A randomised controlled trial to evaluate the impact of supportive text messages from GP practices on self-reported symptoms and inhaler adherence in patients with asthma and/or chronic obstructive pulmonary disease (COPD) who have been prescribed a preventer (daily) inhaler (Inhaler Trial)

Version	2.0
Date:	22 November 2022
IRAS Project ID:	316452
Chief Investigator:	Dr Luke Twelves
Sponsor:	Accurx Ltd 7 Curtain Rd, London EC2A 3LT

Principal Investigator and Service Agreement for the Protocol

Each participating GP practice must assign a Principal Investigator (PI). The PI is responsible for ensuring the research study is carried out in accordance with this protocol and service agreement at their GP practice.

I agree to;

- To assume responsibility for the proper conduct of the clinical investigation at my site, and to conduct the trial in compliance with this protocol, any future amendments, and with any other trial's conduct procedures provided by the sponsor or authorised representatives.

- Not to implement any deviations from or changes to the protocol without agreement from the sponsor and prior review and favourable opinion from the ethics committee and approval from the competent authority, if applicable, except where necessary to eliminate an immediate hazard to the subject(s), or for administrative aspects of the clinical investigation (where permitted by all applicable regulatory requirements).

- To ensure that all persons assisting me with the clinical investigations are adequately informed about the protocol and of their trial-related duties and functions.

- hereby adhere and accept the terms and conditions set out in the attached Participant Identification Centre agreement (v1.1, January 2021).

……

Principal Investigator Name

……..……..…..

Principal Investigator Signature and Date

…..……

GP Practice Address

The signatures below constitute the approval of this protocol and the attachments

DocuSigned by: Dr Luke Twelves 0694BF7DB220470...	04 January 2023 | 06:31 PST
Dr Luke Twelves **Chief Investigator**	**Date**
DocuSigned by: Victoria Fussey D0DD8EC7F7764FB...	04 January 2023 | 14:31 GMT
Victoria Fussey **Accurx**	**Date**

Contents

1 ABBREVIATIONS

App	Application
CI	Chief Investigator
COPD	Chronic Obstructive Pulmonary Disease
e-Consent	Electronic consent
EDC	Electronic Data Capture
ICH	International Conference on Harmonisation
LH	Lindus Health
GCP	Good Clinical Practice
GP	General Practitioner
PIS	Patient Information Sheet
REC	Research Ethics Committee
RCT	Randomised Clinical Trial
SAP	Statistical Analysis Plan
QOF	Quality and Outcome Framework

2 STUDY SYNOPSIS

Title	A randomised controlled trial to evaluate the impact of supportive text messages from GP practices on self-reported symptoms and inhaler adherence in patients with asthma and/or chronic obstructive pulmonary disease (COPD) who have been prescribed a preventer (daily) inhaler (Inhaler Trial)
Short Title	A research study to explore the impact of GP support via text messages to patients with asthma and/or COPD
Protocol Number	Accurx-001
Sponsor	Accurx, 7 Curtain Road, Shoreditch, EC2A 3LT
Purpose	To evaluate the impact of text message support sent to patients from GP practices on self reported symptoms and preventer inhaler adherence for patients with asthma and/or COPD
Study Description	A 6-month randomised controlled trial to evaluate the impact of text message support on symptom control and inhaler adherence for patients with asthma and/or COPD
Number of Study Participants	Approximately 4,000 participants with either asthma and/or COPD (study participants is defined as those who have consented and completed the baseline survey) will be randomly allocated to either the treatment or control group (1:1 ratio)
Study Design	The study is divided into an intervention and control group. Both groups will continue to receive their usual care for the duration of the study. Participants (patients with asthma and/or COPD) who choose to participate will be randomly allocated to either the intervention or control group. Randomisation will be at the individual level. The *intervention group* will receive a series of supportive text messages over the 6 month trial period, varying in content and frequency. They will also be asked to provide self reported data on their symptoms and their adherence at 3 points in time (start, mid-point, and end of trial). The *control group* will receive no supportive text messages over the period of the trial. They will be asked to only provide self reported data on their symptoms and their adherence at 3 points in time (start, mid-point, and end of trial).

