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Screening and early warning system for chronic obstructive pulmonary disease with obstructive sleep apnoea based on the medical Internet of Things in three levels of healthcare: protocol for a prospective, multicentre, observational cohort study

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ABSTRACT

Introduction Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are prevalent respiratory diseases in China and impose significant burdens on the healthcare system. Moreover, the co-occurrence of COPD and OSA exacerbates clinical outcomes significantly. However, comprehensive epidemiological investigations in China remain scarce, and the defining characteristics of the population affected by COPD and OSA, alongside their intrinsic relationship, remain ambiguous.

Methods and analysis We present a protocol for a prospective, multicentre, observational cohort study based on a digital health management platform across three different healthcare tiers in five sites among Chinese patients with COPD. The study aims to establish predicative models to identify OSA among patients with COPD and to predict the prognosis of overlap syndrome (OS) and acute exacerbations of COPD through the Internet of Things (IoT). Moreover, it aims to evaluate the feasibility, effectiveness and cost-effectiveness of IoT in managing chronic diseases within clinical settings. Participants will undergo baseline assessment, physical examination and nocturnal oxygen saturation measuring. Specific questionnaires screening for OSA will also be administered. Diagnostic lung function tests and polysomnography will be performed to confirm COPD and OSA, respectively. All patients will undergo scheduled follow-ups for 12 months to record the changes in symptoms, lung functions and quality of life. Primary outcomes include the prevalence and characteristics of OS, while secondary outcomes encompass OS prognosis and the feasibility of the management model in clinical contexts. A total of 682 patients with COPD will be recruited over 12–24 months.

Ethics and dissemination The study has been approved by Peking University Third Hospital, and all study participants will provide written informed consent. Study results will be published in an appropriate journal and presented at national and international conferences, as well as relevant social media and various stakeholder engagement activities.

Trial registration number NCT04833725.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ In this study, the prevalence and characteristics of obstructive sleep apnoea (OSA) among patients with chronic obstructive pulmonary disease (COPD) in China are investigated.
⇒ The Internet of Things (IoT) is applied in the management of COPD and OSA, covering a wide range of patients attending three different levels of care and community populations in China.
⇒ The feasibility, effectiveness and cost–benefit of IoT are measured in a real-world context, which enhances the generalisability of the findings.
⇒ Due to COVID-19, people may have limited access to healthcare, lung function and polysomnography, which may affect the study results.
⇒ The study may be less representative of people who do not use smartphones or live in rural areas as they may not have access to IoT technology.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common chronic disease with characteristics of persistent respiratory symptoms and airflow limitation.[1] As the third leading cause of global mortality,[2] it affects approximately 100 million individuals in China, with a prevalence of 13.7% among those aged 40 years or older.[3] The association of COPD with comorbidities

amplifies morbidity and mortality rates. Obstructive sleep apnoea (OSA), the most prevalent sleep breathing disorder, commonly complicates COPD.[4 5] Marked by daytime sleepiness and nocturnal snoring accompanied by apnoea, OSA results in nocturnal hypoxaemia and hypercapnia, substantially diminishing quality of life and escalating the risk of cardiovascular and cerebrovascular disorders, consequently elevating mortality rates.[4 5] Globally, OSA affects over 20% of the population, with an annual increase in incidence.[6 7] In China particularly, the situation is dire, with an estimated 176 million individuals afflicted by OSA, ranking the country foremost in OSA prevalence worldwide.[8]

OSA is diagnosed by polysomnography (PSG), which is mainly implemented in tertiary hospitals in China. However, the number of patients with OSA who actually receive diagnosis and treatment is limited due to low awareness and limited resources. This shortfall impedes active prevention strategies and fails to meet the comprehensive needs of patients beyond tertiary hospital settings. Thus, moving the threshold of OSA diagnosis and treatment to primary care is essential, where appropriate screening can be conducted and provide opportunities for early intervention. In China, the promotion of OSA screening in primary care settings has gained traction. In 2022, expert consensus on screening and management of a high-risk population of adults with OSA was published to support and guide the screening for high-risk populations with OSA.[9] Questionnaires such as STOP-Bang, the Epworth Sleepiness Scale (ESS) and the Berlin Questionnaire (BQ) have been recommended for screening.[9]

