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Maximising Adherence and Gaining New Information For Your COPD (MAGNIFY)

Submission date
22/07/2019

Recruitment status
No longer recruiting

Registration date
25/07/2019

Overall study status
Completed

Last Edited
17/01/2025

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
How well a patient takes their medication as prescribed, usually referred to as adherence, is a widespread issue affecting patients irrespective of their condition or type of treatment. Poor adherence to medication can lead to persistent symptoms, poor control of disease, reduced quality of life and poor health outcomes for patients. In the case of Chronic Obstructive Pulmonary Disease (COPD), patients who do not take their COPD medication (inhaler) as prescribed can result in a worsening of symptoms, increased risk of lung infections and increased risk of hospital visits and admissions. Treatment guidelines recommend that poor adherence and inhaler technique of patients should be addressed before changing or increasing the medication prescribed. A common reason for poor adherence is that patients simply forget to take their medication. New technologies are now available that can be used to remind patients to take their medication. In a survey by the COPD Foundation, 66% of patients reported that they would like a tool to help them track their medication use. Previous studies in asthma have shown the benefits of inhaler reminders in reducing forgetfulness and improving health outcomes for patients. However, no similar studies have been conducted in patients with COPD. The challenge with assessing adherence in research studies is that if patients are aware that they are participating in a study, this can influence their behaviour and increase their adherence. Adherence and its impact on patient outcomes can only be reliably assessed in studies that resemble real life as closely as possible. Various inhalers are available for the daily management of COPD. New technology to support taking medication has been introduced for the Ultibro Breezhaler inhaler. This technology consists of a sensor device that a patient will attach directly to the inhaler, and a mobile phone application (‘app’) that connects with the sensor device through a wireless Bluetooth connection. The sensor detects and records when a patient inhales and the mobile app also reminds them if they have not taken their daily medication. This technology, developed by Propeller Health, is currently available in the UK through healthcare providers (including GP practices) taking part in a programme with Propeller Health. The aim of this study is to find out whether this technology can improve the treatment and clinical outcomes of people with COPD.

Who can participate?
Patients with COPD and poor adherence to treatment

What does the study involve?
This study aims to recruit over 176 GP practices in the UK and collect non-identifiable or anonymous data for 1,312 patients from the electronic medical records of participating practices. Half of the participating practices are randomly allocated to receive access to the adherence support technology and offer the sensor device plus mobile app to suitable patients with COPD. The other half of the participating practices continue their usual routine patient care for their patients with COPD without providing adherence support technology. The study does not require patients to attend their GP practice outside of their usual routine care. Each practice takes part in the study for 12 months and anonymous data is extracted from their electronic medical records at the beginning of the study and regularly until the end of the study. All data are stored in a research ethics approved database – Optimum Patient Care Research Database (https://opcrd.co.uk).

What are the possible benefits and risks of participating?
The results from this study are expected to provide real life evidence that provision of adherence support technologies can provide benefits in patients with COPD. The results from this and other studies can be expected to help patients and healthcare professionals make better decisions about their treatment to improve patient health and quality of life, and reduce healthcare costs associated with the treatment of patients. The trial will have no impact on patients at the participating sites allocated to the control group as they will continue to receive their usual care. The researchers therefore do not expect there to be any risks or benefits to these patients. Similarly, at the sites allocated to the adherence support, patients will continue to receive their usual care, but commercially available adherence technology devices will be made available to these GP practices at no cost. The sites will then be able to offer this technology to patients who are suitable for and might benefit from adherence support, i.e. patients with poor adherence and frequent exacerbations who are clinically suitable for a dual bronchodilator therapy with Ultibro. Indeed, the correct intervention according to treatment guidelines for these patients is to address adherence and inhaler technique, not to step up therapy. The researchers do not expect the study to have any risks or benefits to those patients who do not receive the adherence device. If the patient receives the device, this may help improve their treatment adherence, which could then improve their clinical outcomes.

Where is the study run from?
Observational and Pragmatic Research Institute (UK)

When is the study starting and how long is it expected to run for?
April 2019 to November 2024

Who is funding the study?
Novartis

Who is the main contact?
The MAGNIFY Team, magnify@opri.sg

Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
260690

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
OPRIUK-1803, IRAS 260690

Study information

Scientific Title
A pragmatic, cluster randomized trial evaluating the impact of an enhanced adherence package (dual bronchodilator + add-on + app) on time to treatment failure and other clinical outcomes in exacerbating COPD patients with poor adherence to mono or dual therapy over one year

Acronym
MAGNIFY

Study objectives
Can technology use improve the treatment and clinical outcomes in people with Chronic Obstructive Pulmonary Disease (COPD)?