	For all participants we will analyse prescription data. Both groups will continue to receive their usual standard of care for the duration of the trial.
Treatment	This is a behavioural intervention. The intervention will consist of a series of supportive text messages over the period of the trial. The messages will vary in frequency from 2 or 3 in the first weeks of the trial to only 1 or 2 a month in the final months of the trial. The content of the messages will vary; some will contain information about how to use a preventer inhaler, some will emphasise the importance of using it, and some will provide simple reminders to patients to take their inhaler.
Objectives	**Primary objectives:** 1. Improved self-reported medication taking as measured by the MARS-5 Questionnaire **Secondary objectives:** 1. Improved control of asthma symptoms as measured by the Asthma Control Test 2. Improved control of COPD symptoms as measured by the COPD Assessment Test 3. A reduction in the interval between patients requesting preventer inhaler prescriptions 4. Difference in emergency admissions 5. Differences in NHS utilisation
Outcome Measurements	**Primary outcome measures**: 1. Changes in the MARS-5 Questionnaire from baseline to 13 and 26 weeks **Secondary outcome measures:** 1. Changes in the Asthma Control Test from baseline to 13 and 26 weeks (for asthma patients) 2. Changes in the COPD Assessment Test from baseline to 13 and 26 weeks (for COPD patients and patients with both asthma *and* COPD) 3. Reduction in days between consecutive preventer inhaler prescription requests from baseline to 13 and 26 weeks 4. Differences in the number of emergency admissions between the intervention and control group over 26 weeks

	5. Differences in the utilisation of NHS resources between the intervention and control group
Key Inclusion and Exclusion Criteria	**Inclusion criteria:** Participants eligible for enrollment in the study must meet all the following criteria: 1. Willing and able to provide informed consent and to comply with the study instructions 2. Male and females age 18 or older 3. Confirmed diagnosis of asthma and/or COPD as recorded in the patient's GP medical record 4. Currently prescribed a preventer inhaler 5. Access to a mobile phone 6. Ability to check text messages on phone 7. Ability to read **Exclusion criteria:** 1. Inability to understand the study procedures 2. Inability or reluctance to provide responses to the study questionnaires 3. Inability to receive and respond to text messages
Key safety arrangement	All participants will continue to receive standard of care for the duration of the trial.
Trial registration	The trial will be registered on the ISRCTN clinical trial registry

3 BACKGROUND AND RATIONALE

3.1 Background

Accurx provides software that allows NHS healthcare teams and patients to seamlessly connect with each other. Through the integrated platform, NHS professionals can manage their patient care and communication. They can use Accurx to send SMS messages and patient questionnaires, provide appointment reminders and referrals, hold video consultations, and manage virtual wards, outpatient clinics and follow-up pathways.

Accurx's Behaviour Change Team focuses on developing tech solutions which can improve patient outcomes, and medication adherence is one of the focus areas for the team. This focus was chosen based on the high prevalence of asthma and COPD in England, along with the well documented issues in medication adherence in these patients with asthma and/or COPD and the evidence in support of text message interventions to improve adherence.

3.2 Rationale

Asthma and COPD are lung conditions that affect a considerable proportion of the UK population. Asthma affects around 5.4 million people across the UK,[1] and approximately 1.17 million people in England have been diagnosed with COPD.[2] Both conditions can have a huge negative impact on patients' quality of life. There are treatments available for both asthma and COPD but research has found controlling these conditions to be a persistent challenge, for example 2.17 million people are estimated to have uncontrolled asthma in the UK.[3]

Nonadherence to medication is a major impediment to achieving optimum outcomes in chronic illness. It is estimated that only approximately 50% of medications for chronic disease are taken as prescribed,[4] and adherence for asthma and COPD medication may be even lower than this.[5] Research suggests that text message interventions can help improve adherence to medication in patients with a range of conditions including hypertension, diabetes, coronary heart disease, and asthma.[6,7,8,9]

Given this evidence around the effectiveness of text message interventions to improve medication adherence, we developed a text message intervention to be sent via the Accurx platform on behalf of a patient's GP practice, supporting them to take their medication as prescribed. All participants will continue to receive their normal standard of care for the duration of the trial.

4 OBJECTIVES AND OUTCOME MEASURES

4.1 Primary objective and measurement

Objective	Measurement
The primary objective of the trial is to assess the difference in adherence of self-reported medication taking as measured by the MARS-5 Questionnaire	Changes in the MARS-5 Questionnaire from baseline to 13 and 26 weeks will be measured in the intervention and control group

