 2019a [117]	audio signals	MATLAB	Offline	3	Accuracy = 95.9%
Navarro-Martínez et al., 2021 [118]	pulse oximetry	Epworth sleepiness scale, STOP-BANG questionnaire, and C-reactive protein screening	Online	117	Sensitivity = 80% Specificity = 92%
Patel et al., 2018 [119]	PSG	ApneaLink Air devices	Online	106	Sensitivity = 82% Specificity = 92%
Magalang et al., 2019 [120]	Nasal pressure	Fifteen HSAT	Offline	-	-
Muñoz-Ferrer et al., 2020 [121]	PSG	Sleepwise (SW)	Online	38	Accuracy = 84%
Light et al., 2018 [122]	EEG and PSG	Sleep physicians	Online	207	Accuracy = 95%
Oceja et al., 2021 [123]	PSG	HRP	Online	320	-
Di Pumpo et al., 2021 [124]	-	WatchPAT	-	-	-
Hoshide et al., [125]	PSG	CPAP therapy	Online	105	Accuracy = 86.9%
Hui et al., 2018 [126]	PSG	Respiratory polygraphy	Online	-	Accuracy = 95%

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Goldstein et al., 2018 [127]	PSG	Sleep physicians		196	Accuracy = 84%
Jensen et al., 2022 [128]	PSG	NightOwl™	Offline	150	Accuracy = 95%
Simonds 2022 [129]	Body movement, respiratory rate, heart rate, snoring, and breathing pauses	Withings Sleep Analyzer	Online	67,278	Sensitivity = 88% Specificity = 88%
Rajhbeharrysingh et al., 2019 [130]	PSG	Machine learning	Online	14	Accuracy = 82.9% Sensitivity = 88.9%, Specificity = 76.5%
Facco et al., 2019 [131]	PSG	Sleep physicians	Online	43	80.0%
Kristiansen et al., 2021 [132]	PSG and PG	Sleep physicians	Online	34	Sensitivity = 97.2% Positive prediction value = 94.2%.
Li et al., 2021 [133]	PSG	Sleep physicians	Online	43,780	-
Massie et al., 2022 [134]	PSG	MATLAB	Offline	261	Sensitivity = 87% Specificity = 89%
Hart et al., 2021 [135]	PSG	CPAP	Offline	18	-
da Rosa et al., 2021 [136]	PSG	Sleep physicians	Online	94	Accuracy = 80.7%
Ashley Suniega et al., 2019 [137]	PSG	HRP	Online	430	Accuracy = 95%
Mosquera-Lopez et al., 2018 [138]	PSG	Machine learning	Offline	14	Accuracy = 86.96% Sensitivity = 81.82% Specificity = 91.67%.
Lipatov et al., 2019 [139]	PSG	HSAT devices	Offline	141	-
Silva et al., 2021 [140]	PSG	SPSS software	Offline	427	-
Bonnesen et al., 2018 [141]	Audio	Portable device	Online	23	Sensitivity = 75%, Accuracy = 60%
Green et al., 2022 [142]	PSG	Online video technician	Online	100	-
Ben Azouz et al., 2018 [143]	PSG	Equivital™ EQ02 LifeMonitor	Online	32	-
Honda et al., 2022 [144]	Respiration activity	wearable sensor	Offline	-	-
Ghandeharioun 2021 [145]	ECG and SpO_2	Sleep physicians	Online	155	Accuracy = 85%

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Labarca et al., 2018 [146]	PG	HSAT an Embletta®	Online	198	-
Lee et al., 2021 [147]	PSG	HSAT	Offline	154	Sensitivity = 85% Specificity = 95%
Huysmans et al., 2020 [148]	ECG and RIP	CNN	Online	81	Kappa score = 0.48
Barriuso et al., 2020 [149]	Respiratory polygraphy	HRP	Online	301	-
Mashaqi et al., 2018 [150]	PSG	HSAT, RYGB and LSG	Online	10	Accuracy = 94%
Takao et al., 2019 [151]	Audio	Autoencoder	Offline	5	Accuracy = 94.7%
Borsini et al., 2021 [152]	PG	Apnea Link Plus and Air	Online	3854	Accuracy = 90%
Gu, W., & Leung 2018 [153]	PPG	pulse oximeter	Online	23	Accuracy = 97%
Mieno et al., 2020 [154]	PSG	PulSleep LS-140	Offline	58	Sensitivity = 96.4% Specificity = 100%
Arguelles et al., 2019 [155]	PSG	HSAT	Online	88	Accuracy = 98%
Stretch et al., 2019 [156]	PSG	k-nearest neighbors algorithm	Offline	415	Sensitivity = 0.43% Specificity = 0.96%
Iqubal & Lam 2020 [157]	PSG	HSAT	Online	88	Sensitivity = 98% Specificity = 76%
Tanaka et al., 2020 [158]	PSG	WP device	Offline	774	-
Kay et al., 2021 [159]	PSG	HSAT	Online	1	-
Bollu et al., 2020 [160]	PSG	nox-T3 sleep monitor and Nomad HSAT	Online	178	-
Yeh et al., 2020 [161]	PSG	Sleep physicians	Offline	-	-
Sterner et al., 2020 [162]	-	WatchPAT	-	-	-
Iakoubova et al., 2020 [163]	PSG	Sleep physicians	Online	900	-
Arguelles et al., 2018 [164]	PSG	Sleep physicians	Online	60	Accuracy = 90%
Gamaldo et al., 2018 [165]	PSG	HSAT	Online	147	-
Journal et al., 2019 [166]	PG	Sleep physicians	Online	1055	-

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
He, Mendez, and Atwood 2020 [167]	PSG	WatchPAT	Online	295	-
Pinheiro et al., 2020 [168]	PSG	HST	Online	1013	Sensitivity = 95.8% Specificity = 94.3%
Anderer et al., 2020 [169]	PSG	Deep Learning	Online	472	Accuracy = 95%.
Zeineddine et al., 2020 [170]	PSG	HSAT	Online	33	-
F. Facco et al., 2018 [171]	PSG	HST	Online	34	Accuracy = 90.5%
Zhongming et al., 2021 [172]	PSG	HSAT	Online	31	-
Carey et al., 2020 [173]	PSG	WPHST	Online	62	-
Aydin et al., 2020 [174]	PSG	APAP	Online	43	-
Homan et al., 2021 [175]	SpO_2	HSAT	Online	558	Accuracy = 90%
Rudock et al., 2019 [176]	PSG	HSAT	Online	-	-
Bliznuks et al., 2022 [177]	SpO_2	CPAP	Online	16	-
Thomas et al., 2021 [178]	PSG	HSAT	Online	297	-
Kazaglis 2018 [179]	Audio	Noxturnal T3 device	Offline	2	-
Arguelles et al., 2019 [71]	PSG	HSAT	Online	11	Accuracy = 95%
Fynn et al., 2020 [180]	PSG	sleep physicians	Online	246	-
Wenbo et al., 2019 [181]	PSG	ring-type pulse oximeter	Online	32	Accuracy = 95.0%
Gutiérrez-Tobal et al., 2018 [182]	SpO_2	SAHS	Online	200	Sensitivity = 83.8% Specificity = 85.5%
Stretch et al., 2020 [183]	PSG	NN approach	Offline	1329	79%
Johnson et al., 2018 [184]	-	HSAT	-	-	-
Sever et al., 2018 [185]	PSG	Sleep physicians	Online	1	-
Martinot et al., 2020 [186]	PSG	Machine learning	Online	192	Accuracy = 84%
Haaland et al., 2018 [187]	PSG	Apnealink	Online	1021	-

Table A1. *Cont.*

Authors	Signal	Detection Method	Online/Offline	Number of Participants	Detection Performance
Do et al., 2022 [188]	PSG	HSAT	Online	505	-
Stanchina et al., 2020 [189]	PSG	APAP	Online	238	-
Perriol et al., 2018 [190]	PSG	CPAP	Offline	66	-
Krause-Sorio et al., 2021 [191]	HR and SpO_2	Telephone screening	Offline	5	-
Mahmood et al., 2018 [192]	PSG	HST	Offline	454	-
Robinson et al., 2018 [193]	PSG	HSAT	Offline	961	Sensitivity = 97.1% Specificity = 100%
Ferreira 2019 [194]	PSG	CPAP	Online	191	-

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Appendix 12 Accurate Detection of Sleep Apnea with Long Short-Term Memory Network Based on RR Interval Signals.

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Accurate detection of sleep apnea with long short-term memory network based on RR interval signals

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ABSTRACT

Sleep apnea is a common condition that is characterized by sleep-disordered breathing. Worldwide the number of apnea cases has increased and there has been a growing number of patients suffering from apnea complications. Unfortunately, many cases remain undetected, because expensive and inconvenient examination methods are formidable barriers with regard to the diagnostics. Furthermore, treatment monitoring depends on the same methods which also underpin the initial diagnosis; hence issues related to the examination methods cause difficulties with managing sleep apnea as well. Computer-Aided Diagnosis (CAD) systems could be a tool to increase the efficiency and efficacy of diagnosis. To investigate this hypothesis, we designed a deep learning model that classifies beat-to-beat interval traces, medically known as RR intervals, into apnea versus non-apnea. The RR intervals were extracted from Electrocardiogram (ECG) signals contained in the Apnea-ECG benchmark Database. Before feeding the RR intervals to the classification algorithm, the signal was band-pass filtered with an Ornstein–Uhlenbeck third-order Gaussian process. 10-fold cross-validation indicated that the Long Short-Term Memory (LSTM) network has 99.80% accuracy, 99.85% sensitivity, and 99.73% specificity. With hold-out validation, the same network achieved 81.30% accuracy, 59.90% sensitivity, and 91.75% specificity. During the design, we learned that the band-pass filter improved classification accuracy by over 20%. The increased performance resulted from the fact that neural activation functions can process a DC free signal more efficiently. The result is likely transferable to the design of other RR interval based CAD systems, where the filter can help to improve classification performance.

Acronyms

AUC	Area Under Curve
BMI	Body Mass Index
CAD	Computer-Aided Diagnosis
CNN	Convolutional Neural Network
CSA	Central Sleep Apnea
ECG	Electrocardiogram
EDR	ECG-Derived Respiration
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
FIR	Finite Impulse Response
GPU	Graphics Processing Unit
GRU	Gated Recurrent Units
HRV	Heart Rate Variability
IIR	Infinite Impulse Response
K-NN	K-Nearest Neighbor
LSTM	Long Short-Term Memory
OSA	Obstructive Sleep Apnea
PAP	Positive Airway Pressure
PPP	Palato Pharyngo Plasty
PSD	Power Spectral Density
PSG	Polysomnography
RNN	Recurrent Neural Network
ROC	Receiver Operating Characteristic
SVM	Support Vector Machine

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1. Introduction

Sleep is a fundamental human activity which is characterized by reduced or suspended consciousness. Hence, the ability to avoid or correct disturbances, such as sleep disordered breathing, is reduced [1]. Sleep apnea is a common cause for sleep-disordered breathing. In the middle-aged workforce about 2% of women and 4% of men were apnea patients in 1993 [2]. In 2003, about 4% of the US population had sleep apnea [3]. The worldwide prevalence was estimated to be 6% in 2008 [4]. It is predicted that this upward trend will continue. Without diagnosis and adequate treatment patients might be exposed to an increased risk of cardiovascular diseases [5], such as stroke and hypertension [6,7]. Apnea might also disturb recreational activities and by doing so cause mental suffering and in some cases clinical depression [8]. Apnea is also linked to narcolepsy, insomnia, and obesity [9]. Studies show that patients with apnea have a higher chance of being involved in a road traffic accident [10]. The disease is also a risk factor for complications during operations under anesthesia [11]. Finally, patients with untreated apnea have a significantly higher mortality risk when compared to a control group with the same age, sex and Body Mass Index (BMI) [4].

Current diagnostic methods depend on Polysomnography (PSG). The measurements include ECG, Electroencephalogram (EEG), Electrooculogram (EOG), Electromyogram (EMG), respiratory effort, airflow and oxygen saturation (SaO_2) [12–14]. To capture these signals, the patient must sleep with intrusive measurement equipment in a clinical environment [15,16]. The process requires supervision by medical specialists. The PSG process makes apnea diagnosis expensive and inconvenient. To improve this situation new methods are required which are less intrusive and more cost effective, but equally accurate. Mobile technology and advanced physiological signal measurement methods might be able to address the intrusiveness and cost issues. One promising measurement technology is single lead ECG for signal acquisition and mobile soft processing for beat-to-beat (RR) interval extraction. As such, that measurement setup has a significantly lower complexity when compared with PSG. Furthermore, it is notably cheaper to communicate and process the resulting RR interval signals, when compared with the multitude of physiological signals measured during PSG. However, major issues remain with the diagnosis support quality provided by these systems. One critical component to ensure diagnosis support quality are the algorithms which extract the relevant information or provide decision support.

With this study we investigate the diagnosis support quality of deep learning algorithms for sleep apnea. To achieve that, we created a test setup which takes in RR interval signals and returns a decision on whether or not specific signal segments show signs of sleep apnea. The processing structure contains a pre-processing and a classification step. In the pre-processing step, the signal was band-pass filtered with an Ornstein–Uhlenbeck third-order Gaussian process. Subsequently, the filtered signal is partitioned with a sliding window. The resulting signal blocks were passed on to an LSTM network which classifies them into either apnea or non-apnea. The setup was designed with a benchmark dataset from the MIT-BIH Polysomnographic Database. With 10-fold cross-validation, we established an accuracy of 99.80%, a sensitivity of 99.85%, and a specificity of 99.73% for the proposed system. By itself, this result is significant, because it indicates that good diagnostic support is possible even with a less complex data acquisition setup. Apart from these results we also want to report a significant design achievement. We found that low- and high-pass filtering the RR interval signal improved the classification accuracy by over 20%. Filtering, as part of the pre-processing for RR interval signals, might help to improve the detection quality for a wide range of CAD systems, because it allows the deep learning algorithms to focus on the Heart Rate Variability (HRV).

To support these claims, we outline our design of an apnea detection algorithm. The next section introduces the medical background of sleep apnea. Section 3 details the methods used to construct the test setup. Thereafter, we present the results achieved while testing the proposed diagnosis support system. In the Discussion section, we relate our work to other studies done on similar topics. Having this extended scope allows us to show how the RR interval filtering might help to improve the classification accuracy for other detection tasks. The conclusion summarizes the work and puts forward the highlights of the study.

2. Background

During apnea the patient ceases to breath for 10 s or more. Obstructive Sleep Apnea (OSA) and Central Sleep Apnea (CSA) are the two main causes for the pauses in breathing. The pauses usually occur during rapid eye movement sleep. An OSA event occurs when the airway is blocked completely. The blockage might be due to fatty tissue, musculus geniohyoideus, or musculus genioglossus. In contrast, a CSA event is characterized by a lack of respiratory effort, i.e. there is a problem with respiration control [17]. OSA is diagnosed more often than CSA [18]. There are several therapies for sleep apnea, such as Positive Airway Pressure (PAP) and Palato Pharyngo Plasty (PPP) [15,19]. In general, these therapies are more effective when sleep apnea is detected early [16,20].

