STUDY REPORT

Cardiorespiratory Diagnostic Study

A longitudinal observational study to investigate the patterns of change in the Tidal Breathing Carbon Dioxide ($TBCO_2$) waveform, measured using the N-Tidal C handset, in patients with Chronic Obstructive Pulmonary Disease (COPD) compared to patients with other common cardiorespiratory conditions.

TidalSense
Cambridge, 2022
tidalsense.com

TidalSense

Our Team

- **Chief Investigator**
  Dr Elango Vijaykumar

Sponsor
TidalSense

Ameera Patel, Chief Executive Officer
Julian Carter, Director of Engineering
Alla Kitov, Head of Product & Design
Henry Lim, Machine Learning Engineer
Henry Broomfield, Machine Learning Engineer
James Barr, Senior Software Engineer
Tom Feist-Hassan, Senior Software Engineer

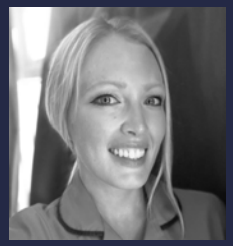
Partner
uMed

Matt Wilson, Founder & Chief Executive Officer
Abi Dhillon, VP Commercial Operations
Sian Organ, Head of Provider Growth and Operations
Glen Swinfield, Head of Engineering
Yun Hsuan Chang, Clinical Informatics Lead / Clinical Safety Officer
Hannah Sharp, Head of Clinical Operations
Marie Appleby, Senior Research Nurse

Investigators

- Dr Ameera Patel – Chief Executive Officer, Cambridge Respiratory Innovations
- Julian Carter – Director of Engineering, Cambridge Respiratory Innovations
- Dr Tom Ko - Clinical Lead for Research at SSP Health