Both COPD and OSA are prevalent respiratory diseases with concerning increasing trends and well-defined impacts on quality of life. Research indicates a substantial proportion of patients with COPD concurrently experience Obstructive Sleep Apnea Syndrome (OSAS),[4 10–13] yet the specific correlation between the two conditions remains elusive. The concept of overlap syndrome (OS), which refers to individuals suffering from both COPD and OSA, has attracted great attention due to its association with a higher risk of mortality, more frequent cardiovascular events, poorer quality of life, increased risk of COPD exacerbation and higher medical costs.[4 14–17] Global studies reported that the prevalence of OS ranges from 1.0% to 3.6% in the population aged 40–89 years old.[4 5] The prevalence of OSA among patients with COPD is between 56.45% and 78%, while the coexistence of COPD in patients with OSA leads to a prevalence of 11.9%–23.2%.[14] Given the large populations of COPD and OSA, it is estimated that there is also a huge potential population of OS in China; however, the specific prevalence or epidemiology of OSA among patients with COPD in China is unknown.

Despite substantial variation in reported prevalence estimates for OS between epidemiological studies thus far, few studies have been conducted in China. Existing studies predominantly feature small sample sizes, limiting their capacity to comprehensively portray OS prevalence and characteristics in both the COPD and general populations. Conducting large-scale studies on OS in China is imperative. Such studies hold pivotal significance in unravelling the natural history, clinical ramifications and prognosis of this syndrome. Additionally, they aid in patient identification and facilitate the administration of appropriate therapies. Notably, screening assumes crucial importance, given that improved clinical outcomes have been observed in patients with COPD–OSA overlap on receiving treatment.[15] Although studies have demonstrated the feasibility of questionnaires or portable devices to screen for COPD or OSA,[14 18 19] there has been no effective or appropriate method to identify patients with the combination of both COPD and OSA.

Although COPD and OSA are common chronic respiratory diseases, ideally the best management of COPD and OSA occurs in primary care. Regrettably, the current capacity of primary care facilities in China remains inadequate. As a consequence, there exists a notable trend among patients to seek care in larger hospitals, leading to a dearth of COPD or OSA management within primary care settings. In recent years, China has implemented a hierarchical diagnosis and treatment policy in the hope that these diseases can be well treated within the health system; however, there is a lack of effective referral mechanisms between different medical institutions.

The Internet of Things (IoT) is a network of devices and objects equipped with sensors, software, electronics and network connectivity that communicate with each other wirelessly and transmit data to a cloud platform.[20 21] Over the past few years, IoT has experienced rapid development and its usage has extremely expanded in responding to COVID-19 pandemic.[20 22–24] Leveraging the advantages of IoT prompts us to contemplate its application in the management of COPD and OSA. This study endeavours to explore a novel management model using IoT technology to effectively identify OSA among patients with COPD and revolutionise the clinical approach to these chronic respiratory conditions.

Aims

The aim of the study is to establish a screening and early warning system for COPD with OSA based on IoT.

Objectives

- To evaluate the prevalence and describe the characteristics of OSA among patients with COPD.
- To assess the feasibility, effectiveness and cost-effectiveness of IoT-based long-term management for COPD and OSA in clinical settings.
- To establish a two-way referral channel between primary care and superior hospitals for COPD and OSA based on IoT.

METHODS/DESIGN

Study design

A prospective, multicentre, observational cohort study will be conducted. The study is registered at https://clinicaltrials.gov (NCT04833725).

The Strengthening the Reporting of Observational Studies in Epidemiology[25] checklist is used to inform the content of the protocol and will also be used to report the results of the study.

Study setting

Participants will be recruited from different levels of healthcare. The general tertiary hospital is Peking University Third Hospital (PUTH), the secondary hospitals are Haidian Hospital and Zhongguancun Hospital, and the primary care facilities are Beixiaguan Community Health Service Center and Huayuan Road Community Health Service Center.

Study population

Inclusion criteria

- Aged 40–80 years.
- Residing in Beijing.
- Patients with stable COPD registered at the study sites.