Not taking medications as prescribed is an issue affecting patients irrespective of disease and treatment type and can lead to poor clinical outcomes such as worsening symptoms. In COPD, guidelines have noted the importance of supporting patients with their regular inhaler use as part of COPD management. The study will focus on patients with COPD that have poor treatment adherence and frequent flare-ups often triggered by cold or similar events.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 06/11/2019, East Midlands - Derby Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; Tel: +44 (0)207 104 8109; Email: nrescommittee.eastmidlands-derby@nhs.net), REC ref: 19/EM/0238, IRAS: 260690

Study design
Pragmatic cluster randomized trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Current interventions as of 17/01/2025:

This is a pragmatic real-life study which does not involve any study visits outside routine care. All patient contact and visits during the study will be part of routine COPD management at the patients' own GP practice, in accordance with NICE recommendations which state that patients with mild/moderate/severe COPD should be reviewed at least once a year. The hypothesis is that patients at sites that have availability of adherence support technology together with the Ultibro inhaler, will demonstrate better clinical outcomes than patients at sites that continued their usual routine care without access to the adherence support technology. The researchers will use anonymised data extracted from 176 GP practices' electronic health records to assess the study outcomes. Data will be extracted by Optimum Patient Care (OPC) who are an organization specialized in primary care data extraction.

The study will be randomised on a practice-level, which means that instead of randomising individual study participants, the researchers will randomise the participating sites. Randomization will be stratified according to practice list size, deprivation score and the percentage of COPD patients with a spirometry-confirmed diagnosis who were receiving treatment intervention (COPD002); COPD002 is part of a nationally available Quality and Outcomes Framework Indicator for COPD (a marker for achievement of COPD patient care). Sites will be randomised in 1:1 ratio to the control arm or to the adherence support arm (ASA). As this study aims to collect real-life data on the impact of Ultibro + adherence technology, sites in the control arm will continue to administer their usual routine care. Particularly for studies looking at real-life impact, a cluster randomised study design can offer various benefits over a traditional randomised controlled trial (RCT) design, where individual patients (rather than sites or clusters) are randomised. Firstly, in a traditional RCT the same investigator is treating patients in both treatment groups. This can result in contamination. For example, in the case of this study, in a traditional RCT setting the same doctor would be required to offer adherence support to some of their patients, while providing usual care for others. It is likely that the "usual care" provided by this doctor could be affected by the fact that they have received training on the adherence support technology and are therefore more aware of adherence issues. Second, traditional RCTs usually require that all study participants are informed and consenting volunteers. This requirement likely pre-selects individuals who are at a lower risk for non-adherence, particularly for RCTs of behavioural interventions. Indeed, patients enrolling in clinical trials may be systematically different regarding adherence levels than those declining to

participate. Furthermore, the clinical trial process means that patients are fully aware of adherence monitoring, and such knowledge could result in patients modifying their adherence behaviour.

Methodology
The following steps will take place at the participating sites:
1. Medical record data will be extracted by OPC to collect baseline data
2. Using the extracted data, OPC will run an algorithm to obtain a list of patients that meet the study suitability criteria at each site. The list will contain unique identifiers which can only be linked to identifiable patient information at the GP practice
3. Each site is randomized to treatment arm centrally by the Sponsor's research team
4. If the site is randomised to the control arm, they will continue their usual routine care
5. If the site is randomised to the adherence support arm (ASA), they will be provided with the Propeller Health adherence support devices and will be trained on its use and functionalities by the Sponsor or by Propeller Health. Potentially eligible patients (identified by the OPC algorithm) will receive a remote pharmacist review, and patients deemed eligible during the remote review will be offered the adherence technology support package (Ultibro+Addon device+App). A specific read code for inhaler aid device should be recorded in patient notes for any patients provided the adherence support device.
6. At the end of the study, data from all sites will be extracted to obtain the data for the 12-month outcome period

OPC will provide support to practices in both arms and this includes mail out, or administration at routine COPD review appointments, of Optimum Patient Care (OPC) COPD review questionnaire to patients with COPD. Data collected with the review questionnaire by OPC will not be shared with the Sponsor. The questionnaire will only be sent out at 12 months at the control group sites in order to eliminate any impact that completing this questionnaire could have on patient behaviour and adherence. At ASA sites, this questionnaire can be administered at Baseline COPD reviews at discretion of the site, but the data will not be used for the purposes of this study and will not be shared with the Sponsor. The sites will be required to sign an agreement with OPC for the collection and use of COPD review questionnaire data. This agreement is separate to the main study agreement with the Sponsor.