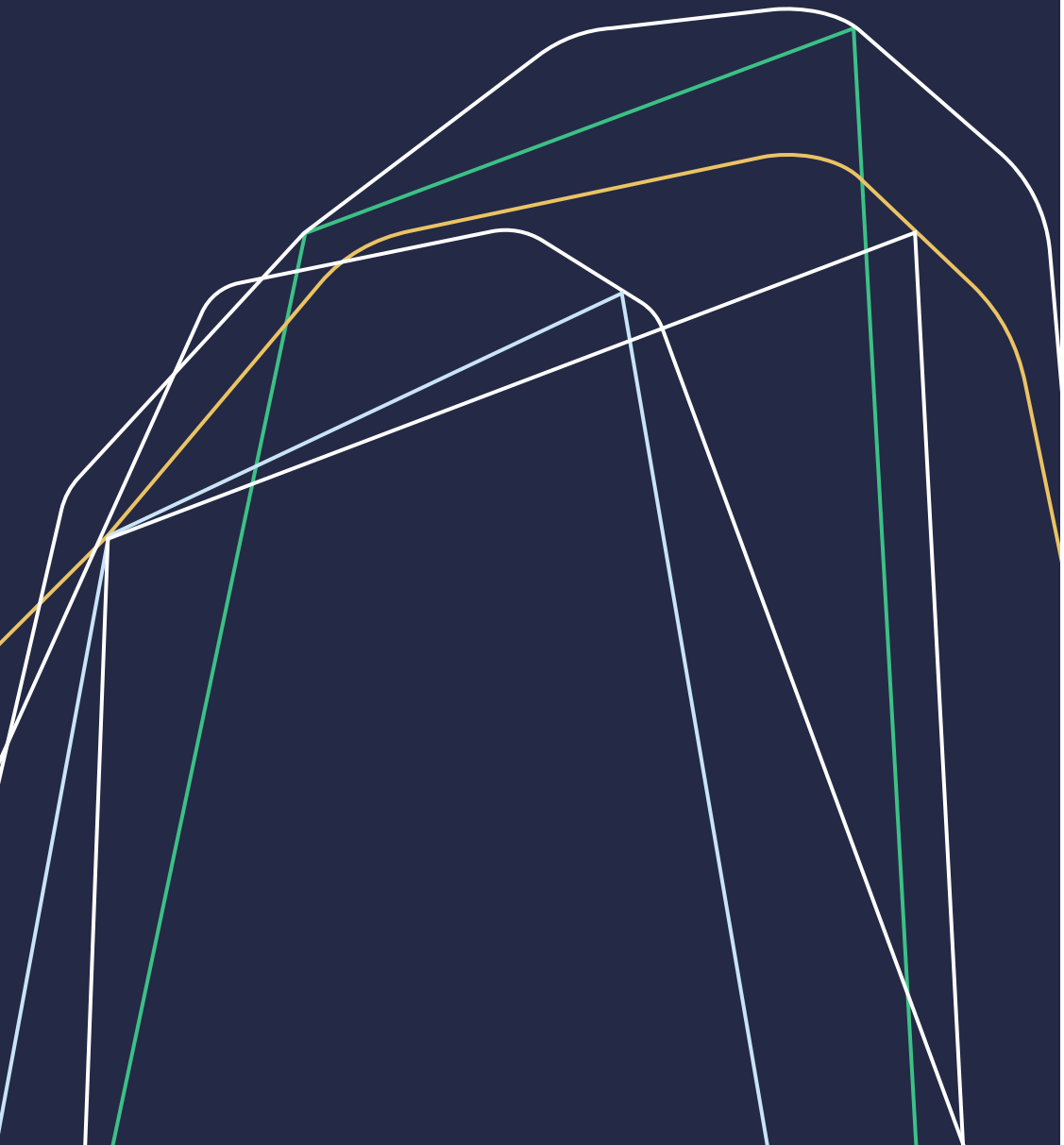
Study Nurses



- Hannah Sharp
  Lead Research Nurse
  uMed

- Marie Appleby
  Research Nurse
  uMed

Why was the research needed



Study aim

Chronic Obstructive Pulmonary Disease (COPD) is a chronic respiratory disease which results in reduced lung function and airflow to the lungs over time. It is in the top five causes of death worldwide, and in 2015, it was estimated that over 174 million people had COPD. In the UK, COPD is estimated to be the second highest cause of emergency hospital admissions and that up to 2 million of the 3 million who are thought to have COPD in the UK don't know that they have it.

Why this study is important to people with asthma?

Under-diagnosis of COPD is due to the lack of a robust and reliable test to identify those individuals who have COPD at an early stage. Currently, individuals with symptoms of COPD are diagnosed with spirometry: an effort-dependent test that is both unreliable and non-specific (i.e. many respiratory conditions can produce similar patterns on spirometry). As a result, the misdiagnosis rates of COPD around the world are high. In Europe, the under-diagnosis rates of COPD are estimated to be anywhere between 66% and 95%, and over-diagnosis rates between 26% and 60%.

In addition, reliable use of spirometry requires supervised use, by a specifically trained medical professional, in a clinic-based environment. As a result, diagnosis of COPD is often late in the natural course of the condition, which misses an opportunity to intervene early and slow progression of the condition. If a simple, safe, reliable, and precise test existed that could identify COPD at an early stage, this could result in significant patient benefit (in terms of accurate diagnosis and early treatment). Such evidence could also be used to provide health-economic arguments to support implementation of a national screening programme for COPD.