In current clinical practice, polysomnograms, which result from PSG sleep studies, are used to evaluate an index score. The score value determines the apnea severity [21,22]. An important component of these index scores is the airflow signal and blood oxygen content [23,24]. However, measuring these signals is intrusive and inconvenient for the patient. To reduce the inconvenience, apnea detection methods were developed using respiratory and single-lead ECG signals [20,25]. In response, PhysioNet held a competition called CinC Challenge 2000 [26,27], which provided ECG data with minute-by-minute labeling [28,29]. After the challenge, the training dataset, with 35 recordings, was made publicly available by PhysioNet. Over the years, the dataset was used to design apnea detection algorithms and it is now considered a benchmark that can be used to compare individual method performances.

Digital biomarkers fail to capture all sleep apnea induced morphological changes [30,31], because transient abnormalities appear randomly, and long-term abnormalities are difficult to quantify [32]. Deep neural networks can refine the information even further and provide medical decision support which can help to diagnose sleep apnea [33–38]. The research provided precedents of employing Convolutional Neural Network (CNN) to detect disease using ECG signals. In apnea detection tasks, directly feeding original ECG signals to deep neural networks is adopted by some researchers [39–41], but the high ECG data rate limits the network depth. As such, the RR interval signal is derived from the ECG extracting the beat-to-beat record of RR-intervals and is, as a time series, irregularly sampled. Studies show that there is a physiologic link between the breathing rate and the beat-to-beat variations of the human heart [42–44]. Hence, it is possible to detect sleep disordered breathing based on RR interval signals. The next section describes the methods we have used to detect apnea induced sleep disordered breathing based on RR interval signals.

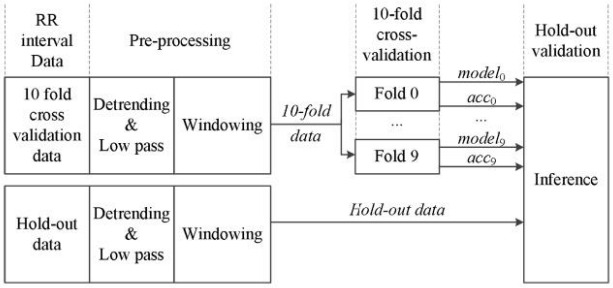

Fig. 1. Block diagram for training and validating the deep learning model.

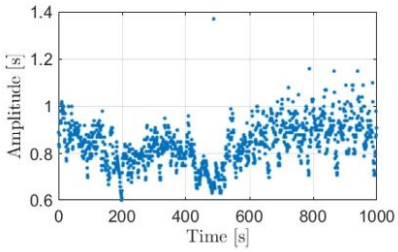

Fig. 2. RAW RR interval data from record a01.

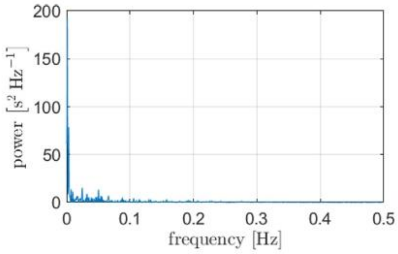

Fig. 3. PSD of the RAW RR interval data.

Table 1
Number of beats and signal name for 10-fold cross-validation and hold-out-validation data from the Physionet Apnea-ECG Database.

10-fold cross-validation No. beats=935462						Hold-out-validation No. beats=169959	
Name	Beats	Name	Beats	Name	Beats	Name	Beats
a01	29639	a12	33829	b05	26937	a11	32953
a02	34931	a13	39723	c01	27643	a15	33948
a03	33966	a14	28212	c02	32137	a17	36131
a04	30902	a16	34948	c03	23758	b01	35081
a05	28740	a18	29970	c04	28089	c07	31846
a06	27199	a19	38738	c05	27957		
a07	37462	a20	34246	c06	28062		
a08	41102	b02	34877	c08	30360		
a09	31318	b03	28918	c09	31179		
a10	32263	b04	24379	c10	23978		

3. Methods

This section describes the methods used to create the sleep apnea detection system. This is done by describing the data and the methods which process the data to refine and ultimately extract diagnostically relevant information. The block diagram, shown in Fig. 1, provides an overview of the system that was used to train and validate the deep learning model. The processing steps are represented by blocks, and the arrows between the blocks represent the data flow. The following sections introduce both processing steps and data in more detail.

3.1. RR interval data

The deep learning model was trained and validated with data from the Apnea-ECG Database [26,27]. The dataset consisted of 35 records (a01 through a20, b01 through b05, and c01 through c10). The individual recordings vary in length from slightly less than 7 h to nearly 10 h. Each record consists of an ECG signal of varying length, and corresponding R beat labels that were generated with automated QRS detection. The shortest signals are just below 7 h in length and the longest one is almost 10 h. The subjects of these recordings are men and women between 27 and 63 years of age, with weights between 53 and 135 kg (BMI between 20.3 and 42.1). Crucially for this work, the records also contain apnea annotations established by human experts based on simultaneously recorded signals such as respiration, that were recorded as part of a PSG. Table 1 provides details about the signals for both 10-fold cross- and hold out-validation. We have partitioned that dataset into *Hold-out data* and 10-*fold data* for the two validation methods outlined in Sections 3.3 and 3.4. The *Hold-out data* contains five records (a11, a15, a17, b01, c07). The 10-*fold data* contains the remaining records. Fig. 2 shows the RR intervals that occur during the first 1000 s of record a01. Note, there is a significant DC bias in the signal. That bias is quantified in the frequency domain as a power level of 192.5 $s^2\,Hz^{-1}$. Fig. 3 shows the Power Spectral Density (PSD) of the RAW RR interval data shown in Fig. 2.

3.2. Pre-processing

The pre-processing of the RR interval signals for both 10-*fold data* and *Hold-out data* was done with a two-step process. The first step is low and high pass filtering. For RR interval signals, high pass filtering is referred to as detrending. The second pre-processing step is windowing, which partitions the data for the classification algorithm.

3.2.1. Detrending and low-pass filtering

From a time series perspective, RR interval signals are nonuniformly sampled. Therefore, conventional signal conditioning using Infinite Impulse Response (IIR) and Finite Impulse Response

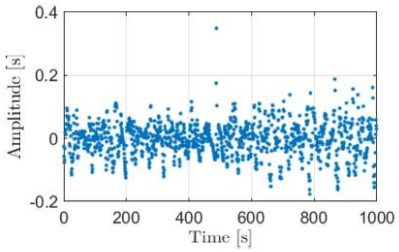

Fig. 4. Detrended and low pass filtered RR interval data.

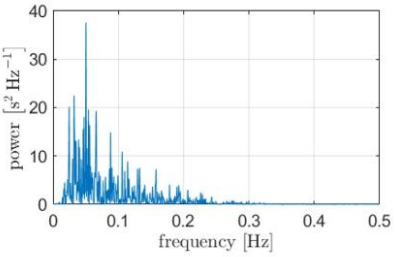

Fig. 5. PSD of the detrended and low pass filtered RR interval data.

(FIR) filters cannot be applied directly. It is necessary to resample the signals such that the resulting samples are at equidistant time intervals, typically at 0.25 s. However, such interpolative resampling introduces noise into the signal, which compromises information quality [45,46]. Filter methods which act directly on irregularly sampled signals can help to prevent the negative effects of resampling.

For our study we have used the detrending and low-pass filter proposed by Fisher et al. [47]. The filter combination is based on an Ornstein–Uhlenbeck third-order Gaussian process which acts on the RR interval signal directly. Fig. 4 shows the filtered version of the unprocessed signal provided in Fig. 2. The DC bias is significantly reduced. This visual observation is confirmed in the PSD plot shown in Fig. 5. The effects of the detrending filter can be observed as the absence of low frequency components up to 0.02 Hz of the normalized frequency. In terms of visual interpretation, removing the DC bias helps to focus on the variability of the RR intervals. In the spectrum plot of the RAW signal, the frequency content caused by that variability was overshadowed by the large DC components. Removing that component allowed us to re-scale the y-axis on the PSD plot which essentially means to zoom in on the spectrum component which hold relevant information for apnea classification.

3.2.2. Windowing

To partition the data for the classification algorithm, we have used a sliding window of 100 RR intervals on the data. The window slides with one RR interval at a time. In other words, the windowing method creates one data block of 100 RR intervals for each beat from the database. This creates a good temporal resolution, and it generates sufficient data to train and test the deep learning algorithm. A window was labeled apnea (positive) if at least 25 RR intervals were labeled apnea. All other windows were labeled non-apnea (negative). The labels for the individual RR intervals came from the Apnea-ECG Database.

3.3. 10-fold cross-validation

10-fold cross-validation aims to mitigate the effects of choosing test samples from an available dataset. Kohavi et al. recommend 10-fold cross-validation for model selection [48]. Hence, this performance measure is relevant for comparing classification models; see Table 3 in Section 5. The basic idea is to partition the labeled data into 10 parts. Each of the cross-validation partitions contained mixed data from the cross-validation dataset (as shown in Table 1). This follows common practice within the machine learning and bioinformatics community for tuning models [49–52]. Once the data is split, the parts are used to generate 10 folds with training and test data. For fold 0, part 0 is used to test and the remaining 9 parts are used to train the network. Similarly, for fold 1, part 1 is used to test and the remaining 9 parts are used to train the network, etc. The left part in the flowchart, shown in Fig. 6, depicts the data arrangement for 10-fold cross-validation.

The model fitting process is structured into 40 epochs. Within each epoch the LSTM network is trained and tested. The training step will result in a *model*, i.e. a set of weights. The LSTM network testing step establishes the prediction quality of the *model*. Based on the prediction quality, the 'Select best model' block decides which model is the best for a particular fold. Once all the epochs are processed, the data from the next fold is loaded. The algorithm returns once all the folds are processed and the K best models, together with their accuracy (acc), are established. The right part in the flow chart depicts the epoch-based fold processing.

3.3.1. Long short-term memory network

Fig. 7 shows a functional diagram of the LSTM algorithm. The upper part of the diagram indicates the Recurrent Neural Network (RNN) loop unrolling, which results in individual LSTM cells. The hidden state vector $\vec{h}_t \in \mathbb{R}^h$ and the cell state vector $\vec{c}_t \in \mathbb{R}^h$ are passed from one cell to the next. The cells consume the input vector $\vec{x}_t$ at different time instances t. Each cell A has LSTM functionality, as indicated in the lower part of the figure.

Each cell incorporates the three gates to establish the LSTM functionality [53]. The forget gate regulates the information content stored within the cell and thereby it plays a vital role in modeling the way humans remember and forget [54]. It is implemented as the first multiplier from the left, highlighted in orange. The input gate is implemented as the second multiplier from the left, highlighted in blue. The output gate is implemented as the third multiplier from the left, highlighted in green.

The weights and biases are established during the training phase and they constitute the LSTM *model*. During the testing phase, the *model* is used to classify an input sequence $\vec{x}_t$. In our case, the model establishes if there are signs of sleep apnea in a block of 100 RR intervals. The methods used for testing the LSTM model are introduced in the next section.

Table 2 shows the model architecture used in this paper. The model used here is a bidirectional LSTM model [55] - where the RR input sequence is passed simultaneously forward through one LSTM model (i.e. samples $x_0, \ldots, x_n$) and backward through another LSTM model (i.e. samples $x_n, \ldots, x_0$). This allows the bidirectional LSTM model to consider time dependencies in both the past and future of a timestep. The outputs of the two LSTMs are then concatenated together and global max pooling (in one dimension) is applied. In these experiments we used both recurrent dropout [56] (with a probability of 0.1) applied to the inputs and hidden states of the LSTM cells and standard dropout [57] (again with a probability of 0.1) applied between the final fully connected layer and the output. These serve to improve the generalization of the model and reduce over-fitting. The model was trained using the Adam optimizer [58] with a learning rate of 1e-3, a batch size of 1024 (providing a good trade-off between

Table 2
Bidirectional LSTM architecture.

Layer	Type	Output shape	Number of parameters
1	Input	100, 1	0
2a	LSTM (forward)	200, 400	161600
2b	LSTM (backward)	200, 400	161600
3	Global 1D max pooling	400	0
4	Fully connected Rectified Linear Unit (ReLU)	50	20050
5	Dropout	50	0
6	Fully connected (Sigmoid)	1	51

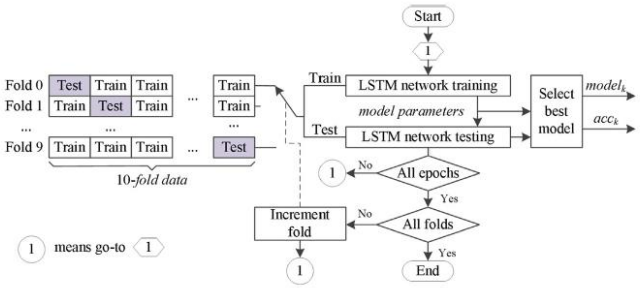

Fig. 6. Flow chart for 10-fold cross-validation, where $model_k$ indicates the best LSTM model for fold k, similarly acc_k is the best accuracy for fold k.

available Graphics Processing Unit (GPU) memory and speed of training), and training performance was evaluated using the binary cross-entropy loss function. The same batch size was used in one of our previous models for LSTM based atrial fibrillation detection in RR interval signals [59]. Models were implemented using the Keras and Tensorflow frameworks [60,61].

3.4. Hold-out testing

The unseen/generalization performance is tested using the held-out dataset (as performed in [52]). During validation we test the best models from each fold with the *Hold-out data*. This is done by accumulating the weighted prediction results. The weight factor reflects the relative prediction accuracy of the specific *model*. It is established by dividing the model accuracy (acc_k) by the sum of all model accuracies ($accAcc$). Eq. (1) defines the accumulated accuracy over all folds.

$$accAcc = \sum_{k=0}^{K-1} acc_k \tag{1}$$

where K is the number of all folds. The *inference* value is established by using the best *model* parameters from the K folds. The prediction result is weight adjusted with the established model accuracy (acc_k) divided by the accumulated accuracies ($accAcc$).

$$inference = \sum_{k=0}^{K-1} \frac{predict(Hold\text{-}out\ data, model_k) \times acc_k}{accAcc} \tag{2}$$

where $predict(data, model)$ used the LSTM algorithm to estimate for a specific *data* based on the *model* parameter.

For hold-out validation testing, the *inference* results are compared with the data block labels. The comparison results are discussed in the next section.