At the GP sites randomised to the adherence support arm, data from patients meeting the following criteria will be included in the primary endpoint analysis: eligible for the trial (see 'Eligibility' section below), during pharmacist review were deemed to be clinically suitable and poorly adherent to inhaled therapy (according to EMR, self-report or clinical judgement), and accepted the Package (i.e. Ultibro + Add-on device+App) at Baseline (these patients will be identified by a specific read code for inhaler aid device).

At the control GP sites, data from patients matched to those in the adherence support arm will be included in the primary endpoint analysis

*Patients in the control GP sites will be matched with replacement to the those in the ASA arm based on having a LABA/LAMA prescription date within 30 days of the date of provision of the technological adherence support package in the ASA arm. ASA arm patients will be matched with up to five controls, as not all controls will provide analysable data

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Previous interventions:

This is a pragmatic real-life study which does not involve any study visits outside routine care. All patient contact and visits during the study will be part of routine COPD management at the patients' own GP practice, in accordance with NICE recommendations which state that patients with mild/moderate/severe COPD should be reviewed at least once a year. The hypothesis is that patients at sites that have availability of adherence support technology together with the Ultibro inhaler, will demonstrate better clinical outcomes than patients at sites that continued their usual routine care without access to the adherence support technology. The researchers will use anonymised data extracted from 176 GP practices' electronic health records to assess the study outcomes. Data will be extracted by Optimum Patient Care (OPC) who are an organization specialized in primary care data extraction.

The study will be randomised on a practice-level, which means that instead of randomising individual study participants, the researchers will randomise the participating sites. Randomization will be stratified according to practice size, deprivation score and the percentage of patients with COPD with a record of FEV1 in the preceding 12 months. Sites will be randomised in 1:1 ratio to the control arm or to the adherence support arm (ASA). As this study aims to collect real-life data on the impact of Ultibro + adherence technology, sites in the control arm will continue to administer their usual routine care. Particularly for studies looking at real-life impact, a cluster randomised study design can offer various benefits over a traditional randomised controlled trial (RCT) design, where individual patients (rather than sites or clusters) are randomised. Firstly, in a traditional RCT the same investigator is treating patients in both treatment groups. This can result in contamination. For example, in the case of this study, in a traditional RCT setting the same doctor would be required to offer adherence support to some of their patients, while providing usual care for others. It is likely that the "usual care" provided by this doctor could be affected by the fact that they have received training on the adherence support technology and are therefore more aware of adherence issues. Second, traditional RCTs usually require that all study participants are informed and consenting volunteers. This requirement likely pre-selects individuals who are at a lower risk for non-adherence, particularly for RCTs of behavioural interventions. Indeed, patients enrolling in clinical trials may be systematically different regarding adherence levels than those declining to participate. Furthermore, the clinical trial process means that patients are fully aware of adherence monitoring, and such knowledge could result in patients modifying their adherence behaviour.

Methodology
The following steps will take place at the participating sites:
1. Medical record data will be extracted by OPC to collect baseline data
2. Using the extracted data, OPC will run an algorithm to obtain a list of patients that meet the study suitability criteria at each site. The list will contain unique identifiers which can only be linked to identifiable patient information at the GP practice
3. Each site is randomized to treatment arm centrally by the Sponsor's research team
4. If the site is randomised to the control arm, they will continue their usual routine care
5. If the site is randomised to the adherence support arm (ASA), they will be provided with the Propeller Health adherence support devices and will be trained on its use and functionalities by the Sponsor or by Propeller Health. The site will then be able to offer this technology to their patients identified as suitable (by the OPC algorithm). A specific read code for inhaler aid device should be recorded in patient notes for any patients provided the adherence support device.
6. At the end of the study, data from all sites will be extracted to obtain the data for the 12-month outcome period

OPC will provide support to practices in both arms and this includes mail out, or administration at routine COPD review appointments, of Optimum Patient Care (OPC) COPD review questionnaire to patients with COPD. The questionnaire includes a question about whether the

patient would use an inhaler that can send reminders on a smartphone, if this was available. Those patients in the control arm that respond Yes to this question, would be considered to represent a matching population to those patients in ASA arm who accepted the adherence technology. This allows us to define the comparator group for the primary analysis.

Other data collected with the review questionnaire by OPC will not be shared with the Sponsor. The questionnaire will only be sent out at 12 months at the control group sites in order to eliminate any impact that completing this questionnaire could have on patient behaviour and adherence. At ASA sites, this questionnaire can be administered at Baseline COPD reviews at discretion of the site, but the data will not be used for the purposes of this study and will not be shared with the Sponsor. The sites will be required to sign an agreement with OPC for the collection and use of COPD review questionnaire data. This agreement is separate to the main study agreement with the Sponsor.