4.2 Secondary objectives and measurements

Objectives	Measurement
Improved control of asthma symptoms as measured by the Asthma Control Test	Changes in the Asthma Control Test from baseline to 13 and 26 weeks (for asthma patients)
Improved control of COPD symptoms as measured by the COPD Assessment Test	Changes in the COPD Assessment Test from baseline to 13 and 26 weeks (for COPD patients and patients with both asthma *and* COPD)
Improved adherence to asthma medication, as indicated by an increase in the frequency with which patients request to refill preventer inhaler prescriptions.	Reduction in the number of days between consecutive preventer inhaler prescription requests from baseline to 13 and 26 weeks
Difference in emergency admissions	Differences in the number of emergency admissions between the intervention and control group over 26 weeks
Differences in NHS utilisation	Differences in the utilisation of NHS resources between the intervention and control group over 26 weeks

The complete survey questionnaire that will be administered to participants can be found in Appendix 7. This appendix includes the full survey questionnaire for (1) asthma and (2) COPD patients, including symptom control as measured through the ACT (for asthma) or CAT (for COPD), medication adherence as measured through the MARS-5 and NHS utilisation questions as measured through a number of questions.

5 STUDY DESIGN

5.1 Study type

This is a non-interventional, randomised controlled trial to evaluate the impact of supportive text messages from GP practices on self-reported symptoms and inhaler adherence in patients with asthma and/or chronic obstructive pulmonary disease (COPD) who have been prescribed a preventer (daily/regular) inhaler.

5.2 Duration

Enrollment period: Second half of 2022 (exact dates will depend on date of ethics approval)
Assessment period: 26 weeks

6. PARTICIPANT IDENTIFICATION

6.1 Study population

Approximately 4,000 patients with asthma and/or COPD of participating GP practices will be included in the trial. A number of GP practices in certain areas have been invited to take part in the trial, and these GP practices will invite their eligible patients to take part (see section 6.2 below). Note that 'study population' here is defined as those who have consented and completed the baseline survey.

6.1.1 Inclusion criteria

Participants eligible for enrollment in the study must meet all the following criteria:

1. Willing and able to provide informed consent and to comply with the study instructions
2. Male and females age 18 or older
3. Confirmed diagnosis of asthma and/or COPD as recorded in the patient's GP medical record
4. Currently prescribed a preventer inhaler
5. Access to a mobile phone
6. Ability to check text messages on phone
7. Ability to read

6.2.2 Exclusion criteria

Participants meeting any of the following criteria are not eligible for inclusion in the study :

1. Inability to understand the study procedures
2. Inability or reluctance to provide responses to the study questionnaires
3. Inability to receive and respond to text messages

6.2 Recruitment of participants

Participating GP practices will invite patients with asthma and/or COPD via the Accurx text message platform to participate in the trial. Only GP practices already using the Accurx platform will be invited to take part in this study (note that over 90% of GP practices in England use Accurx). See section 3.1 for more information on the Accurx text message platform.

7. TRIAL PROCEDURES

Trial procedures are detailed in Appendix 1.

7.1 Eligibility confirmation

Participating GP practices will invite patients that meet the eligibility criteria via text message utilising the Accurx system. Only patients who have asthma and/or COPD of the participating GP practices will be invited to participate in the trial.

7.2 Informed consent

Patients who express interest to participate can access the Patient Information Sheet (PIS), and Informed Consent Form (ICF) via a link in the invitation text message sent to them. Full details and copies of the PIS and ICF are attached as separate documents.

7.3 Eligibility confirmation

Prior to randomisation patients will be required to confirm that they are prescribed a preventer inhaler for their asthma and/or COPD and that they are willing and able to complete the procedures required of participants.

7.4 Randomisation

After participants have signed the ICF they will be randomised into one of the two groups at a ratio of 1:1.

- **Control arm:** Will continue to receive their standard of care
  Will be required to complete the relevant questionnaires as per the study schedule (see Appendices 5 & 6)

- **Intervention arm:** Will continue to receive their standard of care
  Will be required to complete the relevant questionnaires as per the study schedule
  Will receive series of supportive text messages as per the study schedule (see Appendices 3 & 4)

7.5 Assessment period

The assessment period will be over a 26 week period. There will be a final survey sent out via text two weeks after the end of the trial (week 28) offering participants in the intervention group only to provide feedback on the intervention itself via an anonymous survey.

Although assessment will take place over the 26 weeks following the commencement of the intervention, at weeks 13 and 26 all actively enrolled patients' historical prescription request data will be accessed, and this data pull will include refill requests dated up to 6 months prior to the intervention start date.

7.6 End of Study

The study will finish for each participant after 26 weeks for the control group and 28 weeks for the intervention group.