Exclusion criteria

- Contraindicated for spirometry (chest infection in the last 3 weeks, coughing up blood in the last month, severe angina, uncontrolled high blood pressure, pneumothorax or history in the last 3 months of tuberculosis, heart attack, detached retina or surgery on the chest/abdomen/brain/ears/eyes, or previous adverse reaction to salbutamol).
- Unable to perform spirometry (eg, dementia or lack of teeth—cannot make a good seal).
- Unable to perform sleep monitoring.
- Cannot or will not apply the mobile app operation.
- Unable to provide informed consent.
- Judged by the physician as not able to participate.

Recruitment

WeChat, a prominent social media application in China, assumes an active role in scientific research endeavours.[26–28] Leveraging its substantial social influence, this study aims to use WeChat for patient recruitment purposes. The five research sites and their satellite offices will employ WeChat as a platform to advertise the study. E-posters will be displayed on their WeChat platforms, accompanied by targeted messages dispatched to relevant WeChat groups, extending invitations to residents interested in participating. Potentially eligible patients visiting the research sites will be given a brief study introduction by healthcare professionals and invited to attend a baseline assessment, referring to demographic characteristics, questionnaires and tests.

The uncertainty surrounding patients' acceptance of the disease management model and their willingness to participate in the study indeed presents a potential challenge to recruitment. Moreover, the ongoing impact of COVID-19 further complicates matters, potentially limiting access to healthcare services, lung function tests and PSG, potentially causing delays in recruitment. To ensure the study's quality and strict adherence to the protocol, an initial trial phase will occur exclusively at the five designated research sites during the first month of recruitment. This trial period aims for a thorough assessment and potential adjustments to optimise study procedures as needed. On completion of this comprehensive trial phase, the study will proceed according to the refined and optimised protocols. The study flow diagram is shown in figure 1.

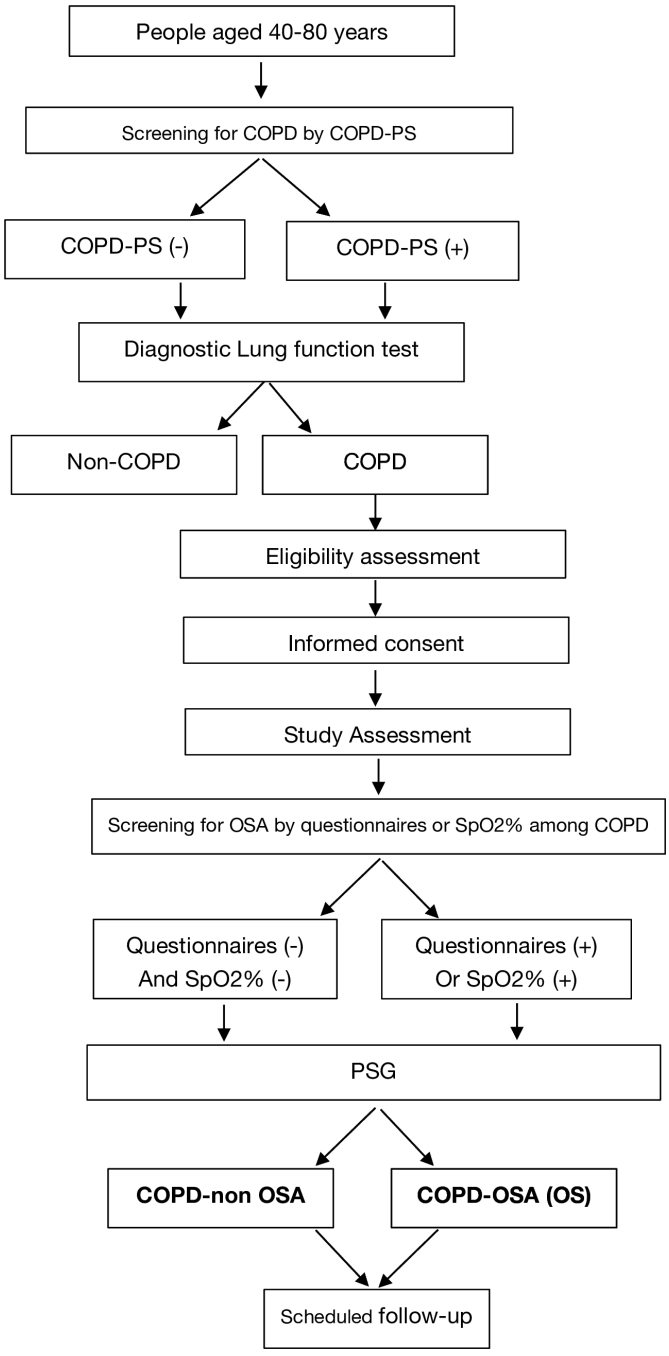

Figure 1 Study flow diagram. COPD, chronic obstructive pulmonary disease; OS, overlap syndrome; OSA, obstructive sleep apnoea; PSG, polysomnography; SpO_2, oxygen saturation; COPD-PS, the Self Scored COPD Population Screener Questionnaire.

Data collection

The data collection process for this study is bifurcated into two phases aligning with the study's objectives. The

initial phase involves identifying patients with COPD and establishing a COPD cohort. Subsequently, screening tools including STOP-Bang,[29] BQ,[30] ESS[31] and nocturnal oxygen saturation (SpO_2%) will be employed to detect OSA among patients diagnosed with COPD. All patients will undergo PSG, thereby enabling the establishment of an OS cohort. Using these data and machine learning techniques, a model will be developed to effectively screen for OSA in patients with COPD. The study's second phase entails a long-term follow-up, using IoT technology to observe and document the natural prognosis of OS and explore the interplay between COPD and OSA. This phase will culminate in the development of an OS prognosis model. Furthermore, the feasibility of an IoT-based management will be comprehensively evaluated. Eligible participants will be registered on a secure IoT platform named BOE (https://copd.boe.com.cn), and data will be entered into the platform.

Baseline assessment

All eligible participants enrolled in the study will undergo a comprehensive baseline assessment covering demographic characteristics such as height, weight, waist and neck circumference, blood pressure, smoking history, comorbidities, exposures, supplemental oxygen usage and medications. Additionally, their health status will be evaluated using the St George's Quality of Life Questionnaire,[32] while respiratory symptoms will be assessed through the CAT (COPD Assessment Test)[33] and mMRC (Modified British Medical Research Council) Dyspnea Scale.[34] These evaluations will be periodically updated during follow-up. Furthermore, the baseline assessment will include laboratory tests, lung function assessments, ECG, chest radiographs and nocturnal SpO_2% measurements using a fingertip pulse oximeter. Additionally, the cost per visit for health-related issues will be diligently recorded. For individuals with a history of COPD, information regarding the frequency of exacerbations within the last 12 months will also be collected. If patients diagnosed with COPD or OSA require treatments that are unavailable at the two community health service centres (CHSCs), they will be appropriately referred to secondary or tertiary hospitals. Standard treatments such as inhalers, continuous positive airway pressure or supplemental oxygen not accessible at the CHSCs will be provided at these higher-level healthcare facilities. After patients are registered on the BOE platform, they will receive labels based on assessment results, and these labels will dynamically change in response to variations in deterministic diagnostic outcomes. The anticipated labels include 'low risk with OSA', 'high risk with OSA', 'COPD', 'OSA' and 'COPD-OSA (OS)'. At any given point, a patient may carry multiple labels, and the platform will diligently track and display the evolution of label changes for each patient. Sleep monitoring recording and lung function test reviewers will be blinded to the above evaluation results to avoid review bias.

Follow-up and outcomes

After the initial baseline evaluation, regular follow-ups will occur every 3 months for all patients following recruitment. Patients who become lost to follow-up (having no response after three reminders), experience severe adverse events, withdraw consent or meet the study endpoints will be considered as having withdrawn from the study.

The follow-up process concludes if any of the following endpoints occur: (1) patient deceases; (2) non-response to assessment after three telephone reminders; and (3) inability to tolerate the required tests. The outlined follow-up schedule is detailed in table 1.

For the long-term disease monitoring, the following indicators will be observed: incidence of acute exacerbation of COPD (AECOPD); visits to healthcare facilities or hospitalisations for AECOPD per year; changes in lung function (forced expiratory volume in 1 s, forced expiratory volume in 1 s:forced vital capacity) and sleep monitoring indicators (ODI (Oxygen Desaturation Index), average nocturnal SpO_2%, minimum blood oxygen saturation, SpO_2% <90% accounted for the percentage of night monitoring time); changes in CAT, mMRC and quality of life assessment; new comorbidities; mortality; and medical cost.

AECOPD is defined as the acute worsening of respiratory symptoms, resulting in additional therapy according to the 2020 Global Initiative for Chronic Obstructive Lung Disease (GOLD).[1]

Screening for OSA

STOP-Bang (≥3),[29] BQ (>2),[30] ESS (>10),[31] nocturnal SpO_2% and heart rate measuring with a finger pulse oxygen instrument (BM2000A, BERRY, China) for one (up to three) night at home are administered to screen for OSA.

COPD diagnosis

At the baseline assessment, all recruited patients will undergo postbronchodilator diagnostic lung function tests (20–60 min after administration of 400 µg salbutamol) by a proficient healthcare professional with lung function certification, and a respiratory physician will diagnose COPD according to the 2020 GOLD.[1] As diagnostic spirometries are readily available at the five designated research sites, lung function tests will be conducted individually at each site. Therefore, standardised diagnostic spirometries across all sites are not mandated for this study. For the research sites where diagnostic lung function tests are not available, participants will be referred to PUTH by the BOE platform for a final diagnosis.

OSA diagnosis

All patients diagnosed with COPD will be referred to the sleep centre at PUTH to perform PSG (Apnealink Air, RESMED, Australia) to diagnose OSA following the American Academy of Sleep Medicine[35 36] and the criteria of the Chinese Sleep Society.[37 38]

Table 1 Follow-up schedule

Item/time	Baseline assessment	Third month	Sixth month	Ninth month	Twelfth month
Follow-up approach	Field investigation	Field investigation or telephone	Field investigation or telephone	Field investigation or telephone	Field investigation
COPD-PS	√				
STOP-Bang	√				
Berlin Questionnaire	√				
Epworth Sleepiness Scale	√				
CAT	√	√	√	√	√
mMRC	√	√	√	√	√
St George's Quality of Life Questionnaire	√	√	√	√	√
Combinations	√	√	√	√	√
Medications or therapy	√	√	√	√	√
Oxygen therapy	√	√	√	√	√
Lung function	√	√	√	√	√
Sleep monitoring indicators	√	√	√	√	√
Events of AECOPD during the last 3 months	√	√	√	√	√
Incidence of AECOPD during the last 3 months	√	√	√	√	√
Visits to healthcare or hospitalisations for AECOPD	√	√	√	√	√
Medical cost related to COPD or sleep breathing disorders	√	√	√	√	√
Referral		√	√	√	√
Withdrawal		√	√	√	√

AECOPD, acute exacerbation of COPD; CAT, COPD Assessment Test mMRC: Modified British Medical Research Council; COPD, chronic obstructive pulmonary disease; COPD-PS, the Self-Scored COPD Population Screener Questionnaire; STOP-Bang, Snoring, Tired, Observed, Pressure, BMI, Age, Neck, Gender.

Resource utilization

To assess the healthcare costs associated with this disease management model, we will conduct a comprehensive analysis of the expenses involved, including equipment and medical professional workers' type and grade. In addition, healthcare costs for patients' hospital admission, costs for IoT medical equipment (like finger pulse oxygen instrument and app on a mobile phone), and IoT platform establishment, maintenance and support will also be evaluated. Additional costs such as the time caregivers spend with the patient addressing health issues (calculated based on local wages) and the expenses incurred by patients during each hospital or CHSC visit will also be meticulously documented.

Statistical analysis plan

Sample size

Given that this study revolves around the construction of a machine learning-based model, we combined conventional sample size calculation methods and machine learning sample size algorithms to confirm the final sample size.

In terms of machine learning, we referred to the previous Time-Aware Long-Short Term Memory (T-LSTM) study,[39] which was a patient subtyping model for analysing sequential and longitudinal patient records. The T-LSTM model was trained and evaluated on the PPMI (Parkinson's Progression Markers Initiative) data set, comprising 654 patients. The COPD and OSA diagnosing and subtyping task and the target deep learning-based diagnostic model to be developed in this study were closely related to the reference research. Therefore, we took the sample size calculation of T-LSTM study as a reference, and finally 654 patients would be recruited in the data collection process to ensure accuracy.

In terms of conventional sample size calculations for clinical studies, the sample size was calculated by the

following formula: $N = \frac{Z_{\alpha}^2 p(1-p)}{d^2}$, where p was the prevalence of OSA among patients with COPD and was given the value of 52.8% based on findings from our previous study.[40] We proposed a confidence level of α=0.05 with a two-sided value in the standard normal distribution Zα=1.96. The relative error was proposed as 0.1 to account for the allowable error, d=0.1×p. We estimated a response rate of 80%, which led to an enrolment target of 430 patients with COPD. In order to do the power analysis for comparing the ability to screen for OSA between sleep assessment questionnaires, nocturnal SpO_2% and PSG, we proposed a sample size of 682 (which was larger than the sample based on machine learning calculation), a prevalence estimated by PSG of 52.8% and a significance level of 0.05. The power to find a difference of 10% in the prevalence of OSA between either of sleep assessment questionnaires and nocturnal SpO_2% and PSG was 96% (pwr package in R), which was acceptable for conducting this study. Based on the above, 682 patients with COPD will be recruited in this study.

Analysis plan

Data will be analysed using Stata V.15.

Descriptive statistics are made for general demographic information. Normally distributed continuous variables will be presented as mean±SD, while non-normally distributed continuous variables will be represented by median and IQR. Categorical variables will be expressed as absolute numbers and percentages (n, %). The differences among the groups are compared using the χ^2 test for categorical variables and t-tests or Wilcoxon rank-sum tests for continuous variables depending on the distribution. Missing data will be analysed using the 'last observation carried forward' method. Differences are considered significant at p<0.05 for all statistical analyses.

The performance of COPD-PS (the Self-Scored COPD Population Screener Questionnaire) to screen for COPD, sleep assessment questionnaires and nocturnal SpO_2% used to screen for OSA will be investigated by presenting 2×2 tables and calculating the sensitivity, specificity, and positive and negative predictive values, along with 95% CI. For the test with a continuous score, a receiver operator curve analysis with the area under the curve (with 95% CI) will be produced.

The primary outcomes are the prevalence and characteristic of OS, hospitalisations for COPD or OSA, incidences of AECOPD, morbidity and mortality.

The secondary outcomes are changes in respiratory symptoms, lung function, sleep assessment, as well as the quality of life, and the cost per true OS detected, the cost per hospitalisation or visit to healthcare avoided.

BOE health digital platform construction

The system contains four functional units: data collection, data storage, data processing, and early warning and message releasing. There are three components: a wearable device (a finger pulse oxygen), disease management platform (BOE) and an app on smartphones. Data collected by wearable devices will be transferred to the BOE platform and the app via Bluetooth and transforming protocol. Lung function tests will also be uploaded to the platform in the form of picture or file. Both patients and medical professionals can conveniently review this information using the mobile app installed on their smartphones or mobile devices. Disease assessment tools and forms to record therapy, medical cost and comorbidities, as well as referral forms are embedded in the platform. Administrators can edit modules according to the needs or requirements of medical care providers. The platform will be updated iteratively on a regular basis. All data are encrypted to protect privacy. What sets this disease management platform apart is its ability to break down information barriers not only between care providers and patients but also among the three levels of care, enabling seamless information sharing. Logical management was set up and the diagnostic criteria for COPD and OSA were embedded in the platform. In this way, the platform can automatically identify patients with OSA among patients with COPD through logical relationships between various data. Another article we are writing on medical engineering would detail the construction of the platform and the operating system, the algorithms applied in the system, the functions of each module, the establishment and implementation of screening and prediction models, and possible application scenarios for the whole system.

Patients are registered on the BOE platform by scanning a QR (quick response) code with their smartphones to connect to the app. Assessment can then be done by filling in relevant information in corresponding modules. When information suggesting changes in disease status is emerging, the platform will automatically integrate the information to form and issue alerts to medical professions, simultaneously reminding patients to consult physicians. In addition, a prediction model of AECOPD will be established based on the instant evaluation of patients' diseases through machine learning to achieve prediction of AECOPD to provide early warnings. (Continual assessment of patients' symptoms and disease conditions during follow-ups enables the use of updated data for timely prediction of potential acute exacerbations. These predictions evolve based on extensive data, allowing for real-time adjustments to the prediction model using any newly imported data into the BOE platform). This feature is being continuously applied and iterated to improve the predictive model's accuracy. The structure of the BOE platform is shown in figure 2.