At the GP sites randomised to the adherence support arm, data from patients meeting the following criteria will be included in the primary endpoint analysis: clinically suitable (see above), and accepted the Package (i.e. Ultibro + Add-on device+App) at Baseline (these patients will be identified by a specific read code for inhaler aid device).

At the control GP sites, data from patients meeting the following criteria will be included in the primary endpoint analysis: clinically suitable (see above), willing to accept the technology*, and received LABA/LAMA, LABA, LAMA or LABA/ICS at Baseline.

*At the control GP sites willingness is determined at the end of the study by assessing the acceptance of technology of the clinically suitable patients. This will be determined by a question in the OPC COPD review questionnaire: If an inhaler was available with technology providing reminders on a smartphone when to take your COPD treatment, would you use it? In order to match the primary populations in the two arms as closely as possible (in terms of both willingness and ability), the response options include “I do not have a smartphone”.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
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Primary outcome(s)
Current primary outcome measure as of 17/01/2025:

The primary endpoint is time to treatment failure. Data will be collected from electronic medical health records. Time to treatment failure is defined as the time (in whole days) from baseline to the first occurrence of:
1. Moderate/severe COPD exacerbation, requiring: an acute oral corticosteroid course prescription, antibiotics prescribed with evidence of a lower respiratory consultation at the same day, respiratory-related hospital attendance/admission (based on GP medical record data), or respiratory-related A&E/ER attendance (based on GP medical record data)
2. Prescription of ICS
3. Prescription of additional chronic therapy for COPD (i.e. theophylline or other

methylxanthines, maintenance oral corticosteroids, PDE4 inhibitors, macrolides (e.g. Azithromycin, Erythromycin), mucolytics (e.g. carbocysteine, N-acetylcysteine), or any other respiratory medication prescribed for COPD)
4. All-cause death

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Previous primary outcome measure:

The primary endpoint is time to treatment failure. Data will be collected from electronic medical health records. Time to treatment failure is defined as the time (in whole days) from baseline to the first occurrence of:
1. Moderate/severe COPD exacerbation, requiring: an acute oral corticosteroid course prescription, antibiotics prescribed with evidence of a lower respiratory consultation at the same day, respiratory-related hospital attendance/admission (based on GP medical record data), or respiratory-related A&E/ER attendance (based on GP medical record data)
2. Escalation of therapy to triple therapy (ICS/LABA/LAMA)
3. Prescription of additional chronic therapy for COPD (i.e. theophylline or other methylxanthines, maintenance oral corticosteroids, PDE4 inhibitors, macrolides (e.g. Azithromycin, Erythromycin), mucolytics (e.g. carbocysteine, N-acetylcysteine), or any other respiratory medication prescribed for COPD)
4. Respiratory-related death

Key secondary outcome(s))

Current secondary outcome measures as of 17/01/2025:

1. Rate of moderate/severe exacerbations over the 12-month trial period (based on electronic medical record data)
2. Proportion of patients with at ≥1 moderate/severe exacerbation over the 12-month trial period (based on electronic medical record data)

Exploratory outcome measures:
1. Adherence based on prescription refill records over 12 months
2. Respiratory-related healthcare resource utilization (HCRU)
3. Acceptance rate of the technological adherence support package at ASA sites

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Previous secondary outcome measures:

1. Adherence, determined as Medication Possession Ratio (MPR) based on electronic medical record data at 12 months
2. Proportion of patients with moderate/severe exacerbations, and total number of exacerbations at 12 months, based on electronic medical record data, where exacerbation is defined as requiring: an acute oral corticosteroid course prescription, antibiotics prescribed with evidence of a lower respiratory consultation at the same day, respiratory-related hospital attendance or admission (based on GP medical record data), or respiratory-related A&E/ER attendance (based on GP medical record data)

Completion date

30/11/2024

Eligibility

Key inclusion criteria

Current inclusion criteria as of 17/01/2025:

For a practice to be eligible for participation, the following criteria should be met:
1. General practice in the United Kingdom (England, Scotland, Wales, Northern Ireland) participating in Optimum Patient Care services that support chronic disease review and provide high-quality respiratory data
2. Willing to use advanced technology as part of clinical practice
3. At least 8 patients suitable for adherence technology
4. Actively prescribing Ultibro® Breezehaler® as a routine clinical care option; (i.e. inhaler compatible with the add-on technology)