7.7 Early discontinuation/Withdrawal of participants

Each participant has the right to withdraw from the study at any time. In addition, the GP or Sponsor may discontinue the participation of a participant from the study at any time, if this is considered necessary for any reason including:

- Pregnancy
- Ineligibility
- Significant protocol deviation
- Significant non-compliance with study requirements
- Withdrawal of consent

During participant withdrawal, participants will be given the opportunity to provide a reason for withdrawal. Providing a reason for withdrawal will be optional and clearly marked as so. Following participant withdrawal, no further outreach will be performed other than an End of Study notification which will be sent via SMS. All data recorded prior to withdrawal will be analysed in line with the analysis plan.

7.8 Definition of end of trial

The end of the study is defined as the date of the last data collection from the last participant in the study.

8. STUDY INTERVENTION

Both the intervention and control group will continue to receive standard of care from their GP practice for the duration of the trial. On signing the informed consent page, all participants who

sign up will receive a confirmation message and will then be randomly allocated to either the treatment or control group (1:1 ratio) after completing the baseline survey.

8.1 Intervention group

Participants allocated to the intervention group will receive supportive text messages for the duration of the study. The frequency of the text messages will vary each week, with one or two messages a week for the first 12 weeks and one message every two weeks for weeks 13 - 26. They will be asked to complete the assessment questionnaires at week 1, 13 and 26. The schedule of the text messages for the intervention group is in Appendix 3 and the text content is in Appendix 4.

8.2 Control group

Participants allocated to the intervention group will not receive supportive text messages. They will then be asked to complete the assessment questionnaires at week 1, 13 and 26 via text message. The schedule of the text messages for the intervention group is in Appendix 5 and the full content is in Appendix 6.

8.3 Adherence

Adherence to the intervention cannot be reliably measured in this trial. The number of participants clicking on the assessment questionnaire links in text messages at 13 and 26 weeks will be assessed, as a proxy measure of adherence to the trial.

9. SAFETY REPORTING

9.1 Adverse events reporting

No adverse event reporting will be conducted for this trial.

9.2 Pregnancy

Pregnancy status will not be collected for participants for the duration of the trial.

10. STATISTICS

The Sponsor/designee will be responsible for the statistical analysis, in accordance with the Statistical Analysis Plan.

10.1 Description of statistical methods

All patients enrolled in the study will be asked to complete a survey at baseline, midpoint (13 weeks) and endline (26 weeks). The survey will consist of the ACT or CAT (depending on whether the participant has asthma or COPD), the MARS-5, and two questions which assess NHS resource utilisation and hospital admissions.

Data collection for this study will conclude at the 26 week mark, after which participants will have one week to complete the endline survey. Prescription data for all actively enrolled patients will also be extracted at 26 weeks. The final dataset will then consist of all patients who initially enrolled, excepting those who explicitly opted out. Where survey data is concerned, the final dataset will consist of those patients who completed both the baseline and midpoint surveys, those who completed both the baseline and endline surveys, and those who completed all three surveys. Data relating to age, sex, and GP practice location will also be collected for descriptive purposes.

Power calculations indicate that a minimum sample size of approximately 4,000 patients with either Asthma or COPD will be required at completion of baseline stage in order to detect a very small change in the CAT score with 80% power. We have used the power calculations for the CAT to calculate the overall required minimum sample size because the CAT measure is that for which we expect the fewest number of participants (there are substantially fewer patients with asthma than COPD). Moreover, we are anticipating a loss-to-follow up of approximately 90-95% (from initial invite to completion of endline measures). Given the relatively low prevalence of COPD compared to Asthma, and given that we are not able to preferentially recruit patients by condition, this study will aim to recruit a large enough overall sample to ensure that 800 patients with COPD are included in the final analysis (400 in each arm). This will require approximately 4000 patients with either Asthma or COPD to complete the initial baseline survey.

All analyses will be conducted using a combination of ANCOVA and independent samples t-tests, where appropriate. Relevant descriptive statistics, as well as raw and adjusted mean differences across treatment arms for all primary and secondary outcome measures will be reported for analyses conducted across the full sample and for any subset analyses. These data will be analysed at both 13 and 26 weeks and will be presented with 95% confidence intervals.

For all outcome measures, the null hypotheses specify no significant difference between the treatment and control arms after accounting for any potential differences at baseline. Where ANCOVA is used, these hypotheses will be rejected if the confidence intervals of the mean adjusted differences do not include zero. Where an independent-samples t-test is used, confidence intervals for raw mean differences that do not include zero will be sufficient to reject the null hypothesis.

Several subset analyses will be conducted to investigate potential differences between sub-populations of interest. More specifically, subset analyses will consider the effect of the treatment on MARS-5 scores in patients with asthma and COPD separately, in addition to examining potential variations in efficacy across patients with different initial levels of symptom control and medication adherence.

Finally, model adequacy will be assessed through residual plots and Shapiro-Wilk tests for normality and Levene's test for homogeneity of variance. Where severe departures from key statistical assumptions are observed, non-parametric methods may be considered.

10.2 The number of participants

The total number of participants recruited into the study will be approximately 4,000. The number of participants recruited into the study is defined as those who have consented and completed the baseline survey. Participants will be recruited in cohorts using a 1:1 ratio (control:intervention). Each member of a given cohort will be randomly allocated into the study, as per computer generated randomisation list using a random number generator as part of the Microsoft .NET framework.

10.3 Criteria for termination of the trial

It is not anticipated that the trial will be suspended or terminated unless on the advice of the TSC in the event of safety concerns or futility such as poor recruitment rates. The study may resume once concerns are addressed and with agreement from the TSC, CI, Sponsor and Ethics Committee.

10.4 Handling of missing and incomplete data

Missing data will be reported with reasons given where available. Depending on the extent of missing values, further investigation may be made into the sensitivity of the analysis results to the method(s) specified.

11. DATA MANAGEMENT

11.1 Source data

Data for the study will be obtained from (1) the surveys that patients complete and (2) patients' medical records pulled from GP practices' Electronic Medical Record systems (EMR).

Patient survey data will be stored in Accurx's production Azure SQL Server database, with access restricted to select authorised members of the Accurx engineering team - as per our ISO 27001 accredited, business operations. This data will then be pseudonymised before being exported to Accurx's analytics Azure SQL Server database, with access restricted to a select group of researchers. Patient prescription data will be stored, pseudonymised, in the same production Azure SQL Server database before also being exported to the aforementioned analytics Azure SQL Server database. Encryption is achieved by combining the patient identifier, organisation identifier, and created date, then hashing using the SHA-256 algorithm.

Other than in their signed consent form, patients will be referred to by a unique ID number.

11.2 Access to data

As described in section 11.1, patient survey data within Accurx's production Azure SQL Server database will be accessible only to a restricted, audited group of the Accurx engineering team (according to the Accurx privileged access management system). The data will also be available through the existing Accurx platform to participating GP practices.

The pseudonymised copy of the patient survey data within Accurx's analytics Azure SQL Server database will be accessible only to a restricted, audited group of the Accurx research team.

Patient prescription data within Accurx's production Azure SQL Server database will be accessible, pseudonymised, to a restricted, audited group of the Accurx engineering team. This pseudonymised data will also be available, from the Accurx analytics Azure SQL Server database, to a restricted, audited group of the Accurx research team.

11.3 Data handling and record keeping

Patient informed consent will be recorded through the Accurx platform when patients consent to participate in the trial. Accurx will store this consent against each patient's unique ID number. This will be stored in Accurx's production database (described in sections 11.1 and 11.2).

The remaining data - survey response data and prescription data - will be collected and stored as described above. There will be no further source available.

Data in the analytics database will be retained for as long as is required by the study. The pseudonymised prescription data will be retained in both the analytics database and the production database for as long as is required by the study. Patient survey data in the production database is required to be stored following the conclusion of the study in order to provide clinical data back to the GP practices as part of the Accurx platform. This survey data will be retained for as long as is required for Accurx to provide this service.

12. QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

12.1 Risk assessment

A risk assessment and categorisation tool will be prepared before recruitment starts and will be reviewed and amended as appropriate during the study, to reflect significant changes to the protocol or to the study conduct.

12.2 Study monitoring

The study will be monitored throughout the period of the trial. Key information will be recorded in the Trial Monitoring Report, which will include detail on the following:

1. Summary of patient engagement and enrollment in the intervention and control group: - Number of patients invited and the number of patients who signed up - Number of patients opting out of the intervention
2. Summary of the extent to which the text message intervention is delivered as conceived and planned in the intervention and control group: - The total number of text messages expected to be delivered per day - The total number of text messages actually successfully delivered per day - The number of failed messages per day
3. Summary of issues and complaints raised by patients or GP practices users, and action taken to resolve these along with any implications for the trial, broken down by: - Issues raised by participating patients, action taken and implications for the trial - Issues raised by participating GP practices, action taken and implications for the trial

13. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the electronic Trial Master File (eTMF), in line with the Sponsor SOPs.

14. SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree

A. the safety or physical or mental integrity of the trial subjects; or
B. the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within one working day. In collaboration with the CI, the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

15. ETHICAL AND REGULATORY CONSIDERATIONS

15.1 Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

15.2 Guidelines for Good Clinical Practice

The Investigator will ensure that this trial is conducted in accordance with relevant regulations and with Good Clinical Practice.

15.3 Approvals

The protocol, patient information sheet, informed consent form and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC) and HRA for written approval. The Chief Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

15.4 Reporting

An Annual Progress Report will be submitted once a year to the REC if required. In addition, an End of Trial notification and final report will be submitted to the REC.

15.5 Participant confidentiality

Accurx will ensure that all patient data is pseudonymised as described in section 11. Study data will only be available to a restricted, audited group of the Accurx research team.

15.6 Expenses and benefits

No expenses are expected for participants in both the intervention and control arm of the study. Participants will also not be remunerated for participation in the trial.

16. FINANCE AND INSURANCE

16.1 Funding

This study will be funded and conducted by Accurx.

16.2 Insurance

The Sponsor has undertaken insurance for this study.

17. PUBLICATION POLICY

The Chief Investigator will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authorship will be determined in accordance with the International Committee Medical Journal Editors guidelines.

No publication or disclosure of study results will be permitted except with explicit approval from the Sponsor, Accurx.

18 REFERENCES

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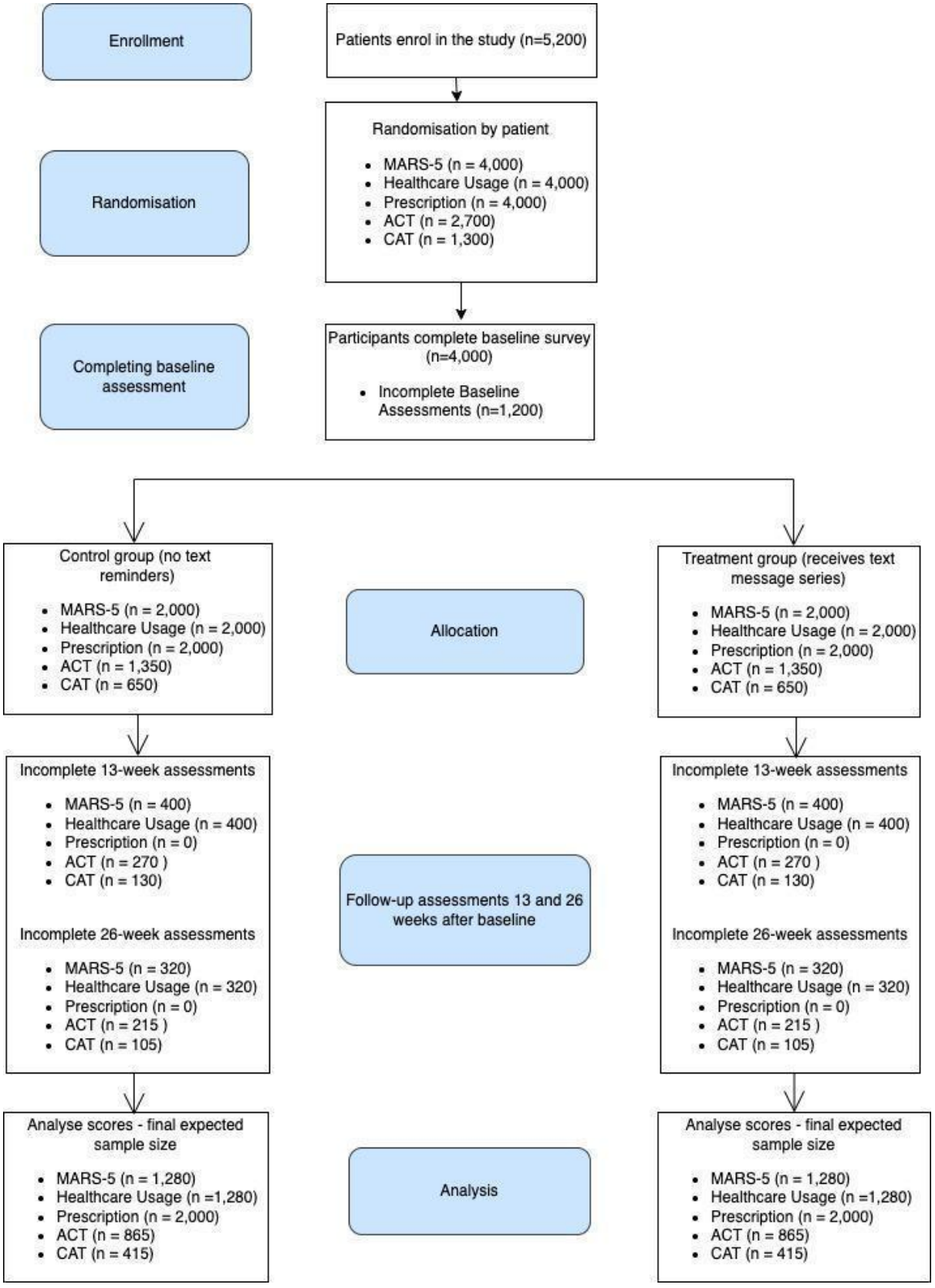
19 APPENDIX 1 - Trial flow chart



20 APPENDIX 2 - Schedule of events table

Schedule of events	Invite	Onboarding Baseline	Assessment period				End of Study
		(Day 0, +/48hrs)	Wks 1 to 12	Week 13	Wks 14 to 25	Week 26	Week 28
Invite to participate	X						
eConsent		X					
Randomisation		X					
Supportive text messages (intervention group only)		X	X	X	X	X	
MARS-5 Questionnaire		X		X		X	
Asthma Control Test (asthma patients only)		X		X		X	
COPD Assessment Test (COPD pts and pts with both asthma and COPD		X		X		X	
Inhaler prescription frequency assessment		X		X		X	
Emergency admissions assessment		X		X		X	
NHS utilisation assessment		X		X		X	
End of study notification (control group)						X	
End of study notification (intervention group)							X
End of study feedback survey (intervention group only)							X

21 APPENDIX 3 - Intervention group: text message schedule

Week	1							2							3							4						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔		✔							✔						✔			✔					✔				
Week	5							6							7							8						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔			✔					✔						✔			✔					✔					
Week	9							10							11							12						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message		✔						✔									✔									✔		
Week	13							14							15							16						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔																✔											
Week	17							18							19							20						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message		✔																	✔									
Week	21							22							23							24						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message			✔												✔													
Week	25							26							27							28						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔											✔										✔						

22 APPENDIX 4 - Intervention group: text message content

Asthma - intervention group		
Hi [name],	Thanks for signing up to take part in the study about your asthma. You'll receive your first message from us in the next few days. A copy of the information sheet is here: [INSERT LINK TO PDF]. You can come back to this at any point. Remember that if you want to opt out at any time during the next 6 months you can do so via this link: https://forms.gle/N7jGrLjQeAeKQ9ee9	Thanks, [Name] [Practice]
Hi [name],	Please take 2 minutes to fill out the questionnaire below. This will help us to understand your asthma symptoms and how you're currently using your preventer inhaler. If you do not complete this survey, you will not be able to take part in the study. Please complete this questionnaire: URL [Asthma ACT Questionnaire] Any messages we send you over the next 6 months will relate to your preventer inhaler (the one that is prescribed to be taken every day) NOT a reliever or rescue inhaler (one only prescribed to take as and when you need to). If you're unsure which inhaler is which, please get in touch with your local pharmacy or the practice.	Many thanks, [Name] [Practice]
Good morning [name],	To make sure you're using your preventer inhaler correctly and getting the maximum benefit from it, please take a few minutes to watch the relevant video on the Asthma UK website below. You can easily search for your inhaler type or name on this site. https://www.asthma.org.uk/advice/inhaler-videos/	Thanks, [Name] [Practice]
Hi [name],	It's important to take your preventer inhaler every day as prescribed, even if you think your asthma is okay. It works by keeping down any inflammation and swelling in your airways. Using the inhaler every day helps you to build up protection over time.	[Name] [Practice]
Hi [name],	This is just a gentle reminder to take your preventer inhaler today to help make sure your asthma is well-controlled.	Thanks, [Name] [Practice]
Good morning [name],	There are many benefits to taking your preventer inhaler every day. For example, you shouldn't need to use your reliever inhaler as much, you should sleep better at night, exercise should feel easier, and you should become less sensitive to your asthma triggers. Please take your inhaler today if you haven't already.	Thanks, [Name] [Practice]
Hi [name],	We know that some patients were diagnosed with asthma many years ago. Watch this short video from Asthma UK for a refresher on what asthma is. https://www.asthma.org.uk/advice/understanding-asthma/what-is-asthma/	Many thanks, [Name] [Practice]
Hi [name],	Do you take your inhaler as part of a routine? Many patients find that incorporating their inhaler into their daily routine can help them remember to take it. If you think this might help you, you could try taking it before you brush your teeth	Many thanks, [Name] [Practice]