4. Results

This section provides the hold-out and 10-fold cross-validation results for the proposed sleep apnea detection method. We report a confusion matrix for each of these tests. These matrices detail

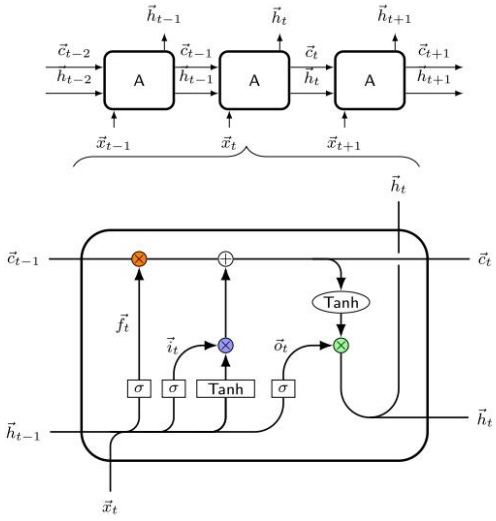

Fig. 7. Overview of the deep learning algorithm. Depicted as RNN loop unrolling and LSTM cell. In the LSTM cell, $\sigma(\ldots)$ is the sigmoid activation function and Tanh(…) is the hyperbolic tangent function.

the number of RR intervals correctly identified as normal (TN), the number of RR intervals falsely identified as apnea (FP), the number of RR intervals falsely identified as normal (FN), and the number of RR intervals correctly identified as apnea (TP). As such, the LSTM network testing algorithm returns a vector with elements in the range of 0 to 1. In order to compare these results with the true labels, we have used a threshold of 0.5, which was established through Receiver Operating Characteristic (ROC) analysis; see Section 4.1. The confusion matrix has the following

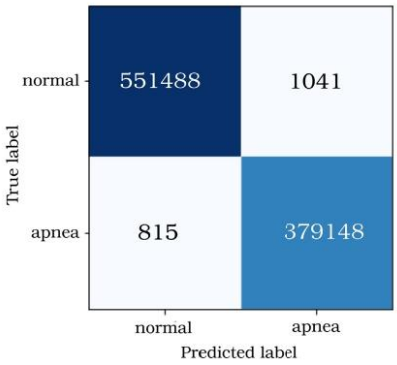

Fig. 8. Confusion matrix for 10-fold cross-validation.

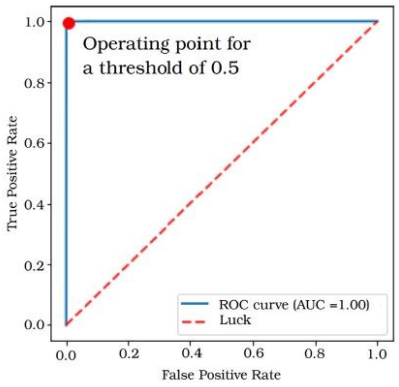

Fig. 9. ROC for the 10-fold cross-validation test.

form:

$$C = \begin{bmatrix} TN & FP \\ FN & TP \end{bmatrix} \tag{3}$$

With these base results, we calculate the following performance measures:

$$\begin{aligned} \text{Accuracy} &= \frac{TP + TN}{TP + TN + FP + FN}, \\ \text{Sensitivity} &= \frac{TP}{TP + FN}, \\ \text{Specificity} &= \frac{TN}{TN + FP}. \end{aligned} \tag{4}$$

In a final step we evaluate sensitivity and specificity at different threshold levels to establish the true positive rate and false positive rate, respectively. The threshold determines the level below which a result is interpreted as negative, and all other results are interpreted as positive. These results are depicted in a ROC curve which plots the true positive rate over the false positive rate.

4.1. 10-fold cross-validation

Fig. 8 shows the confusion matrix for the 10-fold cross-validation, described in Section 3.3. The predicted labels correspond very well with the true labels; this is indicated by the low number of false classifications. The selected operating point maximizes the perpendicular distance between the dashed red line (Luck) the ROC curve. That operating point translates into a threshold of 0.5 which is used to establish the confusion matrix entries. The Area Under Curve (AUC) of 1.00 indicates a perfect result. This outcome indicates that the 1856 misclassifications, reported in the confusion matrix, were not statistically relevant (see Fig. 9).

Fig. 10 shows the accuracy of the models for the test set against the number of epochs. Fig. 11 shows the loss of the model against the number of epochs. These plots show the results obtained with the hold-out validation method outlined in Section 3.4. The performance of the LSTM algorithm is similar across the folds, hence the variance is small. Therefore, the shaded area in the graphs, which indicate the variance, is very small, which makes it barely visible.

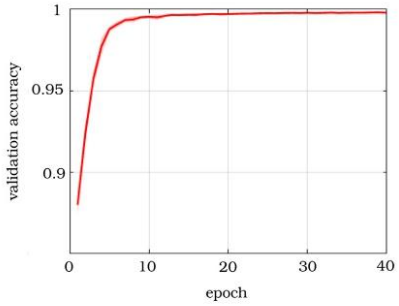

Fig. 10. Validation accuracy over 40 training epochs. The solid red line represents the mean valuation accuracy of the 10 folds and the shaded area indicates the variance.

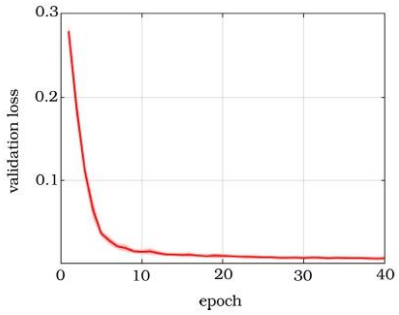

Fig. 11. Validation loss function over 40 epochs. The solid red line represents the mean and the shaded area indicates the variance.

4.2. Hold-out validation

Once the 10 best LSTM models were established during 10-fold cross-validation, we were in a position to conduct the hold-out validation, as described in Section 3.1. The confusion matrix for the hold-out validation is shown in Fig. 12. Based on these measures, the classification performance was established. The last

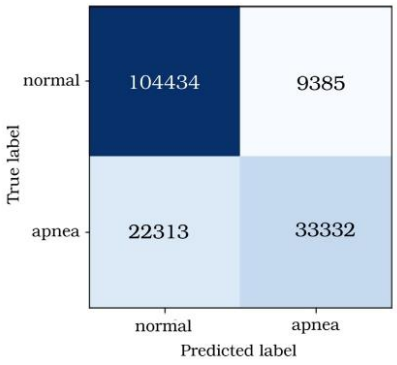

Fig. 12. Hold-out confusion matrix.

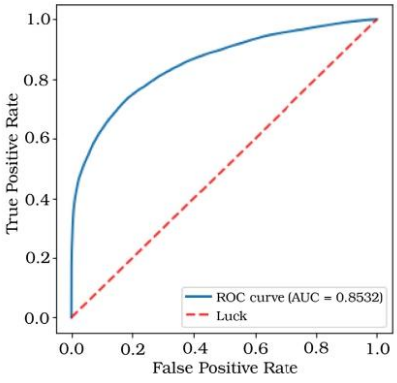

Fig. 13. ROC for Hold-Out validation.

row in Table 3 provides the hold-out performance values. Fig. 13 shows the corresponding ROC curve.

5. Discussion

In this study we show that it is possible to detect sleep apnea through RR interval analysis. The following list details the advantages of the proposed method:

- Low measurement complexity — this translates into low energy requirements, which is beneficial for wireless sensor applications. Furthermore, the measurement can be done in the patient environment, potentially even by the patient.
- Low data rate — It makes RR interval signals energy efficient to communicate, store, and process. In many cases, this energy efficiency translates into cost efficiency.
- Low complexity of the algorithm chain — to classify the RR interval section we use only a two-step process. There is no feature engineering which complicates and in some cases even dilutes the information extraction.
- Real-time processing — RR intervals can be measured, communicated, and processed such that the results are available for efficient diagnostic support, and treatment monitoring can be guaranteed.

This work is based on the assumption that variations in the beat-to-beat interval of the human heart holds information that can help to detect sleep apnea [62]. As a corollary, we assume that all components of the RR signal which do not hold information about the beat variations are irrelevant. With these ground rules in place, we set about investigating appropriate pre-processing methods. Initially, we focused our efforts on detecting and correcting outliers in RR interval data and adjusting the method used for labeling data RR interval blocks. However, with these pre-processing methods, the classification accuracy remained below 80%. Furthermore, the graph which documents the training progress showed a split between training- and valuation-accuracy, which indicates that the network could not extract decision relevant information from the RR interval signal. Only after the band-pass filter, described in Section 3.2.1, initial model fitting tests showed that the valuation accuracy jumped to over 99% and there was no split between the training and valuation performance of the network. As such, detrending the RR interval signals removes a narrow frequency band around DC from the signal. This band does not carry information about the beat-to-beat variability. Hence, the irrelevance reduction does not impact on the beat-to-beat variability as it turns out the opposite effect was observed: detrending improved the classification accuracy significantly. We have selected LSTM as classification algorithm, because previous studies showed that LSTM performed well on time series data. Several researchers have compared the performance of Gated Recurrent Units (GRU) and LSTM model architectures on a range of natural language processing and sequence modeling tasks with no overall winner emerging [63–65]. Generally, GRU models seem to perform better when datasets are small, with LSTM models exhibiting greater expressive power in capturing long term dependencies in larger datasets.

Our study was based on data from the well known PhysioNet Apnea-ECG Database. That enabled us to compare our results with the classification results that are available from other research projects. Table 3 summarizes the outcome of these research projects. Some classical studies were focused on the design of digital biomarkers, which extract in specific properties from the available signals. For example, Varon et al. used orthogonal subspace projections to extracted 7 digital biomarkers from an ECG-Derived Respiration (EDR) signal [66]. Mendez et al. combined an autoregressive model with a K-Nearest Neighbor (K-NN) classifier to achieve a classification accuracy of above 85% [67]. An extreme learning machine was used by Tripathy to classify digital biomarkers, extracted with intrinsic band functions, from both EDR and HRV signals [68]. Song et al. extracted 11 digital biomarkers hidden in the ECG [49]. The resulting values were fed into a Markov model to refine the information further. Janbakhshi and Shamsollahi extracted digital biomarkers from ECG to derive EDR [69]. Other studies used adaptive boosting (AdaBoost) [50] and even threshold methods [70] for apnea detection. Apart from focusing on detection algorithms, researchers also investigated the practicality of such systems by using data from wearable sensors [51] and by analyzing the real-time properties of the information extraction algorithms [71]. Both studies used Support Vector Machine (SVM) for classification.

Wang et al. [52] used five records (a11, a15, a17, b01, c07) as *Hold-out data*. These are the same five records we used for hold-out validation. Thus, the results achieved are strictly comparable. Table 3 shows the hold-out performance measures for both studies. The hold-out performance of our study is 0.7% better than the results from Wang et al. However, the main point is that both studies could not confirm the 10-fold cross-validation results with equally good hold-out results. This and other limitations will be discussed in the next section.

Table 3
Summary of studies on algorithmic sleep apnea detection based RR interval signals from records in the Apnea-ECG Database.

Author	Classifier	Validation method	No. features	Acc. in %	Sen. in %	Spe. in %
Mendez et al. [67]	K-NN	Leave-One-Out	52	85.7	81.4	88.4
Surrel et al. [51]	SVM	10-fold	88	88.4	73.3	87.6
Bsoul et al. [71]	SVM	Variable-folds	111	88.49	96.77	83.62
Song et al. [49]	SVM+LR	10-fold	32	86.2	80.0	89.9
Hassan [50]	Adaboost	10-fold	18	87.33	81.99	90.72
Janbakhshi et al. [69]	Assemble	Cross-validation	85	90.90	89.60	91.80
Chazal et al. [72]	LD/QD	Many-fold	52	92.5	91.4	93.1
Dong et al. [70]	Threshold	Single-fold	6	90.10	88.29	90.50
Wang et al. [52]	Residual network	10-fold Hold-out	0	94.39 80.60	93.04 –	94.95 –
Proposed method	**LSTM**	**10-fold** **Hold-out**	**0**	**99.80** **81.30**	**99.85** **59.90**	**99.73** **91.75**

5.1. Limitations

The main limitation of this work comes about from the low hold validation accuracy of 81.30%. We suspect that the number of training cases was insufficient to extract knowledge concerning sleep apnea changes in the RR interval signal. Therefore, more varied data is needed to improve the knowledge extracted during training and establish robust hold-out testing. Concerning the data used for this study, there is also a shortcoming in terms of instrumentation. The RR intervals were extracted from ECG signals via automated QRS detection. Changing the instrumentation setup might alter the QRS detection algorithm as well. These different QRS detection algorithms can show variations in the RR interval signal produced from the same ECG signal.

Our study is also limited by the rectangular window we use to create data blocks with 100 RR intervals. The window function alters the PSD of the RR interval sequence. The blocks of 100 RR interval blocks might not contain sufficient data to capture all relevant information present in the nonlinear signal characteristics. Hence, the LSTM algorithm might not receive all of the available information. However, the 10-fold cross-validation and the training progress, indicated by the graphs shown in Figs. 10 and 11, indicate the 100 beats were sufficient to answer the apnea non-apnea question with a high degree of accuracy.

5.2. Future work

The 10-fold cross-validation results show that the proposed deep learning model is robust for the datasets it was trained on. However, the hold-out performance needs to be improved in the future. This should be done by training and testing the model with more varied data. Apart from improving the model, there is also scope to extend the role of the deep learning system from detection to prediction. Recent work by Hu et al. indicates that RR interval based sleep apnea detection might be possible [73].

Hypopnea is defined as abnormally slow or shallow breathing [74]. The airways are partially blocked, in contrast for apnea in which the airways are fully blocked. Hence, hypopnea can be considered a milder form of breathing disorder, which makes it harder to detect. However, hypopnea might lead to apnea, and therefore hypopnea detection can help to initiate treatment which prevents patients from developing sleep apnea [1]. Therefore, in the future we plan to train and test our deep learning model with hypopnea data in order to detect this breathing disorder as well in RR interval signals.

6. Conclusion

In this paper we proposed a processing architecture for sleep apnea detection in RR interval signals. In a pre-processing step we filtered the RR interval signal and partitioned it with a sliding window. The resulting RR interval blocks were fed into an LSTM network for classification. Filtering the signal helped the deep learning system to focus on the information contained in the HRV. As a consequence, the LSTM algorithm could extract relevant knowledge from the signal to achieve a 10-fold cross-validation accuracy of 99.80%. The variance between the folds was low. The hold-out accuracy was 81.30%.

Having accurate and robust processing methods for RR interval based sleep apnea detection is prerequisite for cost-effective CAD systems. These systems could be used for the initial diagnosis and during treatment monitoring. In such a CAD setting, the deep learning results constitute an independent second opinion on the data. In the clinical workflow, a human expert should validate the machine decision through an independent review of the evidence, i.e. the measured signal, information from the patient record, and personal interaction with the patient. Having these two independent opinions during diagnosis and treatment monitoring can help to improve safety, reliability, and quality of the decisions. Safety comes from the human interpretation of the algorithm results. The human expert has to decide whether or not the machine results make sense and act accordingly. This allows machine algorithms and human experts to work symbiotically on the sleep apnea detection problem. The machine algorithms provide real-time monitoring of patient data without risk of inter- and intra-observer variability. Furthermore, computer-based systems do not suffer from fatigue, and the results are reproducible. The decision model can be updated, which will improve the decision support over time. The human expert then becomes involved only if apnea is detected. That will improve reliability and efficiency of the clinical process, because both machine algorithms and human experts will work according to their strength. Diligent machine work is then supervised with human creativity and intuition. Hence, accurate detection of sleep apnea with an LSTM network based on RR interval signals has the potential to become a key component for delivering appropriate diagnostic support and convenient uninterrupted treatment monitoring.

CRediT authorship contribution statement

Oliver Faust: Conception and design of study, Acquisition of data, Analysis and/or interpretation of data, Writing - original draft, Writing - review & editing. **Ragab Barika:** Writing - review & editing. **Alex Shenfield:** Writing - review & editing. **Edward J. Ciaccio:** Writing - review & editing. **U. Rajendra Acharya:** Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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All authors approved the version of the manuscript to be published.

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Appendix 13 A Review of Automated Sleep Stage Scoring Based on Physiological Signals for the New Millennia.

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A review of automated sleep stage scoring based on physiological signals for the new millennia

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ABSTRACT

Background and Objective: Sleep is an important part of our life. That importance is highlighted by the multitude of health problems which result from sleep disorders. Detecting these sleep disorders requires an accurate interpretation of physiological signals. Prerequisite for this interpretation is an understanding of the way in which sleep stage changes manifest themselves in the signal waveform. With that understanding it is possible to build automated sleep stage scoring systems. Apart from their practical relevance for automating sleep disorder diagnosis, these systems provide a good indication of the amount of sleep stage related information communicated by a specific physiological signal.
Methods: This article provides a comprehensive review of automated sleep stage scoring systems, which were created since the year 2000. The systems were developed for Electrocardiogram (ECG), Electroencephalogram (EEG), Electrooculogram (EOG), and a combination of signals.
Results: Our review shows that all of these signals contain information for sleep stage scoring.
Conclusions: The result is important, because it allows us to shift our research focus away from information extraction methods to systemic improvements, such as patient comfort, redundancy, safety and cost.

1. Introduction

Sleep is a basic human function, which is characterized by a sequence of alterations in brain, muscle, eye, heart and respiratory activity. That active and regulated process is a prerequisite for physical and mental health. Sleep renews the body by protecting the metabolizable energy, maturing the neuronal connections, as well as consolidating learning and memory. However, when the life rhythm quickens and lifestyle changes, sleepiness and sleep structure disorders threaten people's routine activities and public safety [1]. Apart from these direct, or immediate risk factors, traumatic childhood experiences may also increase the risk for a number of sleep disorders in adulthood [2]. Demographics show that up to 24% of the adult population have regular sleep problems [3]. In a more focused study, Ohayon and Smirne found that 27.6% of the Italian population had sleep disorder symptoms [4]. The 'Sleep Heart Health Study' established that, across the world, patients experiencing difficulty initiating or maintaining sleep or daytime sleepiness have a reduced Health-Related Quality of Life (HRQoL) [5,6]. The impact of sleep problems on health and HRQoL translates into economic consequences [7,8]. Wickwire et al. estimate that the global aggregate cost for sleep disorders exceeds $100 billion USD per year [9]. Ozminkowski et al. found that, within a six month period, the average direct and indirect costs for adults with sleep disorders were about $1,000 greater than for patients without sleep problems [10]. Several scientific studies provide evidence that there is a strong link between fatigue and occupational safety [11]. Léger demonstrated that sleep problems are statisti-

Acronyms: AASM, American Academy of Sleep Medicine; ANS, Autonomic Nervous System; ANN, Artificial Neural Network; AI, Artificial Intelligence; ANOVA, Analysis Of Variance; BR, Breathing Rate; CD, Correlation Dimension; DFT, Discrete Fourier Transform; DSS, Decision Support System; DWT, Discrete Wavelet Transform; ECG, Electrocardiogram; EDF, European Data Format; EEG, Electroencephalogram; EMG, Electromyogram; EOG, Electrooculogram; GMM, Gaussian Mixture Model; HMM, Hidden Markov Model; HR, Heart Rate; HRQoL, Health-Related Quality of Life; HRV, Heart Rate Variability; IoHT, Internet of Health Things; LDA, Linear Discriminant Analysis; NREM, Non-REM; OSA, Obstructive Sleep Apnea; PSG, Polysomnography; PPV, Pulse Pressure Variation; REM, Rapid Eye Movement; SBLE, Behaviour of Local Extrema; SVM, Support Vector Machine; SWS, Slow Wave Sleep; WNR, Wake, Non-REM, REM.

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cally linked to poorer medical status and worse socio-professional indicators [12]. A French study found that employees with sleep problems missed twice as many workdays during a year when compared to normal sleepers [12]. Sleep studies help to establish the diagnosis of pathologies, such as circadian rhythm disorders, epilepsy, sleep apnea, insomnia and hypersomnia [13,14]. Insomnia is the most common sleep problem in industrialized countries [15,16]. For example, the prevalence of insomnia is 23% in Japan and 56% in the United States). Around 50% of insomnia patients did not seek medical attention [17]. Hence, a large number of patients suffer without treatment. To maintain public health and productivity it is of great importance to monitor sleep and analyze sleep stages.

On an abstract level, there are two main sleep stages, Non-REM (NREM) and Rapid Eye Movement (REM). REM sleep occurs 5–30 min at 90 min intervals. During REM sleep the neuronal activity is higher than during NREM sleep. During NREM sleep, metabolic rate, sympathetic activity, blood pressure, and Heart Rate (HR) decrease while parasympathetic activity increases. Sleep experts follow well-established guidelines for sleep scoring based on guidelines from standardization bodies [18,19]. Nowadays, overnight Polysomnography (PSG) is the 'gold standard' for sleep stage evaluation [20]. It is a multi-parametric measurement apparatus that records a wide range of physiological signals in parallel, such as Electroencephalogram (EEG), Electrocardiogram (ECG), Electrooculogram (EOG), Electromyogram (EMG), blood oxygenation, airflow, and respiratory effort. In the majority of cases, the PSG data is captured in the controlled environment of a sleep laboratory. During pre-processing, the data is divided into 30 s epochs, and every epoch is categorized as either wakefulness, REM sleep or one of four states (S1, ..., S4) during NREM sleep [21–23]. In 2012, the American Academy of Sleep Medicine (AASM) published guidelines where the NREM stages S3 and S4 were combined to one stage (S3) [19], also known as Slow Wave Sleep (SWS) [24]. The guidelines for sleep staging, from Rechtschaffen & Kales, suggest the use of two EEG channels[2], two EOG electrodes and one EMG electrode [18]. Despite the efforts to standardize sleep staging, ambiguities still exist. One such ambiguity comes from the fact that the sleep stage definitions leave some space for individual interpretation [25]. Hence, expert based sleep staging is subject to bias and may therefore be unreliable [24]. For example, Danker et al. examined inter-operator variability of human expert scorers and found an interrater agreement of only 76.8% [26]. Another problem is that the physiological mechanisms, which shape the physiological signals recorded during sleep, are not well understood [6]. It is understood that sleep patterns change significantly with age, but what causes these changes is less clear [27]. The lack of well-established causality between physiological processes and the observed signals makes the data interpretation complex. Furthermore, understanding physiological processes is an active research area, hence new and refined relationships have to be learned all the time. Human experts can extract the required information from medical data and make a diagnosis. However, computational methods can be used as assistive devices to detect subtle differences in imagery, speed up the analysis process, and reduce cost. These systems can provide a wide range of results, starting from event labelling[3], over feature extraction, up to the level of suggesting a diagnosis [28]. Despite progress made in the development of diagnostic support systems, fundamental questions still remain, such as 'Which physiological signals contain sufficient information to support a particular diagnosis?' and 'How can we ensure the safety of the diagnosis?'

In this review, we establish that there is a wide range of physiological signals which contain sleep stage related information. This information can be used to support diagnosis, treatment monitoring and drug efficacy tests. However, before we can harvest these benefits, it is necessary to measure the signals and extract the information. The fact that we found a wide range of signal processing methods indicates that there is no standard method for information extraction, and indeed it is unclear which signals provide sufficient information for diagnosis. To address this uncertainty, we reviewed information extraction mechanisms for different physiological signals, to provide an indication of the information that is actually contained in the data. With respect to this focus, we recognized that automated sleep stage scoring is likely to play a leading role in future work. Computer machinery can assist to reduce inter- and intra-observer variability. Supplementing manual analysis with computerized assistance has the potential to provide cost savings. Furthermore, computer based systems can increase the quality of the extracted information including the utilization of decision support systems to assist in signal interpretation. We have discovered a large body of research on automated sleep stage scoring. This research tends to follow a traditional design methodology of feature extraction, and in some cases automated decision making. The feature extraction step must be carefully considered, because it reduces the information available for decision making, and its design process can be error prone. We recognize that automatic sleep stage classification is a starting point for sleep stage scoring. However, its diagnostic quality is usually insufficient in a practical setting, so that the sleep stage recognition technique ultimately requires manual inspection of the polysomnograms by expert human scorers. To improve outcome, we propose a general sleep stage scoring systems design based on deep learning and Internet of Health Things (IoHT) technology, described in more detail herein.

2. Review

This section presents a review of relevant scientific literature on automated sleep stage scoring. We have structured the review such that the results can be used to support our position on computer assisted sleep stage scoring and to justify our vision for future sleep scoring systems. To be specific, we have structured the review in accordance with the physiological signals that underpin sleep stage scoring. An initial analysis of the available literature showed that EEG, ECG, and EOG data were most often used in automated sleep stage scoring systems. The next three sections provide the review results for sleep scoring systems based on these signals. Individual physiological signals can represent only one aspect of sleep stages. Measuring multiple signals provides the benefit of redundant information as well as possibly providing additional uncorrelated information. Hence, a number of scientific studies have investigated automated sleep stage scoring based on multiple signals. Section 2.4 provides the review results for these systems.

2.1. Electroencephalogram

The EEG is a recording of electrical activity of the brain. EEG patterns show different characteristics during sleep stages. These features have been used for development of numerous sleep stage classification systems [29–32]. A wide variety of signal processing techniques have been used to extract sleep- related information from EEG signals including: time-domain features [33–36], spectral features [37–39], time-frequency features [35,40,41] and non-linear features [42,43]. To provide adequate decision support for medical

[2] The AASM manual suggests three EEG channels while keeping all other signals the same.

[3] For example, respiratory and body movement events.

practitioners, several classification methods have been utilised in the reviewed sleep classification studies including: K-means [33], Support Vector Machine (SVM) [41], Ensemble Classification, such as Random Forest [44], Bootstrap Aggregating [45] and Artificial Neural Network (ANN) [46].

Hassan and Bhuiyan decomposed EEG signals and developed a sleep classification system using the Ensemble Empirical Mode decomposition technique and the RUSBoost classifier with an average accuracy of 88.1% for a six class problem [47]. The accuracy is increased to 90.4% for the six class problem using a tunable-Q factor wavelet transform technique together with Random forest classifier [40]. Diykh, Li and Wen decomposed time domain features of EEG signals and employed and identified six sleep stages using the K-means algorithm with 95.9% accuracy [33]. Bajaj and Pachori [48] used time-frequency features of EEG signals and a multiclass least square SVM classifier to solve a six class problem. The classification accuracy was 88.5%. Hsu et al. proposed a system to classify sleep stages using EEG signal energy features and recurrent neural classifier, resulting in 87.2% accuracy [49]. Seifpour et al. [34] proposed a novel approach for multi-class sleep stage classification by using the symbolic analysis concepts to develop a new time domain feature termed Statistical SBLE. They achieved 90.6% and 97.9% accuracy for six-stage and two-stage classification respectively. Principal component analysis [50] and Deep Learning methods [51–53] have also been employed to construct an EEG-based sleep staging system with reasonable accuracy. Table 1 provides a summary of the review results. The table columns are Author, Data, Feature extraction method, Classification method, and Classification results. The columns of the subsequent three tables have the same content. This allows us to contrast and compare automated sleep stage scoring systems that were based on different physiological signals.

2.2. Electrocardiogram

ECG signals are recordings of the electrical activity of the human heart. In the absence of heart diseases, ECG signals are highly structured and individual signal components can be identified through visual inspection [58]. Individual sleep stages manifest themselves in subtle changes in the ECG signal. Yücelbaş et al., Xiao et al., and Kesper et al. proposed that sleep staging with ECG is less complex, but equally accurate, when compared to PSG analysis [59–61]. Redmond et al. provide further support for the validity of ECG based sleep staging by comparing it with EEG based sleep staging [62,63]. Fell et al. made the case for nonlinear analysis of ECG signals for sleep staging [64,65].

Sleep stages are associated with activities of the Autonomic Nervous System (ANS) [66]. To be specific, during REM sleep, the lung tidal volume decreases, and the respiratory rate exhibits a frequent and irregular pattern compared with that in NREM sleep [67]. Therefore, the characteristics of the related physiological information, such as the respiratory rate and HR vary according to the sleep stages. In a clinical setting, the HR is established by measuring successive beat to beat (RR) intervals from ECG signals [68,69]. Heart Rate Variability (HRV) provides one or multiple measures that help to establish the regularity of HR signals [70,71]. These measures provide meaningful information for clinical intervention [72,73], because they reflect the ANS condition [74–76]. During REM sleep, the HR and its variability are increased due to fluctuations between sympathetic and parasympathetic activities [77,78]. Various HRV parameters, calculated with time-, frequency-domain, and nonlinear analyses, revealed significant differences between NREM and REM sleep [79,80]. Trinder et al. analyzed the autonomic activity during sleep with HRV measures [81]. de Zambotti et al. documented the effects of alcohol on sleep by analysing the cardiac autonomic function [82]. Penzel et al. used detrended fluctuation and spectral analysis for sleep stage information extraction [79]. Respiratory sinus arrhythmia, a periodic variation in the HR according to the respiratory cycle, also exhibits different patterns for REM versus NREM sleep [19]. Liu et al. compared HR and pulse rate variability [83]. They found that pulse rate variability contained similar information as HRV. That is of practical importance, because pulse rate is easier to measure than HR. Virtanen et al. analyzed sleep stage changes in postmenopausal women [84]. Crasset et al. and Faust et al. established that HRV changes with age and gender [85,86]. Mendez et al. proposed a real-time Decision Support System (DSS) for sleep stage scoring based on HR signals [87]. Table 2 provides a summary of the review results on automated sleep scoring systems based on ECG signals. That table includes work on HR, because for all relevant studies the HR signal was extracted from ECG signals with appropriate algorithms.

2.3. Electrooculography and respiratory effort

EOG results from the continuous measurement of the corneo-retinal standing potential which can be used to track eye movements. Hence, this signal provides important information for REM stage detection. According to the AASM rules [19], the EOG electrodes are positioned 1 cm lateral to the left and right outer canthi. That placement is straight forward, indeed it can be undertaken by patients [88]. The user led signal acquisition is an important factor for long term monitoring and continuous sleep stage assessment. From this perspective, the work by Virkkala et al. [89] is important, because they demonstrated that EOG signals contain information about NREM sleep stages. Rahman et al. could significantly improve the classification accuracy of EOG based sleep scoring [90].

Respiratory information has been widely used to assess human nocturnal sleep objectively [91–93]. Long et al. used respiratory effort amplitude to establish an automated sleep stage classification system [94]. To improve the classification accuracy, they performed subject specific feature normalization. Such subject specific interventions are an important topic when it comes to long term sleep health monitoring, because of age-related changes to physiological parameters. Table 3 summarizes the review results for sleep studies based on both EOG and respiratory effort.

2.4. Combination of signals

The combination of multiple physiological signals provides redundant information. That is important for human scorers, because a particular bit of information might be overlooked in one signal, but that same information might be detected in another signal. Therefore, PSG incorporates a wide range of physiological signals. As such, it is the standard method to diagnose sleep disorders [95]. Typically, PSG recordings include the EEG, EOG, EMG and ECG. In many cases, these signals are recorded during the entire night [23,96]. With PSG, sleep stage is manually scored on each 30 s epoch throughout the night by trained sleep experts, forming a sleep hypnogram [22].