ASA arm patients included in the study:
1. Aged ≥40 years
2. COPD diagnosis
3. ≥2 exacerbations in the last 2 years or 2 years preceding March 2020
4. Prescribed maintenance inhaled COPD therapy in the last 12 months
5. 2 years' valid EMR data
6. Pharmacist deemed patient to be clinically suitable and poorly adherent to inhaled therapy (according to EMR, self-report or clinical judgement)

Control arm patients included in the study:
1. Matched to intervention patients based on LABA/LAMA prescription date
2. Aged ≥40 years
3. COPD diagnosis
4. ≥2 exacerbations in the last 2 years or 2 years preceding March 2020
5. Prescribed maintenance inhaled COPD therapy in the last 12 months
6. 2 years' valid EMR data

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Previous inclusion criteria as of 06/09/2023:

For a practice to be eligible for participation, the following criteria should be met:
1. General practice in the United Kingdom (England, Scotland, Wales, Northern Ireland) participating in Optimum Patient Care services that support chronic disease review and provide high-quality respiratory data
2. Willing to use advanced technology as part of clinical practice
3. At least 8 patients suitable for adherence technology
4. Actively prescribing Ultibro® Breezehaler® as a routine clinical care option; (i.e. inhaler compatible with the add-on technology)

Patients suitable for adherence technology support:
1. Aged ≥40 years
2. Ever-smoker
3. On the COPD register of participating practices
4. Coded COPD diagnosis and FEV1/FVC ever recorded <0.7
5. At least 2 moderate/severe COPD exacerbations in the last 24 months (or prior to March 2020, if poorer)

6. Total adherence to current mono/dual therapy of ≤50% based on refill Rx data or a clinical EHR code for poor adherence in the last 12 months (or prior to March 2020, if poorer)

Previous inclusion criteria:
For a practice to be eligible for participation, the following criteria should be met:
1. Willing to receive OPC clinical audit and quality improvement services, including IT access for secure software installation and de-identified data extraction
2. Willing to use adherence technology as part of clinical practice
3. At least 16 patients suitable for adherence technology support (see below)
4. A clinician (doctor, nurse, pharmacist, etc) willing to act as a practice lead
5. Prescribing or able to prescribe Ultibro® Breezehaler® as a routine clinical care option i.e. inhaler compatible with the add-on technology

Patients suitable for adherence technology support:
1. Confirmed COPD diagnosis
2. Smoking history
3. At least 2 COPD exacerbations in the last 24 months
4. Poor adherence to single/dual COPD therapy – Total adherence to current mono/dual therapy of ≤50% based on refill Rx data in the last 12 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
40 years

Sex
All

Total final enrolment
3598

Key exclusion criteria
Current exclusion criteria as of 17/01/2025:

Practice exclusion criteria:
1. Consent refusal code indicating opt-out of data used for research
2. Clinically unsuitable for LABA/LAMA therapy
3. Unresolved asthma diagnosis with an inhaled corticosteroid (ICS) prescription in the last 12 months
5. ASA arm only: Unable to use technology (e.g. not having/able to use a smartphone compatible with the technology, not having reliable Internet access)

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Previous exclusion criteria as of 06/09/2023:

Practice exclusion criteria:
1. General practice not prescribing Ultibro® as part of routine clinical care to patients with COPD
2. General practices hosting or affected by research, or other aspects of care, which might significantly influence the practice-wide implementation

Patient exclusion criteria:
1. Patients with a consent refusal code indicating opt-out of data used for research
2. Patients not deemed clinically appropriate for the therapy which is technology-compatible
3. Patients on triple therapy (ICS/LABA/LAMA)
4. Read code for asthma (excluding 'asthma resolved' read codes)
5. Blood eosinophil count >300 cells/µl if blood count available in the last 12 months
6. Unable to use technology (e.g. not having/able to use a smartphone compatible with the technology, not having reliable Internet access)

Previous exclusion criteria:
GP Practice who cannot prescribe Ultibro breezhaler or currently do not prescribe Ultibro breezhaler

Date of first enrolment
18/06/2021

Date of final enrolment
22/11/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Observational and Pragmatic Research Institute
Warren House
Sankence
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United Kingdom
NR11 6UN

Sponsor information

Organisation
Observational and Pragmatic Research International Ltd

Funder(s)

Funder type
Industry

Funder Name
Novartis

Alternative Name(s)
Novartis AG, Novartis International AG

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available due to restrictions on the use of the Optimum Patient Care Research Database (study data source), as outlined within the legally binding data-sharing agreement with the study sponsor. Individual requests for dataset access may be made available for approved researchers on specific requests to the steering committee and with the written approval for data sharing by the ADEPT committee (governing body of OPCRD).

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		24/05/2021	04/06/2021	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes