Official Title

Construction and Validation of an Impulse Oscillometry (IOS)-Based Platform for Screening, Diagnosis, and Management of Chronic Airway Diseases

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1. Research Background and Rationale

Chronic obstructive pulmonary disease (COPD) and bronchial asthma are common chronic airway diseases that pose a serious threat to public health, affecting approximately 600 million people worldwide. In 2015, about 3.2 million people died from COPD and 400,000 from asthma [1]. In China, chronic airway diseases represented by COPD and asthma have become major chronic diseases that seriously endanger public health. The China Pulmonary Health (CPH) study, led by our team, showed that the prevalence of COPD among Chinese adults aged 20 years and older is 8.6% [2], and the prevalence of asthma is 4.2% [3]. Chronic airway diseases impose a huge medical burden. However, although medical expenditures for chronic airway diseases continue to rise, some key clinical outcomes have not improved accordingly [4]. Their prevention and management face three core challenges: low rates of early diagnosis, non-standardized management, and weak diagnostic and treatment capacity at the primary care level.

Conventional spirometry, as the primary method for assessing respiratory function, relies on forced expiratory maneuvers by patients, which limits its application in elderly, pediatric, and severely ill patients, and makes it difficult to sensitively identify small airway dysfunction, an early pathological change. Impulse oscillometry (IOS) is the most widely used type of forced oscillation technique. Based on the spectral relationship between pressure and airflow during tidal breathing, it can non-invasively measure respiratory system impedance, including resistance and reactance parameters [5], and is particularly sensitive to changes in small airways [6]. Because IOS requires minimal patient cooperation and is sensitive to small airway function, it is often considered a complementary tool to spirometry [7-9].

A large number of previous studies have shown that IOS parameters have good application value in the diagnosis and assessment of COPD and asthma. IOS parameters (such as R5-R20, Fres, and AX) are significantly correlated with FEF25-75 measured by spirometry and have higher sensitivity [10]. In subjects with chronic respiratory symptoms and normal pulmonary function, IOS is more sensitive than spirometry in

detecting small airway dysfunction [11]. Recent domestic studies have further explored a new IOS-based severity classification system for COPD (the SAIO grading system) [12]. Huang CH et al. [13] used IOS parameters and multiple machine learning methods to establish a predictive model for distinguishing COPD from asthma. However, the clinical application of this technology in China still faces key bottlenecks: the lack of diagnostic criteria and standardized pathways based on the Chinese population; the unclear value of IOS in dynamic disease management and prognosis prediction; and the lack of high-level evidence on its application effectiveness in real-world settings, especially in primary care institutions. Therefore, conducting systematic research on IOS technology and platform construction is an urgent need to promote the precise and standardized application of this technology and to address current clinical dilemmas.

In our previous work, we further explored the application value of IOS in COPD screening, auxiliary diagnosis, and severity assessment. We were the first to construct a COPD screening pathway based on an IOS-derived prediction model for the forced expiratory volume in one second to forced vital capacity ratio (FEV_1/FVC). The results were published in *The Lancet Regional Health - Western Pacific* [14], and a corresponding invention patent was filed. In asthma patients, we were also the first to discover the effectiveness of combining IOS with FeNO in identifying patients with inadequately controlled asthma symptoms [15]. These preliminary studies have laid a key methodological and evidence base for the systematic construction of a "screening-diagnosis-management" platform in this project.

The lead institution of this project, the Beijing Institute of Respiratory Medicine, and its important component, the Department of Respiratory and Critical Care Medicine of Beijing Chaoyang Hospital, Capital Medical University, is a National Key Discipline in Respiratory Diseases and a National Clinical Key Specialty Construction Project Unit of the National Health Commission. It has a profound foundation in the prevention and treatment of respiratory diseases, especially COPD and asthma. It has served as the responsible institution and led the Ministry of Health Public Welfare Industry Research Project - China Pulmonary Health (CPH) study. It has completed multiple national

science and technology projects, support programs, and four major chronic disease projects during the "10th Five-Year Plan" to the "14th Five-Year Plan" periods, and has achieved multiple research results.

In terms of basic research and the establishment and management of biological specimens, it also has a good preliminary working foundation and software and hardware environment. The Beijing Key Laboratory of Respiratory and Pulmonary Circulation Diseases is affiliated with Beijing Chaoyang Hospital, Capital Medical University. The laboratory has a building area of more than 3,600 square meters and 15 full-time researchers. The center also has a biological specimen bank equipped with 30 -80°C freezers and 30 liquid nitrogen tanks, with dedicated personnel responsible for specimen management, providing the experimental conditions to complete this project. In summary, the direction of this research closely aligns with the national strategy for chronic disease prevention and control. The team possesses full-chain capabilities from basic research to clinical translation, and from technology development to guideline formulation, providing a solid foundation for the smooth implementation of this project.

2. Study Objectives

To construct and validate IOS-based diagnostic models for chronic airway diseases: Participants will be enrolled from the respiratory and critical care medicine outpatient clinics and physical examination centers of multiple centers. Using respiratory specialists' clinical diagnosis as the gold standard, diagnostic models for COPD and asthma based on impulse oscillometry (IOS) parameters will be established, their optimal diagnostic thresholds will be determined, and diagnostic performance indicators such as sensitivity, specificity, and area under the curve (AUC) will be systematically evaluated. In addition, external validation of the COPD and asthma screening models will be conducted in multicenter community populations to determine the optimal diagnostic thresholds and evaluate their sensitivity, specificity, and AUC.

To construct IOS-based prognostic warning models for chronic airway diseases: In patients with confirmed stable COPD or asthma, a 48-week prospective cohort follow-up will be conducted to analyze the association between IOS parameters and the

risk of future acute exacerbations, and to construct a Cox proportional hazards regression prediction model based on IOS parameters for the dynamic management and prognostic warning of chronic airway diseases.

3. Study Sites or Study Population

3.1 Phase 1: Construction and Validation of IOS-Based Screening and Diagnostic Models for Chronic Airway Diseases

Study Nature: Multicenter, cross-sectional study.

Study Sites: Respiratory and critical care medicine outpatient clinics, physical examination centers, and community health service centers in multiple regions across China (Northeast, Central South, East China, Northwest, and Southwest).

Study Population: Participants aged 18–80 years from respiratory clinics, physical examination centers, and community health service centers across China.

3.2 Phase 2: Construction of an IOS-Based Dynamic Management and Prognostic Warning Platform for Chronic Airway Diseases

Study Nature: Multicenter, prospective cohort study.

Study Sites: Respiratory and critical care medicine outpatient clinics in multiple regions across China (Northeast, Central South, East China, Northwest, and Southwest).

Study Population: Patients aged 18–80 years with confirmed stable COPD (meeting GOLD diagnostic criteria) or bronchial asthma (meeting GINA diagnostic criteria) based on clinical and pulmonary function examinations. Stable disease is defined as no acute exacerbation within the past 4 weeks, without the need for systemic glucocorticoids or increased routine medication.

4. Study Design

4.1 Phase 1: Construction and Validation of IOS-Based Screening and Diagnostic Models for Chronic Airway Diseases

This part is a cross-sectional study. It is planned to enroll participants from respiratory clinics and physical examination centers of multiple hospitals across China. Using respiratory specialists' clinical diagnosis of COPD and asthma as the gold standard, diagnostic models for COPD and asthma based on impulse oscillometry (IOS)

parameters will be constructed, and their optimal diagnostic thresholds will be determined. Meanwhile, external validation of the COPD and asthma screening models will be conducted in multicenter community populations.

1) Inclusion Criteria:

- Age 18–80 years;
- Clear consciousness, with basic communication and comprehension ability, able to cooperate with questionnaires and IOS/pulmonary function examinations;
- Willing to participate in this study and sign written informed consent.

2) Exclusion Criteria:

- Confirmed respiratory infection within the past 4 weeks;
- Other diseases that severely affect pulmonary function, such as active pulmonary tuberculosis, extensive bronchiectasis, pulmonary fibrosis, chest wall deformity, lung cancer, etc.;
- Comorbid severe dysfunction of important organs such as the heart, brain, liver, and kidney (e.g., New York Heart Association class III–IV, severe arrhythmia, uremia, etc.) or uncontrolled malignant tumors;
- Cognitive impairment or psychiatric disorders that prevent cooperation with the study procedures;
- Pregnant or lactating women;
- Contraindications to pulmonary function tests (including spirometry, bronchial challenge/bronchodilation tests).

3) Outcome Measures:

Respiratory specialists will make the final clinical diagnosis (COPD/asthma/other) based on a comprehensive assessment of patient symptoms, spirometry results (including bronchodilation/bronchial challenge tests), and other clinical indicators.

4) Predictive Variables:

Based on previous research and literature review, the candidate variables include: age, sex, height, weight, body mass index (BMI), smoking status (pack-years), and IOS

parameters: total respiratory impedance (R5), central airway resistance (R20), peripheral airway resistance (R5-R20), reactance area (AX), and resonant frequency (Fres).

4.2 Phase 2: Construction of an IOS-Based Dynamic Management and Prognostic Warning Platform for Chronic Airway Diseases

This part is a prospective cohort study. The objective is to conduct a 48-week dynamic follow-up of patients with confirmed stable COPD or asthma, analyze the association between IOS parameters and the risk of acute exacerbations, and construct a Cox regression risk prediction model.

1) Inclusion Criteria:

- Age 18–80 years;
- Patients with COPD meeting the Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnostic criteria, or patients with asthma meeting the Global Initiative for Asthma (GINA) diagnostic criteria;
- Disease in a stable phase (defined as no acute exacerbation within the past 4 weeks, without the need for systemic glucocorticoids or increased routine medication);
- Willing to participate in this study and sign informed consent.

2) Exclusion Criteria:

- Comorbid other severe respiratory diseases (such as bronchiectasis, pulmonary fibrosis, lung cancer, active pulmonary tuberculosis, etc.);
- Comorbid severe heart, liver, or kidney dysfunction (such as NYHA class III–IV, end-stage liver disease, dialysis-dependent renal disease);
- Known conditions affecting the accuracy of pulmonary function tests (such as chest wall deformity, pneumothorax, recent thoracic or abdominal surgery);
- Severe cognitive impairment, psychiatric disorders, or communication barriers that prevent cooperation with questionnaires and examinations;
- Planning to move out of the study center coverage area within the next 1

year, or unable to guarantee completion of regular follow-up;

- Pregnant or lactating women.

3) Outcome Measures:

- Primary outcome: Acute exacerbation events (defined as symptom deterioration requiring systemic glucocorticoid use, antibiotic use, emergency department visits, or hospitalization);
- Secondary outcomes: Annual decline rate of pulmonary function, changes in quality of life scores, all-cause mortality, and respiratory-related mortality.

4) Follow-up Plan and Observation Indicators:

Follow-up plan: After enrollment, outpatient follow-up will be conducted every 12 weeks to collect information on respiratory symptoms, acute exacerbations (frequency, severity, and days of hospitalization/emergency department visits), new comorbidities, mortality (COPD/asthma-related and all-cause), and treatment adjustments. At each follow-up visit, questionnaires will be used to assess symptoms and quality of life.

5. Sample Size

5.1 Phase 1: Construction and Validation of IOS-Based Screening and Diagnostic Models for Chronic Airway Diseases

This phase aims to establish diagnostic models for COPD and asthma based on IOS parameters. A total of 14 predictive variables (sex, age, height, weight, and IOS parameters) are planned to be included. According to the principle of subjects per variable (SPV) > 10, the number of subjects initially expected to be included in the linear regression prediction model should be at least 10 times the number of predictive variables. Therefore, the training set requires at least $14 \times 10 = 140$ participants. Based on our previous research, assuming that the prevalence of COPD among the hospital population aged 20 years and older is approximately 25% [14] and the prevalence of asthma is approximately 25%, the total sample size required for the respiratory and critical care medicine outpatient clinics and physical examination centers of multiple

hospitals is calculated as: 140 / 0.25 ≈ 600 cases, including at least approximately 150 COPD patients and at least 150 asthma patients from hospital outpatient clinics.

In addition, external validation of the COPD and asthma screening models is planned in multicenter community populations. The sample size estimation is based on the confidence interval width of the AUC in diagnostic accuracy studies [16]. The confidence level is set at 95% (two-sided), and the width of the 95% confidence interval for the AUC estimate is required not to exceed 0.15. The AUCs of the models for discriminating COPD and asthma are expected to be 0.80 each. Based on literature, the prevalence of COPD among Chinese adults aged 40 years and older is conservatively estimated to be 13.7% [2], requiring at least 55 COPD patients to be included, corresponding to a total sample size of approximately 400 cases. Based on literature, the prevalence of asthma among Chinese adults aged 20 years and older is conservatively estimated to be 4.2% [3], requiring at least 50 asthma patients to be included, corresponding to a total sample size of approximately 1,200 cases. Therefore, in the external validation, a total sample size of approximately 1,200 cases from multicenter community populations is required, including at least 55 COPD patients and 50 asthma patients.

5.2 Phase 2: Construction of an IOS-Based Dynamic Management and Prognostic Warning Platform for Chronic Airway Diseases

The sample size calculation in this study is based on the requirements for constructing a Cox proportional hazards regression model. A total of 14 predictive variables (sex, age, height, weight, and IOS parameters) are planned to be included. According to the principle of subjects per variable (SPV) > 10, the number of subjects initially expected to be included in the linear regression prediction model should be at least 10 times the number of predictive variables. Therefore, the training set requires at least 14 × 10 = 140 participants. According to previous literature, the annual acute exacerbation rate is 40% for COPD patients and estimated to be 30% for asthma patients, with a preset dropout rate of 15%. Based on this, the required sample size for COPD patients from multiple hospitals is calculated as (140 / 0.40) × 1.15 ≈ 400 cases,

including at least 160 cases with acute exacerbations of COPD. The required sample size for asthma patients from multiple hospitals is calculated as (140 / 0.30) × 1.15 ≈ 550 cases, including at least 165 cases with acute exacerbations of asthma. Therefore, a total sample size of 1,000 cases of confirmed COPD or asthma from multiple hospitals is required, including at least 160 cases with acute exacerbations of COPD and at least 165 cases with acute exacerbations of asthma.

6. Data Collection

6.1 Phase 1: Construction and Validation of IOS-Based Screening and Diagnostic Models for Chronic Airway Diseases

1) Demographic data: sex, age, height, weight, body mass index (BMI), smoking status (pack-years), occupational exposure history, and biomass fuel exposure history;

2) Clinical information: respiratory symptoms (cough, sputum, shortness of breath, wheezing, etc.) and their severity, disease duration, personal and family allergy history, and previous diagnosis and treatment history;

3) Screening questionnaires: COPD Population Screener (COPD-PS), COPD Screening Questionnaire (COPD-SQ), and European Community Respiratory Health Survey (ECRHS) questionnaire;

4) Pulmonary function indicators: IOS parameters: R5, R20, R5-R20, AX, Fres, etc., before and after medication; spirometry parameters: FEV1, FVC, FEV1/FVC, MMEF, etc., before and after medication; bronchodilation test/bronchial challenge test results;

5) Inflammatory biomarkers: complete blood count (including eosinophil level), serum total immunoglobulin E (IgE) measurement, and FeNO level;

6) Gold standard diagnosis: final clinical diagnosis made by respiratory specialists (COPD/asthma/other).

Specific Methods:

(1) Impulse Oscillometry (IOS) Testing:

The testing instrument is a portable IOS device (IOS600, UBREATH, China). According to the method recommended by the European Respiratory Society (ERS),

patients should remove tight clothing, relax, maintain an upright upper body, avoid slouching, and practice uniform and calm breathing. After sitting quietly for 20 minutes, the test is performed. The head should be kept natural, horizontal, or slightly tilted upward. A nose clip is worn, both palms press the cheeks on both sides, the teeth bite the mouthpiece tightly, the tongue must not block the mouthpiece, and there should be no air leakage. The patient breathes calmly and relaxed for 45–60 seconds. Daily calibration is performed, and graphical data such as spectral analysis plots and impedance-volume plots are recorded for quality control. Each participant is measured at least 3 times, and the average value meeting quality control standards (e.g., R5 variation < 10%) is taken. The main analysis parameters include: total respiratory impedance (R5), central airway resistance (R20), peripheral airway resistance (R5-R20), reactance area (AX), and resonant frequency (Fres).

(2) Traditional Spirometry:

A portable or non-portable pulmonary function instrument (MasterScreen Pneumo) is used. The procedure is performed according to the recommendations of the American Thoracic Society (ATS)/ERS joint guidelines. Patients must exclude relevant contraindications and are prohibited from eating a large meal 2 hours before the test, smoking 1 hour before the test, and strenuous exercise 30 minutes before the test. The patient is seated and performs tidal breathing, that is, uniform and calm breathing 3–5 times. At the end of tidal expiration, the patient inhales maximally to total lung capacity through a respiratory filter, then exhales explosively and continues to exhale uniformly and completely to residual volume. During forced expiration to residual volume, there should be no interruption or coughing. The patient should exhale as long as possible, for more than 6 seconds or until an expiratory plateau appears, then rapidly inhale maximally to total lung capacity. Thereafter, the results are quality controlled. The above procedure must be repeated at least 3 times, and the best measurement value is recorded. The main indicators include: forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and maximal mid-expiratory flow (MMEF). The bronchial challenge test uses a standard method (such as methacholine),

and the positive criterion is: cumulative provocative dose (PD20) or concentration (PC20) causing a ≥20% decrease in FEV1.

(3) Bronchodilation Test:

After completing baseline IOS and spirometry measurements, all patients undergo a bronchodilation test. The patient exhales air from the lungs to residual volume, begins slow deep inhalation through the mouth at the end of expiration, and simultaneously inhales 100 μg of salbutamol sulfate inhalation aerosol (trade name: Ventolin, manufacturer: GlaxoSmithKline, specification: 100 μg/puff) via a spacer until the end of deep inhalation, holds the breath for 5–10 seconds, then resumes normal breathing, for a total of 4 puffs, i.e., a total of 400 μg of salbutamol sulfate inhalation aerosol. Twenty minutes after the last puff, post-bronchodilation IOS and spirometry examinations are performed. The positive criterion for the bronchodilation test is: FEV1 increases by ≥12% compared with before medication, and the absolute value increases by ≥200 mL.

(4) Fractional Exhaled Nitric Oxide (FeNO) Testing:

According to the method recommended by ATS/ERS guidelines [17], the testing instrument is a nitric oxide analyzer with an electrochemical sensor (NIOX; Aerocrine AB, Stockholm, Sweden). The subject is seated, first exhales completely, then inhales treated air through a nitric oxide scrubber to maximal lung capacity. The subject then exhales against an automatic resistance regulator, which maintains the expiratory flow rate at a constant 50 mL/s. By adjusting the instrument resistance, the upper airway pressure of the subject can be maintained at a level of at least 5 cm H2O throughout the expiratory process. This pressure is sufficient to keep the soft palate closed and expel air from the nasal cavity. FeNO measurement is performed when the exhaled nitric oxide concentration reaches a stable plateau and is maintained for at least 3 seconds. If the expiratory process fails to meet the required flow rate and plateau standards, it is considered an unqualified operation and cannot be measured. In this case, repeated exhalation is required, up to a maximum of 6 repeated measurements, from which 3 qualified measurement results with consistency within 10% are obtained. The

measurement result is the mean of the above three measurement results. The nitric oxide monitor needs to be calibrated every 14 days, and also when the room temperature changes by more than 5°C.

This examination should be completed before other pulmonary function tests.

(5) Blood Tests:

Researchers will collect no more than 20 mL of blood from each participant. Blood will be used for the following tests and analyses: eosinophil level and serum total immunoglobulin E (IgE) measurement.

6.2 Phase 2: Construction of an IOS-Based Dynamic Management and Prognostic Warning Platform for Chronic Airway Diseases

Baseline Indicators:

1) Demographic data: including sex, date of birth, height, weight, living environment, education level/years of formal education; smoking history/passive smoking history; occupational exposure history; biomass fuel exposure history;
2) Clinical information: years since diagnosis of COPD/chronic bronchitis/emphysema/asthma and age of onset; current respiratory symptoms, such as shortness of breath, chest tightness, cough, wheezing, sputum; previous family history; allergy history/atopy;
3) Previous acute exacerbations: acute exacerbations within 12 months before baseline: number of acute exacerbations, severity of acute exacerbations (use of systemic steroids/antibiotics/emergency department visits/hospitalization), and days of hospitalization or emergency department visits;
4) Comorbidities: comorbidities before the baseline visit;
5) Treatment: current medications for COPD/asthma/chronic respiratory symptoms (type/duration of use/dose/frequency), and non-pharmacological treatment, specific concomitant medications (steroids);
6) Symptom and quality of life assessment: Modified British Medical Research Council (mMRC) dyspnea scale, COPD Assessment Test (CAT), Asthma

Control Questionnaire (ACQ), Asthma Quality of Life Questionnaire (AQLQ), and St George's Respiratory Questionnaire (SGRQ);

7) Pulmonary function indicators: IOS parameters: R5, R20, R5-R20, AX, Fres, etc.; spirometry parameters: FEV1, FVC, FEV1/FVC, MMEF, etc.; bronchodilation test/bronchial challenge test results;
8) Inflammatory biomarkers: complete blood count (including eosinophil level), serum total immunoglobulin E (IgE) measurement, and FeNO level;
9) Chest HRCT scan: high-resolution CT in inspiratory and expiratory phases.

Follow-up Plan and Indicators:

Outpatient follow-up is conducted every 12 weeks after enrollment. The follow-up contents are as follows:

1) Respiratory symptoms: shortness of breath, chest tightness, cough, wheezing, sputum;
2) Acute exacerbations: number of acute exacerbations since the last follow-up, severity of acute exacerbations (use of systemic steroids/antibiotics/emergency department visits/hospitalization), and days of hospitalization or emergency department visits;
3) New comorbidities: new comorbidities since the last follow-up;
4) Mortality: death due to COPD/asthma and all-cause death;
5) Treatment: treatment adjustments during follow-up and reasons for adjustment: medications (type/duration of use/dose/frequency) and non-pharmacological treatment, specific concomitant medications (steroids);
6) Symptoms and quality of life: evaluated using mMRC, CAT, ACQ, AQLQ, and SGRQ;
7) Pulmonary function testing is performed again only at week 48 after enrollment:
8) Pulmonary function indicators: IOS parameters: R5, R20, R5-R20, AX, Fres, etc.; spirometry parameters: FEV1, FVC, FEV1/FVC, MMEF, etc.; bronchodilation test/bronchial challenge test results;
9) Specific methods: same as Section 6.1 of Phase 1.

7. Data Management and Statistical Analysis Plan

7.1 Data Management

An electronic data capture (EDC) system will be used for online data entry, with logic checks and range checks configured. All data will be independently entered by two individuals and checked for consistency. Paper case report forms (CRFs) will be properly archived.

7.2 Statistical Analysis

Phase 1: Construction and Validation of IOS-Based Screening and Diagnostic Models for Chronic Airway Diseases

Descriptive analysis: Continuous data will be expressed as mean ± standard deviation or median with interquartile range (for skewed distribution), and between-group differences will be compared using the t-test or non-parametric test (for skewed distribution). Categorical data will be described as percentages (%), and between-group comparisons will be performed using the chi-square test or Fisher's exact test.

Correlation analysis: Pearson correlation or Spearman correlation will be used to analyze the correlation between IOS parameters (R5, R20, R5-R20, AX, Fres, etc.) and spirometry parameters (FEV1, FVC, FEV1/FVC, MMEF, etc.) as well as inflammatory biomarkers (FeNO, blood eosinophil count, total IgE).

Model construction: In the model construction phase, the raw data will first undergo strict preprocessing. Outliers will be removed through clinical verification, and variables with a missing rate of less than 5% will be imputed using multiple imputation, while continuous variables will be standardized. Subsequently, in the feature selection step, LASSO regression or stepwise logistic regression dimensionality reduction techniques will be used, combined with clinical prior knowledge, to screen out the independent factors with the greatest predictive value for the disease from the 14 candidate variables (with emphasis on core IOS parameters). Based on the selected core predictive variables, multivariable logistic regression (with exploratory comparison of machine learning models such as random forest) will be used to construct the "COPD diagnostic model" and the "asthma diagnostic model" separately. Finally, to promote

the clinical translation of the research results, a visual diagnostic nomogram will be drawn based on the determined optimal logistic regression model to assist clinicians in actual diagnostic and treatment decisions.

Model performance evaluation indicators: The constructed diagnostic models will undergo comprehensive and rigorous performance evaluation through a multicenter external validation set. In terms of model discrimination assessment, receiver operating characteristic (ROC) curves will be plotted, the area under the curve (AUC) and its 95% confidence interval will be calculated, and the optimal diagnostic cut-off value will be determined according to the principle of maximizing the Youden Index. The sensitivity, specificity, positive predictive value, and negative predictive value corresponding to this cut-off point will be output simultaneously. In terms of model calibration assessment, calibration curves will be plotted and combined with the Hosmer-Lemeshow goodness-of-fit test to thoroughly evaluate the consistency between the model-predicted disease probability and the actual observed probability. In addition, to further verify the clinical utility of the model, decision curve analysis (DCA) will be introduced to quantify the actual net benefit that can be brought by applying the model to guide clinical screening at different threshold probabilities, thereby comprehensively confirming its value for promotion in the real world.

Comparison and combination of different screening methods: The DeLong method will be used to compare the differences in discrimination ability, sensitivity, and specificity between our established COPD and asthma screening models and screening questionnaires (COPD-PS, COPD-SQ, ECRHS, etc.). Combined diagnostic ROC curve analysis will be used to analyze the combined diagnostic value of the screening models and screening questionnaires.

Phase 2: Construction of an IOS-Based Dynamic Management and Prognostic Warning Platform for Chronic Airway Diseases

Descriptive analysis: Same as Phase 1. Baseline characteristics of those who completed follow-up and those lost to follow-up will be compared, and whether loss to follow-up is random will be analyzed.

Clinical association analysis: Spearman correlation analysis or the Kruskal-Wallis test will be used to analyze the relationship between IOS parameters and symptom scores (mMRC, CAT, ACQ, AQLQ, and SGRQ) as well as GOLD grading/GINA control levels.

Model external validation: Cox proportional hazards regression models will be used to analyze the relationship between IOS parameters (including baseline values and longitudinal change values) and future acute exacerbation risk, and to construct a prognostic risk prediction model. Before multivariable Cox regression, methods such as LASSO regression may be used for feature selection.

Model performance evaluation: The C-index (concordance index) of the Cox regression model will be calculated to evaluate the model's discrimination ability, and calibration curves will be plotted to evaluate the model's calibration. Time-dependent ROC curves will be used to evaluate the model's predictive performance for acute exacerbation risk at different time points (such as 3 months, 6 months, and 12 months).

Software: R software (version 4.3.0 or above) will be used for statistical analysis. All tests will be two-sided, and $P < 0.05$ will be considered statistically significant.

8. Expected Results

1) Establishment of IOS-based diagnostic models for chronic airway diseases:

IOS-based diagnostic models for COPD and asthma will be constructed, and the optimal cutoff values and diagnostic performance (sensitivity, specificity, AUC, etc.) of IOS parameters in the diagnosis of COPD and asthma in the Chinese population will be clarified, providing an objective and quantitative diagnostic reference for clinical practice.

2) Construction of a dynamic management and prognostic warning platform for chronic airway diseases:

Through a prospective cohort study, the relationship between IOS parameters and clinical outcomes of the disease will be clarified, the predictive value of longitudinal changes in IOS parameters for the risk of future acute exacerbations will be analyzed, and a Cox regression risk prediction model based on IOS parameters will be constructed,

forming a new strategy for the management of chronic airway diseases covering the full cycle of "screening-diagnosis-warning."

3) Formation of an evidence base supporting policy and industrial development:

By producing high-quality, localized research results, key high-level evidence-based medical evidence will be provided for the clinical promotion of domestic portable IOS devices, technological iteration, and the formulation of related health policies (such as primary care respiratory disease screening standards and device configuration criteria).

9. Research Progress

Start and End Time	Research Plan Content
April 2026 – June 2026	Preparation and ethics approval
July 2026 – December 2026	Complete enrollment of at least 300 participants from outpatient clinics and physical examination centers of multiple hospitals in Phase 1; simultaneously initiate external validation screening in community populations and complete symptom screening questionnaires, IOS, spirometry, bronchodilation/challenge tests, and biomarker examinations for at least 800 community participants; Complete enrollment of 400 patients with chronic airway diseases in Phase 2 and include them in the IOS-based chronic airway disease cohort management platform
January 2027 – December 2027	Complete the remaining 300 participants from outpatient clinics and physical examination centers of multiple

	hospitals in Phase 1, as well as the remaining 400 community participants for external validation in multiple centers, including symptom screening questionnaires, IOS, spirometry, bronchodilation/challenge tests, and biomarker examinations; Complete enrollment of the remaining 600 patients with chronic airway diseases in Phase 2 and include them in the IOS-based chronic airway disease cohort management platform
January 2028 – June 2028	Conduct data cleaning and analysis, establish IOS-based diagnostic models for COPD and asthma, determine optimal diagnostic cutoff values, and evaluate sensitivity, specificity, and AUC; Complete the 48-week follow-up of all participants in the prospective cohort and construct a Cox regression risk prediction model
July 2028 – December 2028	Paper writing and publication

10. Main References

[1] Collaborators G B D C R D. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015 [J]. Lancet Respir Med, 2017, 5(9) : 691–706. DOI: 10.1016/S2213-2600(17)30293-X.

[2] Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study [J]. The Lancet, 2018, 391(10131) : 1706–1717. DOI: 10.1016/s0140-6736(18)30841-9.

[3] Huang K, Yang T, Xu J, et al. Prevalence, risk factors, and management of asthma in China: a national cross-sectional study [J]. Lancet, 2019, 394(10196) : 407–418. DOI: 10.1016/S0140-6736(19)31147-X.

[4] Martinez F D, Vercelli D. Asthma [J]. The Lancet, 2013, 382(9901) : 1360–1372. DOI: 10.1016/s0140-6736(13)61536-6.

[5] Oostveen E, Macleod D, Lorino H, et al. The forced oscillation technique in clinical practice: methodology, recommendations and future developments [J]. Eur Respir J, 2003, 22(6) : 1026–1041. DOI: 10.1183/09031936.03.00089403.

[6] Kaminsky D A, Irvin C G, Lundblad L, et al. Oscillation mechanics of the human lung periphery in asthma [J]. J Appl Physiol (1985), 2004, 97(5) : 1849–1858. DOI: 10.1152/japplphysiol.00300.2004.

[7] Galant S P, Komarow H D, Shin H W, et al. The case for impulse oscillometry in the management of asthma in children and adults [J]. Ann Allergy Asthma Immunol, 2017, 118(6) : 664–671. DOI: 10.1016/j.anai.2017.04.009.

[8] Shi Y, Aledia A S, Tatavoosian A V, et al. Relating small airways to asthma control by using impulse oscillometry in children [J]. J Allergy Clin Immunol, 2012, 129(3) : 671–678. DOI: 10.1016/j.jaci.2011.11.002.

[9] Cottee A M, Seccombe L M, Thamrin C, et al. Oscillometry and asthma control in patients with and without fixed airflow obstruction [J]. J Allergy Clin Immunol Pract, 2022, 10(5) : 1260–1267.e1261. DOI: 10.1016/j.jaip.2021.12.026.

[10] Chiu H-Y, Hsiao Y-H, Su K-C, et al. Small Airway Dysfunction by Impulse Oscillometry in Symptomatic Patients with Preserved Pulmonary Function [J]. J Allergy Clin Immunol Pract, 2020, 8(1) : 229–235.e223. DOI: 10.1016/j.jaip.2019.06.035.

[11] Li L-Y, Yan T-S, Yang J, et al. Impulse oscillometry for detection of small airway dysfunction in subjects with chronic respiratory symptoms and preserved pulmonary function [J]. Respir Res, 2021, 22(1). DOI: 10.1186/s12931-021-01662-7.

[12] Lu L, Wan Q, Tang G, et al. New Classifications of COPD Severity Based on Impulse Oscillometry: A SAIO Grade Base on ECOPD Cohort in China [J]. Archivos de bronconeumologia, 2025, 61(6) : 334–340. DOI: 10.1016/j.arbres.2024.10.005.

[13] Huang C-H, Chou K-T, Perng D-W, et al. Using Machine Learning with Impulse Oscillometry Data to Develop a Predictive Model for Chronic Obstructive Pulmonary Disease and Asthma [J]. Journal of Personalized Medicine, 2024, 14(4). DOI: 10.3390/jpm14040398.

[14] Liu M, Yao X, Shi Y, et al. Impulse oscillometry-derived equation for prediction of abnormal FEV1/FVC ratio for COPD screening in Chinese population: a multicenter cross-sectional study [J]. Lancet Reg Health West Pac, 2025, 56: 101501. DOI: 10.1016/j.lanwpc.2025.101501.

[15] Yang X, Liu M, Shi H, et al. Detection of Inadequately Controlled Asthma in Adults Using Impulse Oscillometry and Fractional Exhaled Nitric Oxide [J]. J Asthma Allergy, 2025, 18: 637–647. DOI: 10.2147/jaa.S516257.

[16] Hanley J A, Mcneil B J. The meaning and use of the area under a receiver operating characteristic (ROC) curve [J]. Radiology, 1982, 143(1) : 29–36. DOI: 10.1148/radiology.143.1.7063747.

[17] American Thoracic Society; European Respiratory Society. ATS/ERS recommendations for standardized procedures for the online and offline Measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005 [J]. Am J Respir Crit Care Med, 2005, 171(8) : 912–930. DOI: 10.1164/rccm.200406-710ST.