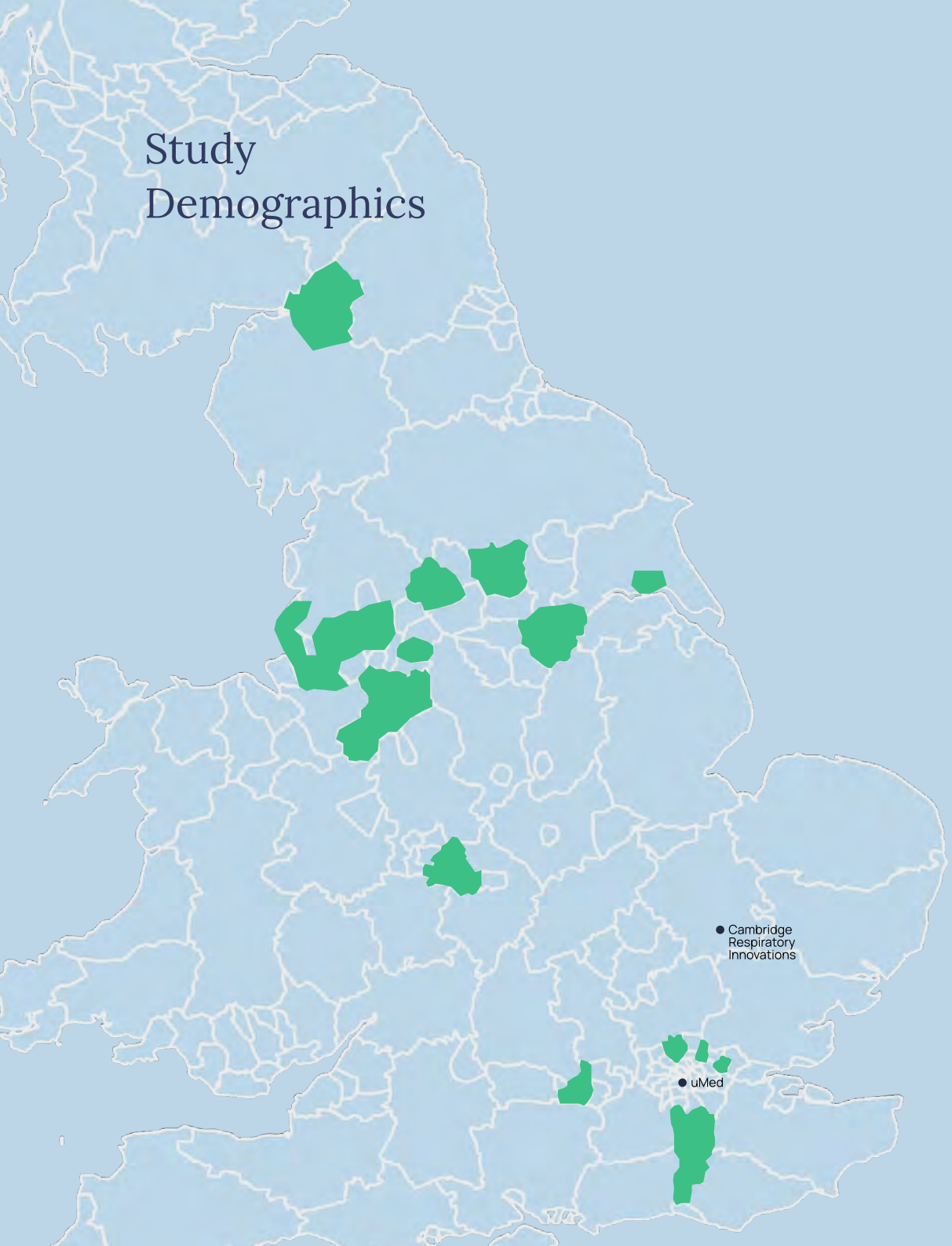
Problem statement

Current methods of diagnosing and measuring disease control in asthma require forced expiratory manoeuvres that can be difficult to perform and equally difficult to interpret, especially during periods of poor asthma control. There is a need for a simple, effort-independent, and accurate method that can easily identify changes in respiratory function that will lead to asthma attacks. This will benefit people with asthma by allowing timely treatment and preventing hospital admissions.

Expiratory capnography is a graphical measurement of carbon dioxide (CO_2) partial pressure during expiration. The characteristic shape of the $TBCO_2$ waveform has been shown to change during asthma exacerbations, reflecting small airway obstruction, which then returns to a normal pattern after treatment and recovery.

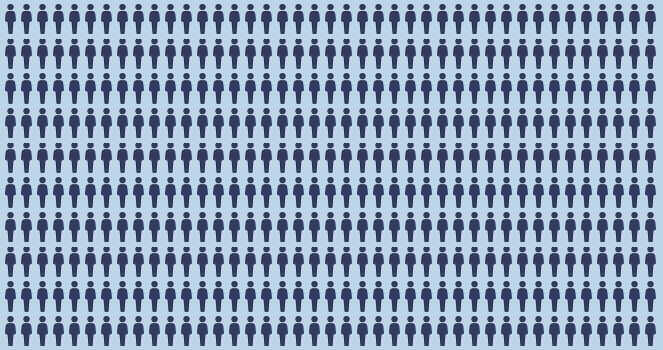
Currently, capnography is invasive, expensive, and can only be recorded in specialist centres, via a nasal cannula and microstream sampling of expired CO_2. The N-Tidal C, a new, hand-held device, has been developed to monitor the user's $TBCO_2$ waveforms whilst in the community, detect changes that would reflect small airway obstruction, and calibrate accurately.