EEG signals in combination with other physiological signals, such as ECG, EOG and EMG have also been used to design automatic sleep stage scoring systems [97,98]. Kishi et al. found that the mechanism which governs NREM sleep stage transitions is also important for the REM sleep rhythm [99].

R.S.T. Leung, studied the effects of OSA on the sleep stages by observing autonomic functions through multiple physiological signals [100]. Tracik and Ebersbach studied the sleep attack pattern of a Parkinson patient [101]. They found a very fast transition from stable wakefulness to S2 without passing through S1. Kushida et al. compared subject reports with sleep patterns extracted from PSG measurements [102]. They could not detect significant differences

Table 1
A summary of the review results for selected research work that used a *EEG signals* to support sleep stage scoring.

Author	Data	Feature extraction method	Classification method	Classification results
Mousavi et al., 2019 [53]	The benchmark Sleep-European Data Format (EDF) dataset	time and frequency-domain as well as sequence to sequence features	Deep learning	84.26% accuracy for a two class problem
Michielli et al., 2019 [52]	The benchmark Sleep-EDF dataset	55 time and frequency-domain features	Deep learning	83.6% accuracy for a two class problem
Sharma et al., 2018 [29]	The benchmark Sleep-EDF dataset	Three-band time-frequency localized wavelet filter bank followed by log-energy, signal-fractal-dimensions, and signal-sample-entropy	SVM	Up to 98.3% accuracy for a two class problem
Seifpour et al., 2018 [34]	The benchmark Sleep-EDF dataset	Novel time domain feature named Statistical Behaviour of Local Extrema	Multi class SVM	Up to 97.9% accuracy
Chriskos et al., 2018 [54]	23 healthy male adults between the ages of 23 and 45 (mean: 29 ± 6 years).	Two novel methods offunctional connectivity estimation: Synchronization Likelihood and Relative Wavelet Entropy	SVM [Highest accuracy], K-nearest parameters, Neural network	Accuracy: 92.93%
Memar and Faradji 2018 [44]	Sleep-EDF database (Pz-Oz channel), St. Vincent's University Hospital and University College Dublin (UCDDB), the Expanded Sleep-EDF database (XSEDFDB)	Nested 5-fold cross validation, subject cross-validation	Random Forest	Accuracy: 95.31% for nested 5-fold and 86.64% for subject cross-validation
Hassan and Subasi, 2017 [45]	Sleep-EDF database -DREAMS	Tunable-Q wavelet transform	Bootstrap aggregating (Bagging)	Accuracy: 92.43% for 6-classes from the Sleep-EDF database
Pillay et al., 2018 [35]	16 preterm and term born newborns of 27–41 weeks gestational age (their age at birth)	Multiple features from the time- and frequency-domain	Hidden Markov Models (HMMs), Gaussian Mixture Models (GMMs)	HMM: mean kappa: 0.62 (±0.16) GMM: mean kappa: 0.55 (±0.15).
Supratak et al., 2017 [51]	Montreal Archive of Sleep Studies, Sleep-EDF database	a deep learning model, named DeepSleepNets on raw single-channel data	No classifier	Sleep EDF: Kappa: 0.76 MASS: Kappa: 0.80
da Silveira et al., 2017 [39]	Sleep-EDF (Pz-Oz channel)	Discrete Fourier Transform (DFT)	Random Forest	Accuracy for 6-state sleep stages: 90.5%
Hassan and Bhuiyan, 2016 [40]	Sleep-EDF database	Tunable-Q factor wavelet transform	Random forest	Accuracy: 90.38%, for 6-classes
Hassan and Bhuiyan, 2017 [47]	Sleep-EDF database	Ensemble Empirical Mode Decom- position	Random under sampling boosting (RUSBoost)	Accuracy of up to 98%
Bajaj and Pachori, 2013 [48]	Sleep-EDF database	time-frequency image based on the Wigner-Ville distribution (WVD)	multiclass least squares sup-port SVM.	Accuracy: 88.47
Diykh et al., 2016 [33]	Sleep-EDF database, Sleep Spindles database	The time domain features and structural graph similarity	The K-means clustering algorithm	Accuracy: 95.93% for Sleep-EDF dataset
Dimitriadis et al., 2018 [38]	Sleep-EDF database	Wavelet decomposition and cross-frequency coupling techniques	multi-class Naive Bayes classifier	Accuracy: 94.4%
Čić et al., 2013 [41]	Twenty healthy Croatian babies aged 3 months	intrinsic mode functions decomposition and generalised zero-crossing methods	SVM	Accuracy: 90%
Shi et al., 2015 [32]	25 adult subjects; Sleep Apnea Dataset provided by St. Vincent's Uni-versity Hospital and University College Dublin.	A two-stage multi-view learning algorithm based on a joint collaborative representation	K-means clustering	Accuracy: 81.10%
Vural and Yildiz, 2010 [50]	International Database PhysioNet Sleep Records	Principle component analysis of time domain and frequency domain	no classifier	41.1, 33.7, 92.6, 76.4, 96.4, 79.7% success rates for 6-classes
Koley and Dey, 2012 [55]	28 subjects aged between 35 and 56 suspected to have sleep apnea	SVM based recursive feature elimination technique	Binary SVMs were combined with a one-against-all strategy.	Accuracy: 85%
Şen et al., 2014 [56]	25 individuals aged 50 ±10 years; Data set provided by provided by St. Vincent's University Hospital and University College Dublin	Hybrid approach	Random Forest	Accuracy: 98.02%
Hsu et al., 2013 [49]	Sleep-EDF (Fpz_Cz channel)	Energy feature extraction using FIR bandpass filters	Elman recurrent neural classifier	Accuracy: 87.2%
Acharya et al., 2005 [57]	Sleep-EDF database	Nonlinear measures	Feature statistics through Analysis Of Variance (ANOVA) test	–

Table 2
A summary of the review results for selected research work that used a *ECG signals* to support sleep stage scoring.

Author	Data	Feature extraction method	Classification method	Classification results
Yücelbaş et al., 2018 [59]	Sleep laboratory of Necmettin Erbakan University database and PhyisioNet	Morphological methods	Random Forest, Wake, Non-REM, REM (WNR)	Up to 87.11% accuracy
Fell et al., 2015 [64]	Data from 12 healthy male	Embedding dimension estimation	–	–
Fell et al., 2015 [65]	Data from 12 healthy male	Correlation Dimension (CD), Kolmogorov entropy, and Lyapunov exponent	–	–
Yoon et al., 2017 [78]	Twenty-one healthy subjects (male: 12, female: 9) and 30 subjects (male: 25, female: 5) with Obstructive Sleep Apnea (OSA) recorded at Seoul National University Hospital	HR Statistical parameters, Spectral power, variability measurements	Threshold, REM duration	Accuracy: 87.54%
Liu et al., 2017 [83]	Seventy-five sleep apnea patients. Data recorded as Shandong Province of Traditional Chinese Medicine Hospital	HR, Time domain statistical parameters, Spectral power, nonlinear measurements	Statistical analysis	Not reported
Kesper et al., 2012 [60]	Apnea-ECG and SIESTA Database	HR, Spectral power evaluated by ANOVA	threshold	Accuracy: 57.8%
Virtanen et al., 2007 [84]	71 healthy postmenopausal women	HR, linear, geometric and nonlinear	Statistical analysis	Not reported
Xiao et al., 2013 [61]	Public database Sleep and Stroke Volume Data Bank	HR, linear statistics, spectral power, nonlinear	WNR, random forest	Accuracy: 88.67%
Redmond and Heneghan, 2006 [62]	37 subjects	ECG derived respiration and HR statistics. EEG sleep staging for comparison	Evaluation of HR parameters during different sleep stages	Not reported
Redmond et al., 2007 [63]	31 male subjects	ECG derived respiration and HR statistics.	WNR, Linear Discriminant Analysis (LDA) and a quadratic LDA.	up to 76.1%
Mendez et al., 2010 [87]	24 subjects	HR statistics Spectral power.	REM-NREM, HMM.	Accuracy: 79.3%
Penzel et al., 2003 [79]	64 patients with symptoms of excessive daytime sleepiness and arterial hypertension	HR statistics, spectral power	Wake, light-, deep-sleep REM. ANOVA	Not reported
Crasset et al., 2001 [85]	26 subjects, 18 normal, 4 with heart transplants	HR Statistical analysis	ANOVA	Not reported
Trinder et al., 2001 [81]	14 healthy subjects	HR spectral power, blood pressure	Statistical analysis	Not reported
de Zambotti et al., 2015 [82]	17 healthy subjects	Statistical analysis of labeled data to find sleep stage transitions	Not reported	Not reported

Table 3
A summary of the review results for selected research work that used a *Electrooculography and respiratory effort* to support sleep stage scoring.

Author	Signals and data	Feature extraction method	Classification method	Classification results
Long et al., 2014 [94]	Respiratory effort from 48 healthy subjects participating in the SIESTA project	Respiratory amplitude, statistics, spectral power, amplitude and volume analysis	Subject specific quadratic LDA, WNR	Accuracy: 79%
Liang et al., 2015 [88]	EOG from 16 healthy experimental subjects	Spectral analysis	LDA for wake, REM, S1, S2, SWS classification	Sensitivity: 82.6%.
Virkkala et al., 2007 [89]	EOG from 265 subjects	Spectral analysis	Thresholds for REM S1, S2 and SWS	Epoch agreement: 72.9%.
Rahman et al., 2018 [90]	EOG Physionet DB	Statistics of Discrete Wavelet Transform (DWT) coefficients	6 classes problem approached with SVM, RUSboost and random forest	Accuracy of up to 91.7% with SVM

between the subjective case reports and the objective sleep staging. Montgomery-Downs et al. studied developmental changes of the sleep patterns in children [103]. Long et al. used actigraphy and respiratory effort to determine sleep and wake states [104]. In their study, they emphasized the nonlinear concept of dynamic warping to improve the classification results. Kirjavainen et al. fused information from both respiratory and body movement signals to determine sleep stages and wakefulness in infants and young adults [105]. The movement signals came from a novel sensor enhanced bed, which could measure body movements unobtrusively. Tripathy et al. [106] and Yildirim et al. [107] used a deep learning system to fuse information from multiple signals. Such an approach might provide better robustness in case of noisy and intermittent data. Table 4 summarizes our review findings for automated sleep stage scoring based upon a combination of signals.

3. Discussion

Information can be defined as a measure of what we can learn from a given amount of data [112]. Hence, the idea of extracting information from physiological signals is vital to sleep stage scoring. With this information centric view, the research question can be

Table 4
A summary of the review results for selected research work that used a *combination of physiological signals* to support sleep stage scoring.

Yildirim et al., 2011 [107]	sleep-edf and sleep-edfx	Convolutional neural network	Up to 97.62%	
Author	Signals and data	Feature extraction method	Classification method	Classification results
Tripathy et al., 2018 [106]	MIT-BIH polysomnographic database	From RR: recurrence quantification analysis and dispersion entropy. From ECG: variance and the dispersion entropy of frequency bands	Deep neural network	95.71% accuracy for REM vs. NREM
Kishi et al., 2011 [99]	Full PSG 11 healthy subjects	Statistical analysis	State machine model for waking, REM sleep, S1, S2, and S3	Not reported
Takatani et al., 2018 [108]	74 newborns and 16 adults	EEG spectral power, HR absolute high frequency component.	Statistical analysis, REM and NREM sleep	–
Fonseca et al., 2015 [109]	Data from 48 subjects	ECG: Spectral power, variability measurements, and network analysis. PSG: Time / frequency, and network analysis	LDA, Wake, NREM and REM	Accuracy: 80%
Helland et al., 2015 [6]	EEG, ECG and respiratory signals from the SIESTA database	HR: statistics. PSG: Time / frequency, and network analysis	LDA, Wake, REM and REM	Accuracy: 80%
Kesek et al., 2009 [110]	EEG, ECG and respiratory signals from 230 habitual snorersand 170 other subjects (all female)	HR: statistics and Spectral power. PSG: manual scoring	Evaluation of HR parameters during different sleep stages	Not reported
Estévez et al., 2002 [111]	11 healthy infants	EEG sleep spindle detection EOG REM detection and EMG muscle tone	Threshold WNR	Not reported
Willemen et al., 2014 [3]	36 healthy subjects	HR statistics and spectral power, Breathing Rate (BR) statistics, and movement statistics	SVM WNR	81%
Long et al., 2014 [104]	Actigraphy and respiratory effort, 115 healthy adults	Statistical analysis of dynamic wrapping of body movement	LDA, binary problem for comparing features to a PSG study	accuracy 95.7%
Kirjavainen et al., 2018 [105]	22 infants or young children	Statistical analysis of body movements	Comparison with PSG, WNR	Not reported
R.S.T. Leung, 2015 [100]	17 healthy subjects	Statistical analysis of labeled data to find sleep stage transitions	Not reported	Not reported
Tracik and Ebersbach, 2001 [101]	Full PSG One subject with Parkinson's disease	Visual scoring of W, S1, S2, S3, and REM	Visual scoring	Not reported
Kushida et al., 2001 [102]	Full PSG 100 patients with sleep disorders	Visual scoring of wake and sleep states	Threshold	Accuracy: 77%
Montgomery-Downs et al., 2006 [103]	542 healthy children in the age range from 3.2–8.6 years	Visual scoring of W, S1, S2, S3, and REM	Visual scoring	Not reported

stated as: 'How much information is needed for sleep state scoring and which signals provide that information?' In the absence of a standardized test for automated sleep stage scoring systems, this question is not readily answered, because each published study investigates a specific aspect and presents novel findings. These findings are based on a particular algorithm setup which is used to process data from specific databases. To shed some light on these questions, we have structured the review in terms of individual physiological signals. Based on this structure, we were able to establish that most of the reviewed work was concerned with EEG data. That focus is justified, because sleep and sleep stages is caused by significant changes in the brain activity [42]. Apart from EEG, all physiological signals measure symptoms of sleep stages. That makes it difficult to detect individual NREM stages. Hence, there are fewer studies which focus on these secondary signals. ECG is likely to be the most prominent secondary signal. It picks up sleep related changes in the ANS. EOG is an important signal for REM phase classification. However, NREM stages are rather complex to classify based on the EOG. Fig. 1 depicts the number of studies which use a particular physiological signal. Apart from the amount of studies, another important fact is that the physiological data for all of the reviewed studies originated from clinical studies. There is as of yet no work on long term sleep stage monitoring, which would inevitably require the home recording of signals. PSG studies are carried out in dedicated sleep labs, where patients are kept overnight. In the sleep lab, the cost for the individual measurement is low, compared to the overall cost of running the facility. Hence, it makes sense to measure as many physiological signals as possible during patient study. To be specific, multiple measurements add redundancy that improves the quality of the diagnosis, especially for human scorers. However, the need for redundancy implies that these systems have to address a problem which may be random in nature. Indeed it is difficult, if not impossible, to predict when a human expert will make an error. As a consequence, a prerequisite for reducing the degree of redundancy, and therefore the amount of resources required for a diagnosis, is to make the process which leads to a diagnosis more reliable. In the next section we outline a generic design of an automated sleep stage scoring system which addresses these shortcomings.

3.1. Future work

This review suggests that use of an automated DSS is one way to establish a reliable diagnosis. Trust in the DSS system should be established with traceability [113,114], i.e. the decision process should be transparent and repeatable. Another important aspect is continuous learning. Just like a human practitioner, a DSS must also learn all the time. Furthermore, there is a need for less intru-

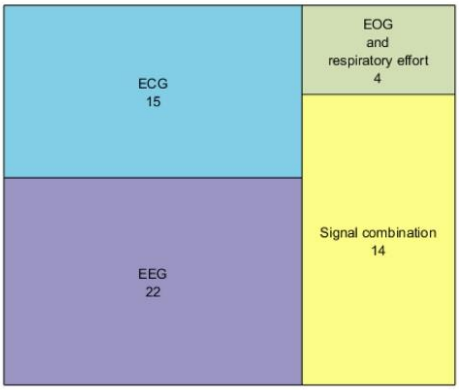

Fig. 1. Treemap representation of the number of studies that used a particular physiological signal. The area of the individual rectangles is proportional to the amount of studies.

sive signal measurement systems, whereby to ensure patient comfort can be improved. In some cases long term monitoring is compromised by patients who fail to wear the sensor equipment, because wearing equipment was uncomfortable. Another important requirement for long term monitoring is real-time analysis [115], since real-time results provide an opportunity to control the therapeutic process.

To address these needs and establish the requirements, we approach the problem from a signal perspective. Recording a physiological signal over multiple sleep cycles implies that the measurement is done in the normal patient environment. EEG signals are impracticable, because the measurement setup must be done by an expert and it is difficult if not impossible for a patient to wear the recording system during the day. EOG is impractical for similar reasons, despite the fact that there are sensor masks that can be applied by patients. The masks, used to measure airflow and respiratory effort, are inconvenient to wear. Long term ECG monitoring is already a standard procedure which could be used to measure multiple sleep cycles. Even more convenient for the patient are HR measurements, because they involve only one sensor attached to a breast strap. That convenience comes from the fact that HR signals can be measured by detecting and encoding the time between two consecutive peaks (R-waves). The R-wave amplitude is rather large, usually in the rage of millivolts, when compared to the remainder of the signal. In contrast, the ECG requires constant recording[4] with a resolution of microvolts. Therefore, the data rate of the HR is much lower[5] when compared to ECG. The lower data rate implies that consumer technology can be used to communicate the HR data. With this technology an unobtrusive sleep stage monitoring, based on the IoHT, can be established [116]. The literature review in Section 2 shows that 5 studies linked HRV with sleep stages. Hence, HR signals contain the required information, i.e. they can be used for sleep staging.

Fig. 2 shows an overview block diagram which captures these requirements. The data is shown flowing from the sensors to a cloud server via mobile technology. From there a deep learning system queries the measured signal in the form of data blocks. These data blocks can be used for automated sleep stage scoring and for learning. The analysis results are disseminated via social networks and other communication apps. This dissemination approach allows us to reach patient, caregivers, and medical staff in a discriminant way. The medical doctor in charge can obtain the raw data independently and review (trace) the decision process of the deep learning system. As such, sensor, mobile device, and cloud storage implement the IoHT. The deep learning system supports the medical practitioner in the process of finding a diagnosis. That diagnosis is disseminated to via the IoHT such that it reaches the correct patient. In this design approach, deep learning takes center stage, because that method considers all of the available information content during both the training and the inference phases [117]. That is an advantage over the traditional machine learning algorithms found in most of the reviewed sleep scoring systems [118]. To be specific, traditional machine learning requires feature extraction to condense the data into a low dimensional feature vector[6], because the decision making algorithms fail to handle high dimensional data. In essence, the feature extraction step is an exercise in information reduction. Hence, traditional machine learning methods never consider all of the available information. Operating on reduced information makes them underperform for unknown data. As a consequence, test result quality, as published in the scientific literature, is difficult if not impossible to achieve in a practical setting. In contrast, deep learning has the potential to excel in such blindfold validation tasks [119]. Hence, deep learning is more suitable for practical applications, such as long term sleep stage monitoring. The decision making algorithm is presented with all of the data containing all the available information. Conceptually, deep learning moves away from information reduction towards knowledge extraction. However, deep learning is computationally complex [119]. Thus, the data must travel to the processing, i.e. physiological data must travel to a data center. Depending on the physiological signal, this might create problems for the communication and storage infrastructure. Hence, we propose HR signals for automated sleep stage scoring. They have the lowest data-rate of all signals taken into consideration.

3.2. Limitations

Traditionally, HR is extracted from ECG signals by detecting the heartbeat (R wave) and subsequently calculating the beat-to-beat (RR) interval [120]. However, the instrumentation effort for measuring HR directly is significantly lower when compared with ECG measurements. In other words, we do not consider the most efficient signal measurement method for scientific studies. That efficiency comes from the fact that the R wave is a readily detected signal deflection. Sensors, which measure the HR directly are efficient, because R wave detection requires less instrumentation effort than ECG measurements. However, this presents a problem, because the heartbeat detection process is not well documented and is oftentimes proprietary to the company which manufactures the sensors. Therefore, it is difficult to establish that direct HR measurements will yield the same beat-to-beat interval sequence as HR extracted from ECG, especially for the subtle signal alterations which are indicative of sleep stage changes. However, none of the reviewed studies is based upon data from HR sensors. All of the relevant research was done by extracting the beat to beat interval from ECG signals. The signals were measured with medical equipment according to measurement standards [121]. Even with standardization, the measurement setup and indeed measurement errors influence the resulting signal [122]. The problem increases if the signal acquisition does not follow medical standards. There is no evidence that direct HR measurements have the same in-

[4] The usual sampling frequency is 256 Hz.

[5] 256 times when we compare the ECG signal with a HR signal of 60 beats per minute.

[6] Typically, less than 10 dimensions.

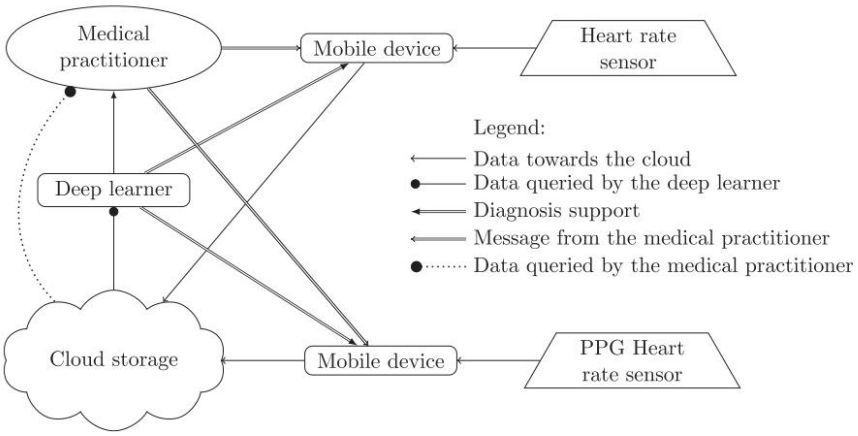

Fig. 2. HR based sleep stage diagnosis support system.

formation content as HR extracted from ECG signals. For example, modern breast strap based HR sensors detect the R wave in hardware[7]. Such a means of detection tends to be less complex when compared to software algorithms that extract the R peaks from ECG [123]. That complexity is required to improve the peak detection quality. Pulse Pressure Variation (PPV) measures HR based on blood flow measurements. It is difficult to establish the measurement quality needed for HRV analysis, because the human circulation system acts as a filter for the heartbeat which pumps the blood. As a consequence, decision making systems that were trained with HR extracted from the ECG might have reduced accuracy when they are used to analyze directly measured HR. Sleep studies are needed which either produce labeled HR signals that are directly measured for the patient or recordings of both ECG and direct HR.

Through the review process, we found that the sleep-EDF database [124] on Physionet [125] has thus far been used in 10 studies. That database contains EEG, EOG, EMG, and respiration signals as well as body temperature. The data provides an excellent opportunity to advance sleep stage technology through cooperation and competition. A common dataset makes the sleep scoring results comparable. Unfortunately, there is no ECG database which has a similar prominence. The 'Sleep HR and SV Data Bank'[8] is also a publicly accessible database, but it has thus far been used in only one study. Granting public access to these databases is a step towards open science that leads to improved technology that can benefit a large number of individuals. However, both data amount and diversity of current databases are insufficient to create universal sleep scoring systems. A sustained effort is needed for remedy.

4. Conclusion

Physiological signals contain sleep stage related information. The task of a DSS is to extract and present this information to a human practitioner. Hence, physiological signals and their information content take center stage in sleep stage scoring. The emphasis on physiological signals is also justified by the fact that instrumentation effort, data rate, and cost differ greatly between the individual signals. In our review, we have found that all investigated physiological signals contain sleep stage related information. From this perspective, the current approach of measuring EEG, EOG, EMG and ECG in one PSG sitting makes sense – a maximal amount of information is obtained in a short period of time. However, some of this information is redundant, i.e. the ECG merely confirms information already extracted from an EEG signal. Redundancy however, is assistive in making a system reliable. For example, a human practitioner might miss a sleep stage transition in an EEG signal due to fatigue, but that expert might spot the transition in the ECG signal. However, that redundancy comes at the cost of expert labor and expensive equipment. The cost and the sheer inconvenience for the patient make recordings longer than one night impractical, even though longer recordings might reveal additional sleep disorders and therefore provide a fuller picture of the patient's sleep health. Patient led signal acquisition and DSS support can help to establish long-term unobtrusive sleep monitoring.

DSS can address issues of inter- and intra-observer variability, because an algorithm produces the same output from a given input regardless of space and time. Furthermore, these systems reduce the need for interpreting multiple signals, because they are immune to fatigue related signal misinterpretations. The need for redundancy can be addressed by observing the physiological signals during multiple sleep cycles. This has the added benefit that more sleep abnormalities can be detected. Furthermore, DSS systems can be made aware of the latest research findings via software and hardware updates, which is convenient and cost effective and can be helpful in tandem with training of human experts.

As part of our future work, we propose to combine AI and IoHT technology to create a HR based sleep scoring system. Using HR ensures patient comfort as well as a lower and therefore more manageable data rate. The signals are stored in a cloud server for traceability and continuous learning. The automated decision support is established with a deep learning system which takes account of all of the available data during the decision making process. We believe that any such a system will benefit patients in part by establishing a real-time sleep monitoring system, which provides constant feedback and emergency messages.

Conflicts of interest

None.

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Statements of ethical approval: For this review article, the authors did not undertake work that involved human participants or animals.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cmpb.2019.04.032.

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Appendix 14 A Review of Automated Sleep Stage Scoring

A review of automated sleep stage scoring

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AASM American Academy of Sleep Medicine
CCNN Complex-valued Convolutional Neural Network
CNN Convolutional Neural Network
CRNN Convolutional Recurrent Neural Network
DT Decision Tree
DL Deep Learning
ECG Electrocardiogram
EEG Electroencephalogram
EMG Electromyogram
EOG Electrooculogram
EDF European Data Format
HMM Hidden Markov Model
HNN Hopfield Neural Network
KNN K-Nearest Neighbors
LDA Linear Discriminant Analysis
NB Naive Bayes
NHTSA National Highway Traffic Safety Administration
NN Neural Networks
NREM Non-Rapid Eye Movement
PSG Polysomnography
RF Random Forest
REM Rapid Eye Movement
R&K Rechtschaffen and Kales
SWS Slow Wave Sleep
SVM Support Vector Machine
HVG Visibility Graph and Horizontal

Introduction

Sleep is a basic human function which covers approximately one-third of the human lifespan (**Yan et al., 2021**; **Acharya et al., 2011**). Adequate night sleep is essential for mental and physical health of a person (**Faust et al., 2016**), and prolonged sleep deprivation has been related to neurobehavioral dysfunction (**Yassin et al., 2020**). **Eldele et al. (2021)** show that, humans who get a good night's sleep have superior health and brain capabilities. **Fiorillo et al. (2019)** established that a significant fraction of the world's population suffers from major sleep disorders which require medical intervention. Several studies have discovered a significant prevalence of sleep-related problems, such as insufficient sleep and trouble falling asleep. In the general population, sleep disorders are common, affecting 22%–65% of people (**Yassin et al., 2020**). **Loh et al. (2020)** found that sleep difficulties affect 16.6% of the adult population, or around 150 million people, and they predict that this number will rise to 260 million people by 2030. According to the American Sleep Association (ASA), 50–70 million persons in the United States suffer from sleep disturbances (**Princy, 2021**). Insomnia symptoms affect approximately 33% of the world's population (**Gurrala et al., 2021**). In addition, more than 100,000 car-accidents happen in the United States each year due to drivers falling asleep, according to the National Highway Traffic Safety Administration (NHTSA). Sleep-related difficulties cause 20% of traffic accidents in the United Kingdom and one out of every four incidents in Germany (**Santaji and Desai, 2020**). The high prevalence indicates that there is a need for technical problem solutions which address sleep related health issues. However, before we can think about technology, we must also understand how the disease affects the economy.

Due to their prevalence and disease specific symptoms, sleep disorders have an economic impact (**Imtiaz, 2021**). Sleep disorders require costly treatments, they lower productivity, and if not effectively treated, disease related symptoms pose public safety risks, like increasing the chances of having traffic accidents. Furthermore, they impact also on a range of other sectors that require attentiveness and fast judgment (**Perslev et al., 2021**). According to **Dietz-Terjung et al. (2021)**, the estimated monetary burden of undiagnosed sleep problems in the United States was $149.6 billion in 2016. They predicted that diagnosing and treating every American adult with sleep problems would cost an additional $49.5 billion. In a focused study, **Lin et al. (2021)** found that sleep problems and delayed sleep time affect about half of all older persons. They established that in the United States, the total healthcare expenses for older persons were 47%–51% greater because of delayed sleep. The medical need, together with the economic impact, should shape our approach to screening, detection, diagnosis, and treatment monitoring of sleep disorders.

Currently, many people with sleep disorders go undiagnosed and untreated due to a lack of public awareness and restricted access to sleep care experts (**Watson and Fernandez, 2021**). The polysomnography "sleep stage scoring" method is one of the most widely utilized methodologies in sleep medicine and research. This method has been around for a long time and is still regarded necessary for understanding sleep architecture. One of the most important steps for diagnosis and treatment of sleep-related problems is the classification of sleep stages. Traditional methods employ qualified human sleep scorers who use a manual scoring procedure to produce repeatable analysis results. This is a time-consuming and taxing procedure. Furthermore, even with strict adherence to standardized procedures intra-and inter-observer variability exists which limits the scoring quality. Researchers have been working for years to develop more efficient, reliable, and accurate categorization algorithms. Computer-assisted sleep stage classification systems are increasingly considered crucial for both diagnosing and monitoring sleep-related disorders. These systems have been successfully applied to the problem of sleep scoring over the years. Despite these accomplishments, fundamental questions still exist, such as:

- How do we incorporate automated sleep stage scoring into clinical workflows?
- How do we avoid bias during training and testing of automated decision support systems?
- How do we make more data publicly available which characterizes sleep accurately?

disorder might be present. A sleep disorder diagnosis should rely on objective measurements. Most objective sleep stage detection methods are based on physiological measurements which require a specialized facility, usually in the form of a sleep lab. The cost of sleep labs implies that these facilities can only be used for the most severe cases. Hence, sleep lab-based diagnosis can do little to reduce the overall cost to society. Furthermore, sleep-lab measurements are taken for only one night under special conditions. This might not represent normal sleep behavior. We adopt the position that current sleep stage scoring methods fail to address the medical need, because their cost is not justified by the economic benefits. Prolonged physiological measurement in the patient environment might be one way to align our methods for screening, detection, diagnosis, and monitoring of sleep disorders. Automated sleep stage scoring takes center stage during this paradigm shift, because only automated analysis and diagnosis support guarantees low levels of intra- and inter-observer variability as well as low cost, with the potential to scale up and meet current healthcare needs.

In this article, we provide an expert review of automated sleep stage scoring. We introduce methods and materials before the review of original work on automated sleep stage scoring is presented. That might benefit the reader, because having an overview of the mechanics for automated sleep stage scoring can help to appreciate and even understand well established scientific work on that topic. An understanding of current research is prerequisite to formulate relevant research questions and identify adequate research gaps. Addressing these research gaps might lead to studies which increase the knowledge of automated sleep stage scoring. The discussion section of this article puts the review work into context with the wider research field of artificial intelligence in medicine. During the discussion we also highlight limitations and give pointers for future work. This article concludes with a summary and our review findings.

Background

The method of obtaining sleep cycle information from electrophysiological signals is known as sleep staging or sleep scoring. This operation is currently done by hand, although efforts to automate it are well underway. In this section, we provide the necessary background on sleep and sleep stage scoring to form a foundation for understanding the automatization approaches. The two most prevalent standards for defining sleep stages are described. The "gold standard" approach for sleep monitoring and sleep stage scoring, polysomnography (PSG), is also described. Following that, we will go through how PSG technologies are used to diagnose sleep disorders.

Sleep staging is an essential approach for diagnosing many sleep related illnesses and disorders (**Satapathy and Loganathan, 2021**). Automated sleep stage scoring systems have been developed to aid sleep scoring in human and animal models since the late 1960s (**Grieger et al., 2021**). Sleep stage scoring is an elementary step during PSG analysis (**Krauss et al., 2021**). Until now, sleep stage scoring has been based on a wide range of physiological signals, such as electroencephalogram (EEG), electromyography (EMG), electrooculography (EOG). During the staging process, these signals are separated into 30 s intervals, called sleep epochs. Each epoch is manually classified by sleep specialists (**Sokolovsky et al., 2020**) and labeled as wake, light sleep, intermediate sleep, deep sleep, and Rapid Eye Movement (REM) sleep (**Perslev et al., 2021**). These labels follow the recommendations from the American Academy of Sleep Medicine (AASM) (**Yan et al., 2021**).

According to a system proposed by Rechtschaffen (R) and Kales (K) in 1968, sleep was split into five stages (**Hussain et al., 2021**). R&K was the first standard which defined commonly agreed rules for sleep stage scoring (**Malafeev et al., 2018**). R&K provides guidelines to break down sleep cycles into five separate stages: non-rapid eye movement (NREM) which can be further classified as sleep stages 1, 2, 3, and 4, and REM stage. Since the 2012 revision of the standard, published by the AASM, stages S3 and S4 should be represented as a single Slow Wave Sleep (SWS) class (**Chriskos et al., 2021**; **Michalek-Zrabkowska et al., 2021**; **Yildirim et al., 2019**). A normal sleeper transits between these sleep stages during night sleep. Meta analysis shows that S2 is the most prevalent sleep stage (**Malik et al., 2018**). The NREM sleep stage takes up 75%–80% of total sleep time, while the REM sleep stage takes up 20%–25% (**Sharma et al., 2021**).

Review

In this part, we provide an overview of automated sleep stage scoring. Conceptionally, we have structured this section in terms of the individual processing steps that lead to automated sleep stage scoring. Any work on this topic starts by identifying a suitable data source. Once the data source is established, a pre-processing step is needed to prepare the data for decision support methods. Broadly speaking, these decision support methods incorporate either traditional machine learning or deep learning (DL) algorithms. These algorithms yield a classification result for a given data segment. For the problem at hand, the classification result will be a sleep stage. That result can be used to support the physician led sleep stage scoring process.

Signal data

During sleep, humans' transition through sleep stages and for sleep stage analysis we are interested in measurements which can document these transitions. Cost and practical obstacles render imaging methods unsuitable for sleep staging. Physiological signals are the logical choice for sleep stage scoring because they can document physiological changes over long periods of time.

During PSG, physiological data is collected from subjects while they are sleeping. A collection of signals is recorded, including EEG, ECG, EOG, and EMG (**Satapathy and Loganathan, 2021**). Automated sleep stage scoring is predominantly based on EEG and EOG measurements. Therefore, we provide more detail for these signals in the subsequent sections. The discussion on signal data concludes with a short review of benchmark datasets.

Electroencephalograms (EEG)

EEG is a technique that measures and records the electrical activity of the brain. During sleep stage scoring, EEG signal records are employed. These signals are indicative of brain activity. The nature of EEG signals is very irregular, nonlinear, and nonstationary (**Acharya et al., 2015**). As a result, EEG signals are appropriate for evaluating sleep disorders (**Faust et al., 2019**). Because of its simplicity single-lead EEG has recently become popular for sleep monitoring (**Acharya et al., 2005**). At least three EEG channels are employed in PSG for sleep staging to collect signals from various regions on the scalp. These electrodes are connected to a machine that records the electrical impulses via wires. The data are printed or presented on a computer screen, and they are used to diagnose epilepsy, sleep disorders, and brain tumors, among other conditions. Delta, theta, alpha, and beta wave bands can be used to structure brain waves which are a morphological feature in EEG signals (**Grieger et al., 2021**). According to the AASM standard, relative signal levels in different frequency bands provide objective information about different sleep stages. For example, alpha waves have a frequency band of 8 Hz–13 Hz, amplitudes of 2 mV–10 mV, and a sinusoidal shape. It can be seen in people who are awake but have closed their eyes and are physically and mentally relaxing. Delta waves occur in settings of very low brain activity, such as profound sleep and general anesthesia, and have a frequency band of 0.5 Hz–4 Hz with amplitudes of 20 mV–400 mV (**Acharya et al., 2015**; **Grieger et al., 2021**).

Once picked up by the electrodes, the signals are fed into a front-end electronic system comprised of amplifiers, filters, and other data gathering hardware before being digitized. EEG signals can be used for assessing brain health as well as diagnosing various sleep and neurological problems. Each 30 s epoch is carefully examined by sleep specialists before being classified into one of five stages (four sleep stages and wake state) (**Eldele et al., 2021**). Measurement complexity and human EEG analysis makes sleep scoring expensive, time-consuming, and error prone (**Santaji and Desai, 2020**). Furthermore, EEG recordings might suffer from interference caused by other physiological measurements that were acquired as part of a PSG (**Santaji and Desai, 2020**). When compared to ECG, EMG, and EOG signals, EEG signals contain more significant and noticeable information. However, it is difficult to use because of limitations caused by electrode displacement and noise (**Imtiaz, 2021**).

Electrooculograms (EOG)

An EOG is a signal produced by eye movements and recorded with electrodes positioned near the eyes. The EOG electrodes are placed 1 cm lateral to the left and right outer canthi, according to AASM guidelines. That placement is straightforward, and patients can do it themselves (**Faust et al., 2019**). EOG signals can be used to identify wake and REM stage, because there are substantial eye movements throughout these stages. Generally, sleep depth is correlated with eye movements—the movement slows down during deeper sleep (**Imtiaz, 2021**).

Benchmark datasets

The Sleep-EDF and EDFx databases include EEG, EOG, and chin EMG signals, as well as event markers. They are available online from the PhysioNet website [https://physionet.org/content/sleep-edfx/1.0.0/]. The EEG signal records are collected from the Fpz-Cz and Pz-Oz channels with a 100 Hz collection frequency, resulting in a data sample length of 3000 for a signal epoch of 30 s. Furthermore, the sleep records originate from two sorts of subjects: those who are in good physical health and those who have modest sleep disorders (**Jain and Ganesan, 2021**).

EDF database

Physionet's Sleep-EDF database contains sleep data from eight participants, four of whom are healthy and four of whom have slight trouble falling asleep. Horizontal EOG, Fpz-Cz, and Pz-Oz EEG channels captured at 100 Hz make up these recordings. Experts have scored each 30 s epoch in accordance with R&K.

EDFx database

The Sleep-EDF database has been expanded and is now available on Physionet. This is an expanded version of the Sleep-EDF database, featuring 197 PSG sleep recordings, 153 from healthy participants and 44 from patients who have slight difficulties sleeping.

Pre-processing

Pre-processing is used to prepare raw measurement results for the classification step. Down sampling, band-pass filtering, and windowing are some of the common procedures in data pre-processing (**Roy et al., 2019**). During our review of scientific studies on automated sleep stage scoring, we discovered that each study used different pre-processing methods.

Apart from these signal conditioning methods, artifact reduction (to eliminate or lessen the effects of artifacts on physiological signals) and segmentation are two of the most prevalent procedures in the pre-processing step (**Seifpour et al., 2018**).

After the pre-processing step, the data is ready for machine classification for medical decision support. The next section reviews common methods that provide the required functionality.

Medical decision support through artificial intelligence

The measured physiological signals must be analyzed to extract diagnostically relevant information. Artificial intelligence is an attempt to automate this analysis step. The idea is that an artificial intelligence algorithm takes a pre-processed signal segment and generates a sleep stage result. However, prior to realizing this automatization, it is necessary to train and test the algorithm. The training and testing process

implies that labeled data was available. For most practical design challenges this is the case, i.e., it is possible to incorporate one or multiple benchmark databases during the design. While training and testing artificial intelligence for sleep stage scoring is not controversial, firm guidance on what algorithms to use for medical decision support is more complex. To start, there are two types of artificial intelligence algorithms that can be used for sleep stage scoring, namely traditional machine classification and DL. Each method has advantages and drawbacks. As such, the selected method will generate the classification results and it will also impact on validity as well as transferability of these results. To reflect on these far-reaching implications, we dedicate the remainder of this section to a review of machine classification and DL for sleep stage scoring.

Machine classification

In recent years, several machine learning techniques have been proposed to categorize sleep stages. One of the benefits of employing machine learning for sleep is the high accuracy, which is especially useful for recognizing disorders and sleep stages. Many researchers have used traditional machine learning algorithms to categorize sleep stages. **Table 1** lists some of the machine learning approaches that are often used for sleep stage classification (**Santaji and Desai, 2020**).

Common to the design of all automated sleep stage scoring systems are data and pre-processing steps. Unique to machine classification are feature engineering and statistical analysis for feature selection (**Eldele et al., 2021**). These two steps prepare the data for machine classification. As such, they are necessary because traditional machine classification algorithms cannot handle high dimensional data. **Fig. 1** depicts the entire procedure with a block diagram. The next sections introduce feature engineering, feature selection, and classification in more detail.

Feature engineering

After the dataset is cleaned through pre-processing, raw data must be transformed into meaningful features that represent the information carried by the signal. Various algorithms for extracting useful information from sleep data have been developed. Furthermore, for identifying significant information, more complicated techniques have combined EOG and EMG signals with EEG. These techniques can be divided into four groups: temporal features, spectral features, time-frequency features, and nonlinear features (**Seifpour et al., 2018**).

Feature selection

Specific sleep stage characteristics or features have been extracted from the epochs as described in the preceding section. The retrieved features are chosen such that they mirror the visual staging guidelines stated in the AASM sleep manual, at least to the extent that an automated system can identify specific traits.

Classification

The process of classifying data into meaningful groups is known as classification. The initial step in the classification process is to find features or qualities that will allow the different categories of data to be distinguished (**Fiorillo et al., 2019**).

Several research groups have developed approaches to automate the sleep staging and apnea/hypopnea event detection processes (**Motamedi-Fakhr et al., 2014**). Until recently, only small data sets were available for algorithm training, see **Table 1** for data requirements per specific algorithm, thus, the analysis methods relied on standard machine learning techniques like K-Nearest Neighbors (kNN) (**Mendez et al., 2010**), Support Vector Machine (SVM) (**Kalaivani, 2020**), and linear discriminant analysis (LDA) (**Ravelo-garcía et al., 2015**). In addition, K-means, decision tree (DT), random forest and hidden Markov models (HMM) are some of the more common techniques in this category (**Elgart et al., 2021**).

Santaji and Desai (2020) suggested an efficient technique for sleep stage classification based on EEG signal analysis utilizing machine learning algorithms with 10 s epochs. Using band-pass filters, EEG data are filtered and divided into frequency sub-bands. With

Table 1 Machine learning approaches that are often used for sleep stage classification.

Techniques	*Technique variations*
Statistical	LDA, SVM, hidden Markov model, Bayesian
Instance	KNN
Decision tree	DT
Ensemble	Ada-boost, random forest
Clustering	K-means clustering

Fig. 1 Generic block diagram for machine learning based sleep staging.

different testing dataset percentages, statistical features were retrieved and extracted using DT, SVM, and random forest methods. The method, suggested by **Santaji and Desai (2020)**, was compared to methodologies used by other researchers as indicated in **Table 2**.

Table 2 provides a comparison between systems that used machine learning methods for automated sleep stage scoring.

Santaji and Desai (2020) categorize sleep stages during that work, they found that RF outperforms both SVM and DT algorithms in terms of classification accuracy. As demonstrated in **Table 2**, the proposed method is compared to methodologies used by other researchers.

Table 3 compares the results from a study by **Loh et al. (2021)** to those of other sleep stage classification studies. This study employed 6075 EEG signal samples, which was less than other studies that used the sleep-EDF database. It should be noted, however, that research using the Sleep-EDF and Sleep-EDFX databases achieved classification accuracies of 92%–95%, but the classification accuracy in this study was achieved for a 3-class problem, i.e., three sleep phases were identified. The classification accuracy was reported as 90.46%. This could be because the EEG signals employed in this study had a sample frequency of 512 Hz, which was five times greater than the other investigations (100 Hz). Another factor could be the quantity of samples utilized; this study used 6075 samples, but other studies used 14,963–127,512 samples.

Deep learning

DL is a branch of machine learning which is characterized by one or more hidden layers in the artificial neural network structure (**Roy et al., 2019**). In general, DL can provide a solution for most machine learning problems. DL is a crucial step in comprehending physiological information (**Faust et al., 2018**). **Perslev et al. (2021)** have used Convolutional Neural Networks (CNNs) for this task. Recently, DL has been used in a variety of fields, demonstrating its superiority over traditional machine learning. This encouraged researchers to use DL techniques to classify sleep stages automatically (**Eldele et al., 2021**). DL algorithms learn optimal characteristics from data. This has improved scoring accuracies for the classic sleep stages of Wake, REM, and Non-REM in recent years. During data analysis, it has been realized that transitional stages, such as pre-REM which occurs between Non-REM and REM, may provide additional insight into the physiology of sleep, and are currently being thoroughly researched (**Grieger et al., 2021**). DL tools were used in approximately 75% of research on automated sleep stage classification (**Loh et al., 2020**).

Deep neural networks can handle high dimensional data. Hence, there is no need for feature extraction and feature selection during the design process. The pre-processed data is directly fed to the classification algorithm for training and testing the network. **Fig. 2** shows a block diagram which depicts the methods needed for DL based sleep staging.

For automatic sleep stage scoring, a variety of classifiers have been utilized, including CNN, deep neural networks (DNNs), and even numerous combinations of them, such as CNN + RNN or DNN + RNN. Most of the experiments used CNN and RNN to process raw PSG data. Other approaches, that have demonstrated promising results, include using precomputed spectrograms (spectral representations expressing the frequency content of signals across time) in combination with CNN and RNN.

Table 2 Comparison of the proposed method with existing sleep classification techniques.

Authors	*Techniques employed*	*Number of stages classified*	*Signal, size*	*Accuracy (%)*
Xi et al. (2013)	HNN	3-NREM = 3	EEG 10 subjects	80.64
Obayya (2014)	Fuzzy clustering	4-NREM/wake/ REM=6	EEG 12 subjects Cairo sleep database	92.27
Zhu et al. (2014)	SVM	4-NREM/wake/ REM=6	EEG 8 subjects sleep EDF database	87.5
Liang et al. (2012)	SVM	2-NREM/wake/ REM=4	EEG-MIT-BIH database	96.2
Ebrahimi et al. (2008)	NN-packet coefficient	3-NREM/wake/ REM=5	EEG 7 subjects sleep EDF database	93.0
Aboalayon et al. (2015)	DT,SVM,NN,NB,KNN	3-NREM/wake/ REM=5	EEG 20 subjects sleep EDF database	97.30
Santaji and Desai (2020)	RF-SVM-DT	02-NREM/REM = 1	EEG 125 subjects sleep EDF database	97.80

Table 3 Summary of the author's findings from automated sleep stage classification research using three classes (W, NREM, and REM).

Authors	*Sampling frequency*	*Datasets*	*Approach*	*No. of samples*	*Accuracy (%)*
Zhu et al. (2014)	100 Hz	Sleep-EDF	HVG + SVM	14,963	92.60
Sharma et al. (2018)	100 Hz	Sleep-EDF	Wavelet filter + SVM	15,139	93.50

Fig. 2 Generic block diagram for deep learning-based sleep staging.

Convolutional neural networks (CNN)

CNNs are modeled on the human visual perception system. Convolutional layers, pooling layers, and fully connected layers are the three functional components that make up CNNs. Each layer applies a function to the data vectors it receives as input, this will change the output data which is passed on to the following layer (**Sokolovsky et al., 2020**). There has been a lot of research into using CNN to classify sleep stages over the last few decades. Furthermore, CNNs are statistical learning models that are versions of neural networks (NNs) that have been effectively applied to image recognition tasks, attaining current state-of-the-art results in picture categorization (**Sokolovsky et al., 2020**). Some scientists have utilized CNN to identify human ailments. Although the CNN architecture has worked admirably in the classification sector, several scientists have tweaked it to distribute classification jobs more evenly (**Yang et al., 2018**). Although a small group has lately begun to use CNN for EEG categorization, there are still significant research gaps (**Cintas et al., 2017**).

Long short-term memory (LSTM)

One of the drawbacks of CNNs is that they are not aware of the temporal unfolding of signals. In other words, CNNs lack memory. During training the weights are updated, but once the training process is completed the network becomes static. This is not ideal for time series analysis, because the signal morphology in the future and indeed in the past might be relevant to classify a current signal segment. LSTM network is the most frequent type of RNN (**Faust et al., 2018**). LSTM algorithms aim to solve this problem by incorporating memory cells. As such they have been extensively used to analyze time series data. Natural language processing, speech recognition, and handwriting recognition are just a few of the applications where it has been applied. Information can cycle via a loop between neighboring time-steps thanks to the links between LSTM units (**Oh et al., 2018**; **Fu et al., 2021**). The memory cell in an LSTM algorithm is made up of five parts: a memory cell (a new variable computed for each timestep), a candidate value for replacing the memory cell at each timestep, and three gates (update gate, forget gate, and output gate) (**Faust et al., 2018**). During the training process, the memory cell is useful for remembering certain values for a long time. The three gates can only take values between 0 and 1, and during the training process, a weight matrix and a bias term will be adjusted for each of them. The forget gate allows to choose which information should be discarded (**Michielli et al., 2019**).

Recurrent neural network (RNN)

RNN architecture is a full-featured deep learning classification algorithm that works well with sequential data. In natural language processing and speech recognition, RNNs are currently the most advanced approaches. Language data can be thought of as sequences, such as words (letter sequences), sentences (word sequences), and documents (document sequences) (sequence of sentences). RNNs are a type of artificial neural network that has the advantage of being able to simulate time series with long-range structural dependencies. RNNs work on the principle of adding a time delay unit and a feedback connection so that information from prior states can be used in later states (**Michielli et al., 2019**).

Table 4 shows the sleep database utilized in prior research for automated sleep stage classification using DL methods. The following is a summary of the DL methods and accuracy acquired from the respective sleep databases: **Table 4**: Sleep-EDF (expanded Sleep-EDF) (**Table 5**). **Tables 4** and **5** show that all automated sleep stage classification studies followed the AASM guidelines and categorized sleep into five stages. **Table 4** shows the subset of PSG recordings that were utilized to train DL models for automatic sleep stage classification.

Table 5 shows an overview of the findings obtained using the same CNN model for various combinations. The two-class (C = 2) dataset employing single-channel EEG signals with the sleep-EDF dataset had the highest identification rate of 98.33%. When the EEG and EOG signals were combined, the best results were achieved for the remaining classes. For the dataset containing six classes, a recognition performance of 91.00% was attained. The sleep-EDFx database yielded the highest accuracy for each class when single-channel EEG data was used. In this database, the greatest identification rate for the six-class stages was 89.43%.

Yildirim et al. (2019) also include a comparison of other studies on the classification of sleep stages using sleep-EDFx data. **Yildirim et al. (2019)** used 127,512 samples of sleep-stage signals from the sleep-EDFx dataset in this investigation. They achieved accuracies for two to six sleep classes of 97.62%, 94.34%, 92.33%, 90.98%, and 89.54%, respectively, utilizing single-channel EEG + EOG data. The accuracy rates achieved with EEG + EOG signals were slightly higher than those obtained with single-channel EEG and single-channel EOG signals.

Tables 3 and **6** compare the results from **Loh et al. (2021)** to those of other sleep stage classification studies. This study employed 6075 EEG signal samples, which was less than other studies that used the sleep-EDF database.

Discussion

This section delves into the strategies that are used for automatic sleep stage scoring. Limitations and further work are also discussed in this section.

Table 4 Summary of automated sleep stage categorization algorithms in the sleep-EDF dataset using DL and PSG recordings.

Authors	*Signals*	*Samples*	*Approach*	*Tools/programming languages*	*Accuracy (%)*
Zhu et al. (2020)	EEG	15,188	Attention CNN	–	93.7
Qureshi et al. (2019)	EEG	41,900	CNN	–	92.5
Yildirim et al. (2019)	EEG	15,188	1D-CNN	Keras	90.8
Hsu et al. (2013)	EEG	2880	Elman RNN	–	87.2
Michielli et al. (2019)	EEG	10,280	RNN-LSTM	MATLAB	86.7
Wei et al. (2018)	EEG	–	CNN	–	84.5
Seo et al. (2020)	EEG	42,308	CRNN	TensorFlow	84.9
Zhang et al. (2020)	EEG	–	CNN	PyTorch	83.6
Supratak et al. (2017)	EEG	41,950	CNN-BiLSTM	–	82.0
Phan et al. (2019)	EEG	–	Multi-task CNN	–	81.9
Tripathy and Rajendra Acharya (2018)	EEG + HRV	7500	Autoencoder	MATLAB	73.7
Biswal et al. (2018)	PSG	10,000	RCNN	PyTorch	87.5
Xu et al. (2020)	PSG	–	DNN	–	86.1
Zhang and Wu (2018)	EEG	–	CUCNN	MATLAB	87.2

Table 5 Summary results of the research on the classification of sleep stages using sleep-EDFx and EDF dataset.

Author	*Number of channel(s)/signals*	*Samples*	*Approach*	*Accuracy (%)*				
				Sleep classes (C)				
				C = 2	*C = 3*	*C = 4*	*C = 5*	*C = 6*
Yildirim et al. (2019)	1 EEG	127,512	1D-CNN	97.85	94.23	92.24	90.48	89.43
	1 EEG	127,512	1D-CNN	97.13	93.35	90.19	88.75	87.08
	1EEG+1EOG	127,512	1D-CNN	97.62	94.34	92.33	90.98	89.54
Author	*Number of channel(s)/signals*	*Samples*	*Approach*	*Accuracy (%)*				
				Sleep classes (C)				
				C = 2	*C = 3*	*C = 4*	*C = 5*	*C = 6*
Yildirim et al. (2019)	1 EEG	15,188	1D-CNN	98.33	94.20	91.39	90.82	89.51
	1 EEG	15,188	1D-CNN	98.06	93.76	91.88	89.77	88.28
	1EEG+1EOG	15,188	1D-CNN	98.06	94.64	92.36	91.22	91.00

Table 6 Summary of the author's findings from automated sleep stage classification research using three classes (W, NREM, and REM).

Authors	*Sampling frequency*	*Datasets*	*Approach*	*No. of samples*	*Accuracy (%)*
Yildirim et al. (2019)	100 Hz	Sleep-EDF	1D-CNN	15,188	94.20
Loh et al. (2021)	512 Hz	CAPSLPDB	1D-CNN	6075	90.46

Sleep stage scoring is an essential approach for diagnosing sleep related illnesses and disorders. That sparks a significant demand for automatization which can help by providing accurate diagnosis and disease management support.

Much research has been published that use machine learning and DL approaches to classify sleep stages using two common sleep databases: Sleep-EDF and Sleep-EDFx. **Tables 2** and **6** show a comparison between a method proposed by **Santaji and Desai (2020)**

with existing sleep classification techniques. **Santaji and Desai (2020)** categorized sleep stages. During their work, they found that RF outperforms SVM and DT algorithms in terms of accuracy. **Table 2** indicates that the proposed method is compared to methodologies used by other researchers. It should be mentioned, however, that research employing the Sleep-EDF and Sleep-EDFx databases achieved classification accuracy of 92%–95%, whereas **Yildirim et al. (2019)** reached a classification accuracy of 90.46% for 3-class sleep phases classification as shown in **Table 6**. This could be because **Yildirim et al. (2019)** employed EEG signals with the high sampling frequency of 512 Hz, which is five times greater than the other research (100 Hz). Another factor could be the quantity of samples utilized; this study used 6075 samples, but other studies used 14,963–127,512 samples.

Limitations

Most studies employed data from only one sleep database to train and test the model, comparing different models and identifying the best performing strategy is difficult. Furthermore, we found that other PSG recordings, such as EOG, EMG, or ECG signals, have not been used in any investigations. Studies that employed PSG recordings did not perform as well as those that solely used EEG signals. As a result, the use of these PSG recordings in real-world applications for automatic sleep stage classification is limited.

Another limitation arises from data driven performance assessment. All studies we reviewed employed some form of data driven performance assessment, usually these were based on accuracy calculations. However, this implies that the classification method was tested with data from the same sample space. For example, the classification method was assessed with data from the same benchmark database that was used for training. This is a problem especially for automated sleep stage scoring because the limited amount of patient specific data might not be sufficient to represent the cohort of all potential patients. What we can hope for is that the classification algorithms have extracted transferable knowledge that is useful even for completely unknown data. However, none of the reviewed studies has tested that assumption.

Transferability of extracted knowledge is a problem for traditional machine learning algorithms. This problem is rooted in the fact that these algorithms can only process low dimensional input vectors. In effect, feature engineering condenses high dimensional signal vectors into low dimensional feature vectors which are used to train and test traditional classification algorithms. It is inevitable that information is lost during this operation. That statement holds true even if we use best practice feature selection methods, because the feature selection is driven by statistical methods rather than classification. As discussed in **Feature engineering** section, feature engineering aims to extract relevant information from pre-processed signal segments. A situation might arise where two feature extraction methods measure the same information, and that information is quite relevant for sleep stage scoring. Hence, including both features into a feature vector used for training and testing the classification algorithm constitutes a missed opportunity to include a different information measure. Missed opportunities such as that constitute a fundamental restriction when it comes to extract transferable knowledge.

DL algorithms are an attempt to address this problem through classification driven feature selection. As such, feature extraction is hidden in the DL algorithm which takes a high dimensional signal segment as input. Having feature extraction functionality within the algorithm allows us to steer the feature selection based on classification results. This avoids the problems introduced by statistical feature selection. We can be sure that all extractable information is used for classification. Therefore, DL algorithms tend to extract more transferable knowledge and if this is the case they perform better, when compared to traditional machine learning algorithms, for completely unknown data. However, classification driven feature selection requires large amounts of data—usually more than the amount of data which is available from benchmark databases. A potential solution is to use multiple benchmark databases. Another solution might be to consider data augmentation techniques.

Future work

Future research efforts should focus on establishing a standalone system that is tailored to the home environment, which would necessitate the development of a hardware component to complement the software. Significant progress has already been made in this area, as evidenced by various scholarly articles (**Gaiduk et al., 2020a,b**). We also intended to develop a system that can distinguish sleep stages and can be used in the house without incurring excessive financial or manpower expenditures. We will investigate using DL to automatically classify sleep stages and the prospect of putting automated sleep analysis software on portable or wearable devices. Furthermore, the system should be easy to use, which led to the selection of signals that may be gathered without being intrusive. This type of device might be widely used to give medical practitioners essential information, allowing for early detection of sleep issues and, as a result, increasing the population's sleep quality.

Conclusion

This review accumulates evidence and identifies future research trends that will clarify the tools and methodology used for automatic sleep staging.

Sleep is an essential part of human and animal species' lives. There is an increasing number of people suffering from sleep disorders around the world. In sleep labs, physiological signals such as EEG, EMG, ECG, and EOG are utilized to diagnose and treat sleep problems, among other things. Visual assessment by a sleep specialist is the most common method for sleep stage classification. This is an extremely time-consuming and difficult task. This approach can be aided by automatic sleep stage classification. Non-REM and REM sleep stages are classified into two categories. Non-REM sleep is separated into three stages: NREM1, NREM2, and NREM3. In this article, we present data using single-channel EEG to automatically score sleep stages. We also introduced and compared two DL-based approaches for automated sleep stage assessment using single channel EEG. Limitations arise from data-driven performance evaluation.

All the studies we looked at used some sort of data-driven performance evaluation, which was mainly based on accuracy calculations. This does, however, imply that the classification approach was validated using data from the same sample space. This is an issue for automated sleep stage scoring, because the limited amount of patient-specific data may not be enough to represent the entire cohort of potential patients.

In the future, research efforts will be employed on automated sleep stage scoring in the home environment. This might necessitate the development of measurement equipment for patient led data acquisition. The development of such automated systems could replace clinical PSG recordings. Hence, there is the potential to diagnose and treat significantly more sleep disorders. This might benefit patients, healthcare providers, and society at large.

Uncited references

Gao et al., 2008; Tong et al., 2015; Weiss et al., 2011.

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