For the warning model of OSA in patients with COPD, different core data are selected as indicators of disease diagnosis and status. The changes in each indicator over time have different weights to the analysis of the patients' conditions. For example, blood oxygen saturation mainly reflects the severity of apnoea, and it is a priority reference in screening for OSA. Another article we are writing on medical engineering will detail the

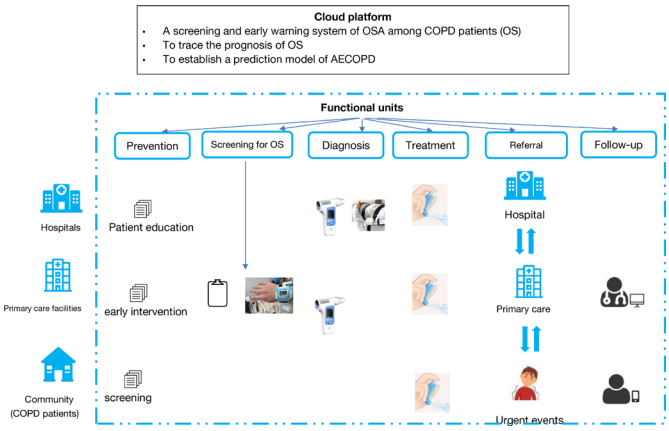

Figure 2 Structure of the BOE platform. AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease; OS, overlap syndrome; OSA, obstructive sleep apnoea.

construction of the platform and the whole operation system.

Data management and quality control

All researchers involved in the study are medical professionals affiliated with the five research sites. A comprehensive 1-week training session will be conducted to ensure adherence to standardised study processes. This training will encompass various facets, including study protocols, assessment methodologies, respiratory and sleep physiology knowledge, as well as proficiency in conducting PSG and spirometry lung function tests. An expert will over-read spirometry traces to ensure sufficient quality before recruitment commences. ZP will over-read all spirometry tests during the study period to ensure quality is maintained. PSG will be conducted at PUTH by a professionally certified technician (YH) with 10 years of experience in sleep monitoring. A scheduled regular monitoring site visit plan is set up to ensure researchers adhere to the study protocol. Researchers will visit the sites monthly or quarterly based on the implementation quality. In every visit, especially during site initiation visits, the study team will observe a complete study assessment. The study will conduct monitoring site visits throughout the study period (from the recruitment of the first patient to the end of the last follow-up of the last patient, which will be from March 2021 to December 2023).

Patient and public involvement

No patient or public will be involved in the study design and implementation, reporting or dissemination plans of our research.

ETHICS AND DISSEMINATION

Ethics and informed consent

The study has been approved by the Ethics Review Committee of Peking University Third Hospital (2020-R-235-01) (online supplemental file 1). Medical ethics committee approvals have also been obtained from the other four research sites (Ethics Review Committee of Haidian Hospital, Ethics Review Committee of Zhongguancun Hospital, Ethics Review Group of Beixiaguan Community Health Service Center and Ethics Review Group of Huayuan Road Community Health Service Center) before the initiation of recruitment. Written informed consent will be obtained from all participants (online supplemental file 2) before the assessment.

Dissemination and publication policy

Study results will be published in peer-reviewed journals and presented at conferences and relevant stakeholder engagement activities. There will be no information that can identify participants in any publication. Participants who explicitly express a wish to be informed about the research outcome will be contacted and offered to receive an article or poster with a lay summary of the study.

DISCUSSION

This study aims to establish a screening and early warning system for COPD with OSA based on IoT, covering primary care facilities and secondary and tertiary hospitals.

Considering the large population of patients with COPD and OSA in China, it is reasonable to estimate that there is a great potential population of COPD patients with OSA, despite the lack of accurate epidemiological data on the prevalence of OS. To address knowledge gaps in the prevalence and characteristics of OSA in patients with COPD in China, our study will provide robust evidence on the profile of the combination and the association between COPD and OSA. As far as we know, this is the first study with a large sample size focused on OSA among patients with COPD in China. Previous studies primarily concentrated on patients within tertiary hospitals, with only a limited representation of the community population. This is also the first study to leverage IoT for COPD and OSA management during the COVID-19 epidemic, which covers a wide range of patients, including those presenting to three distinct levels of care and community populations.