Study Demographics

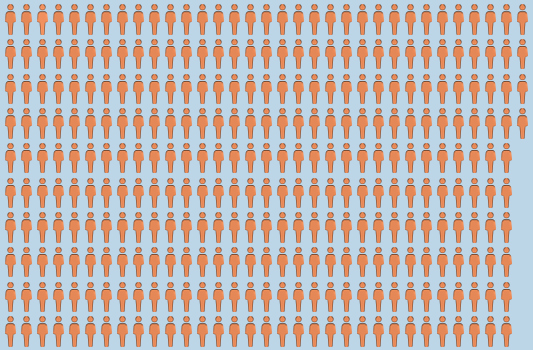


Participants

The recruitment for this research study took place in the primary care setting, but all of the data collection using the N-Tidal C handset took place in a home environment. Participants with different respiratory conditions were recruited from an adult population from GP practices around the UK. Patients were identified and engaged through the uMed platform via participants' GPs.



410
women
56%



324
men
44%

734
number of participants that took part in the study

0-14 years	15-24 years	25-64 years	65+ years
0 children	8 youth	424 adults	302 seniors

19 years old
youngest

96 years old
oldest

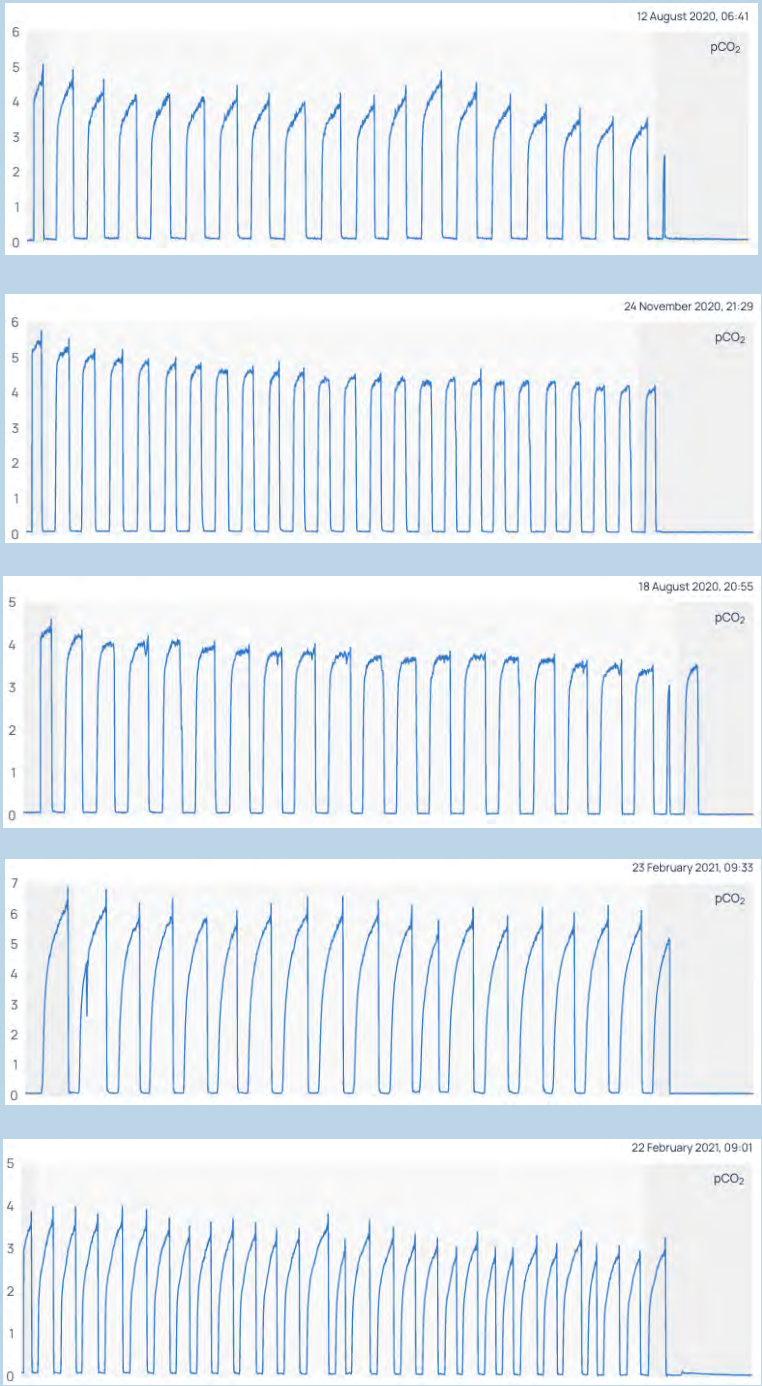
Study design

The N-Tidal C, a new, hand-held device, has been developed to monitor the user's TBCO2 waveforms whilst in the community, detect changes that would reflect small airway obstruction, and calibrate accurately. This technology offers new possibilities to detect airflow limitation in asthma, allowing early attack detection in an effort-independent manner.

The handset was used in accordance with the N-Tidal C Instructions for Use. Participants used the handset twice daily before using their inhalers (morning and evening). The CO_2 partial pressure recordings were automatically communicated to the secure database via 4G network.

Participants held the handset and breathed at their normal, relaxed rate through a mouthpiece for 75 seconds. They were asked to do this twice a day for two weeks. The handset was not supposed to be used in crowded rooms, near a vehicle exhaust, open flames, cigarettes, immediately after drinking a hot beverage or a fizzy drink, or where there was a strong breeze. These conditions may have interfered with the data capture of the handset.

Patients were able to participate from home. uMed supported the study with remote training and handset delivery and collection.

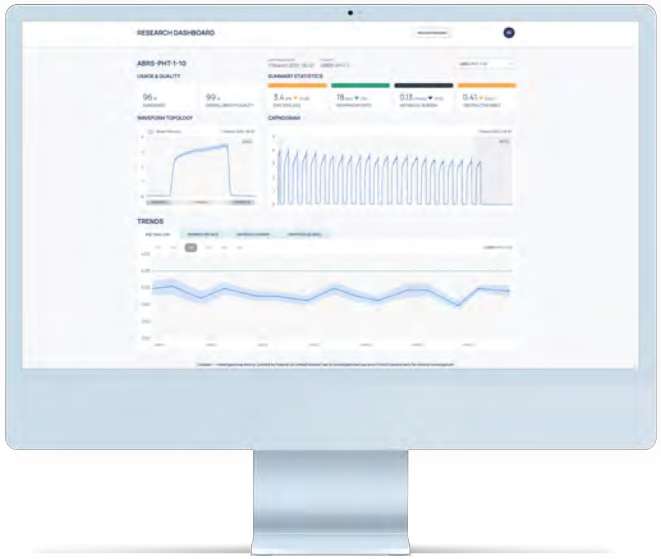


Monitoring

The participants' use of the N-Tidal C handset data collector was monitored remotely throughout the study. The study team checked that the participant was using the handset correctly and provided additional training if needed. The usage of the N-Tidal C handset was reviewed with the participant.

The study team used the Research Dashboard (below) to monitor breath records and parameters such as Adherence and Breath quality (you will read more about these in the coming sections). uMed provided additional training and support for participants as required.

Expiratory capnography is a graphical measurement of CO_2 partial pressure during expiration. The characteristic shape of the $TBCO_2$ waveform has been shown to change during asthma exacerbations, reflecting small airway obstruction, which then returns to a normal pattern after treatment and recovery. Currently, capnography is invasive, expensive and can only be recorded in specialist centres, via a nasal cannula and microstream sampling of expired CO_2.



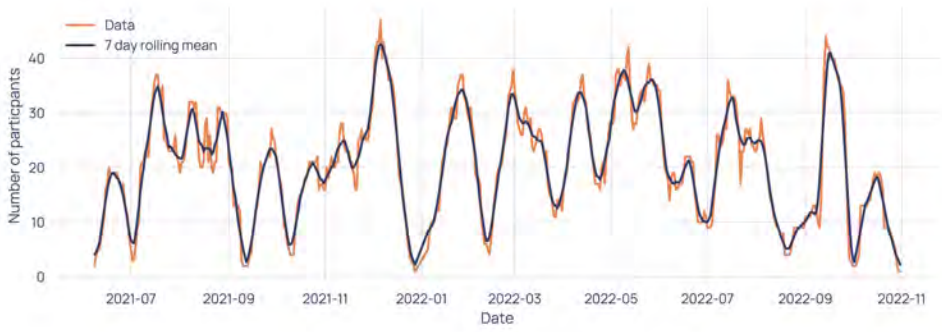
Days on a study

Participants were asked to spend 14 days on the study and use the N-Tidal C handset twice a day everyday.

14

average number of days a participant was on the study

Number of active participants



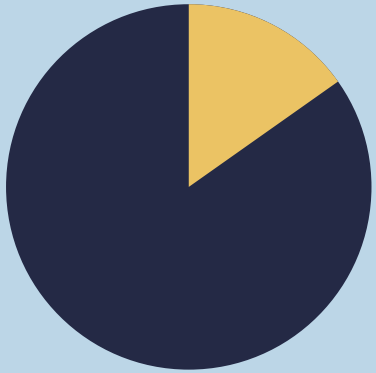
Capnography metrics

18,892

breath records
were collected on this study between 1 June 2021 — 31 October 2022

383,931

number of identified individual breaths taken

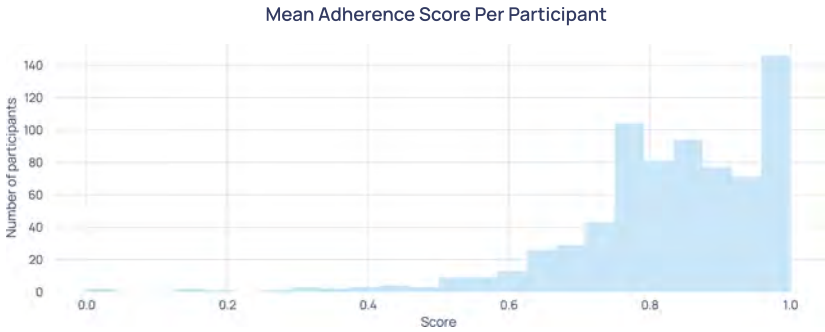


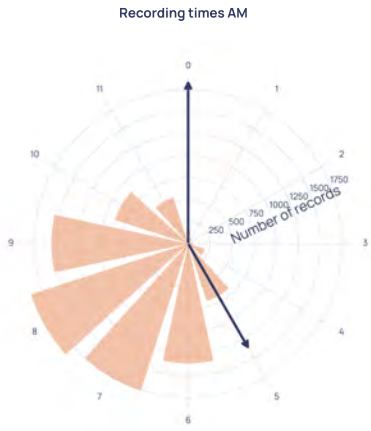
50,744 (13.2%)
low-quality individual breaths were filtered out

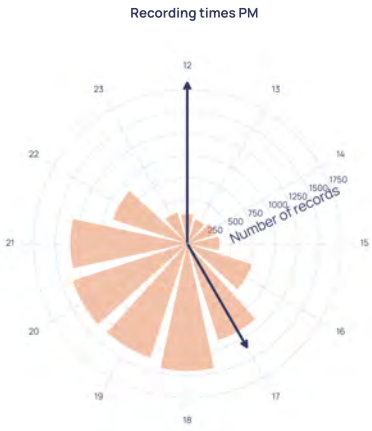
333,187 (86.8%)
high-quality individual breaths were used for data analysis

Adherence

Adherence is a cumulative measure of how consistently participants were using the handset over their study period. Participants were asked to use the N-Tidal C handset twice a day every day. A score of 1 (100%) means that a participant was using it twice a day every day for their whole duration on the study. A score of 0.8 (80%) means that a participant used it twice a day in 80% of their days on the study. The mean adherence score for all participants on the study was 82%, which highlights an excellent consistency to handset usage. The maximum mean adherence score was 100%. Reasons for lower adherence scores were identified to include: hospitalisation and worsening of exacerbations and other respiratory symptoms.







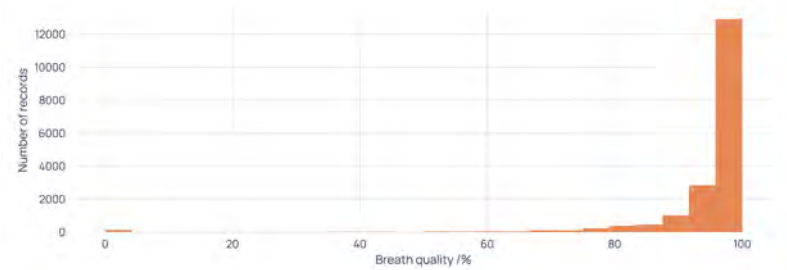
Breath quality

The Breath quality measure indicates the percentage of high-quality breaths captured during the latest breath record (i.e. the participant was not nose breathing, not swallowing, not coughing, etc.). This measure helped study coordinators observe how well participants were using the handset and whether they required a retraining on how to deliver breath records.

95.3%
mean breath quality per record

94.3%
mean breath quality per participant

Breath quality per record



Mean breath quality per participant