In the last two decades, we have seen IoT grow enormously, especially in medicine.[41–43] Studies investigating the application of IoT in COPD and OSA have been documented.[44–50] However, minimal attention has been given to OS. While these studies have highlighted the explicit performances of devices or technologies in research settings, their practical functionality in clinical practice settings remains largely unexplored. Meanwhile, there is lack of economic evaluation of IoT. In the study, we will evaluate the system's performance in clinical settings, including a detailed economic analysis, which will objectively and comprehensively evaluate the feasibility, effectiveness and cost-effectiveness of IoT in clinical settings. Moreover, the study duration covers the COVID-19 pandemic, effectively providing practical evidence for IoT management of COPD and OSA in terms of feasibility and patients' acceptance of the management

model. Over the past decades, numerous health management platforms have emerged, yet their clinical application often falls short of anticipated effectiveness. Many of these platforms have been abandoned post scientific research tasks due to issues such as poor data quality and low utilisation, resulting in significant resource wastage. Our study aims to conduct a comprehensive investigation to validate the long-term efficacy of IoT in reducing costs and enhancing the quality of life for individuals affected by COPD, OSA and OS. Presently, studies concerning IoT in medical care are predominantly conducted in high-income countries, creating a notable gap in IoT research within low-resource settings.[42] By filling this gap, our study will offer critical evidence regarding the practical application of IoT in resource-limited areas.

Since the health system in China is different from that of Western countries, people can choose medical institutions according to their own wishes without requirements for referral. Generally, individuals tend to favour tertiary hospitals, consequently undermining the significance of primary care. While primary care has been an integral part of China's healthcare system since its inception, it took decades for people to truly recognise its significance.[51] Recently, hierarchical diagnosis and treatment is a public health issue with great concern in the management of common chronic diseases (like COPD). However, in reality, the implementation is not ideal, primarily attributed to the lack of available and effective referral mechanisms or referral channels, resulting in a poor interface between primary care facilities and hospitals. In this study, a two-way referral system is integrated in the BOE platform, making it possible to refer patients to hospitals and back to primary care facilities and pushing the implementation of hierarchical diagnosis and treatment for COPD and OSA.

In regular clinical practice in primary care in China, COPD-PS is recommended to screen for COPD,[52] but there is lack of validation of the questionnaire. Although screening for COPD is not the main purpose of this study, COPD-PS is embedded in the platform to further assess the accuracy in clinical settings. Research has indicated that the Oxygen Decrease Index can serve as a screening tool for OSA.[53 54] In China, the use of sleep monitoring tools is recommended for OSA screening, provided the availability of resources permits.[55] However, the performance of such tools in clinical practice is unclear. Moreover, even though STOP-Bang, BQ and the ESS have been widely validated in different countries,[56] there is a lack of validation in Chinese population. In the study, we systematically evaluated the performance of questionnaires and sleep monitoring device for screening, which will provide persuasive evidence for the effectiveness of these tools in different clinical settings.

Predicting AECOPD remains critical and challenging in COPD management. Meanwhile, patients with OS are at higher risk of AECOPD. Previous studies have developed IoT-based AECOPD prediction models, yet these investigations either relied on small sample sizes or exclusively involved hospitalised patients.[44 57 58] The external validation of these models remains inadequate, particularly in primary care settings. In this study, AECOPD prediction models applicable to three different levels of medical care will be established and validated generally and will provide practical evidence for early detection of AECOPD.

Similar to other studies in this domain, this research encounters common challenges prevalent in IoT investigations, including technical hurdles, social disruptions and regulatory considerations.[41 42] In anticipation of potential challenges, we have devised corresponding countermeasures. These include comprehensive training for research staff, detailed participant explanations, an efficient communication system enabling patients to promptly contact researchers if system issues arise, and continuous and vigilant data monitoring throughout the study to uphold data integrity and accessibility. During the study, the devices and the system will be iterated to ensure accuracy in measurements and technical issues. These limitations are speculative and subject to change based on the actual research process. A timely feedback mechanism has been put in place to respond to potential challenges that may arise during the implementation of the study. Lastly, the study may be less representative of people who do not use smartphones or live in rural areas as they may not have access to IoT technology.

In conclusion, this study will provide detailed OS epidemiological data, build disease prediction models and referral channels, and perform economic evaluation of IoT to provide rich evidence for IoT-based clinical practice.

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