	every day.	
Hi [name],	Just a quick reminder to use your inhaler today if you haven't already. By using your preventer inhaler every day, you are helping us to keep your asthma under control.	[Name] [Practice]
Hi [name],	Last week we suggested you try and incorporate taking your preventer inhaler into your daily routine. Today take a moment to reflect on how that is going. Have you remembered to take your inhaler more this week now that it is part of a routine?	[Name] [Practice]
Hi [name],	Remember to pick up a new prescription before your preventer inhaler runs out. If you haven't already, you can arrange repeat prescriptions directly with the practice or through your local pharmacy to make things easier.	Thanks, [Name] [Practice]
Hi [name],	Are you finding these messages useful? Let us know by answering two quick questions via the link below. Please complete this questionnaire: [GOOGLE FORM] If you no longer want to receive the messages, you can opt out at [link to opt out].	Many thanks, [Name] [Practice]
Hi [name],	You can reduce the risk of symptoms like wheezing, breathlessness and a tight chest by using your preventer inhaler every day. Please use your inhaler today if you haven't already.	[Name] [Practice]
Good morning [name],	Have you taken your preventer inhaler yet today? Please remember to take it if you haven't already.	Thanks, [Name] [Practice]
Hi [name],	Asthma flare ups can have a negative impact on your day-to-day life. Using your preventer inhaler today - and every day - lets you gain greater control of your symptoms to help avoid these flare-ups. If you haven't already, please use your inhaler today.	[Name] [Practice]
Hi [name],	Some people tell us that they mean to use their inhaler every day but simply forget. If you struggle with this too, try keeping it somewhere where you'll see it every day, such as by your toothbrush, next to the kettle, or on your bedside table.	Thanks, [Name] [Practice]
Hi [name],	Hopefully you're finding that your asthma is better controlled now that you've been taking your preventer inhaler regularly. We know that many patients find it difficult to remember to take their preventer inhaler when their symptoms improve, but please try to keep taking it as prescribed to help stop your symptoms getting worse and reduce the risk of a flare-up.	Thanks, [Name] [Practice]
Hi [name],	We've been sending you these messages for 3 months now, and we hope that you're finding them helpful. Please answer the short questionnaire below about your asthma to help us understand your symptoms and how you're using your preventer inhaler. Please complete this questionnaire: florey.url ACT/CAT	Many thanks, [Name] [Practice]
Good morning [name],	Make sure your asthma is well-controlled by using your preventer inhaler today - and every day. Remember that if you no longer want to receive the messages, you can opt out at [link to opt out].	Thanks, [Name] [Practice]

Hi [name],	Remember that you need to take your preventer inhaler every day. Taking your inhaler every day will reduce your risk of experiencing asthma symptoms and help build up protection in your airways over time.	Thanks, [Name] [Practice]
Hi [name],	Your preventer inhaler is designed to prevent asthma symptoms. It's important to use it every day, as prescribed, and not only when you experience asthma symptoms. Please try to take it even when your asthma doesn't feel particularly bad.	[Name] [Practice]
Hi [name],	Please remember to take your inhaler today if you haven't taken it yet. By taking your preventer inhaler today - and every day - you are helping to keep your asthma under control.	Thanks, [Name] [Practice]
Good morning [name],	Don't forget to pick up a new prescription before your preventer inhaler runs out. If you haven't already, you can arrange repeat prescriptions with your local pharmacy to make things easier.	Thanks, [Name] [Practice]
Good morning [name],	Just a quick reminder to take your inhaler today if you haven't already. Using your inhaler regularly helps us keep your asthma under control.	Thanks, [Name] [Practice]
Hi [name],	You've now received these messages for the past 6 months. Please let us know how you're feeling by answering the short questionnaire below about your asthma. It should only take you 3 minutes and it will really help us to understand whether these reminders benefit patients. Please complete this questionnaire: florey.url ACT/CAT	Many thanks, [Name] [Practice]
Hi [name],	Final step! Tell us how you found receiving messages from us at Accurx on behalf of your GP practice over the last 6 months. Please could you take 2 minutes to share your feedback through the anonymous survey link below? The deadline for completing the survey is [date]. [survey link] Thank you for taking part in this study. This is the last text message we'll be sending you as part of the study.	Thanks, Alex accuRx

COPD - intervention group		
Hi [name],	Thanks for signing up to take part in the study about your breathing condition - COPD. You'll receive your first message from us in the next few days. A copy of the information sheet is here: [INSERT LINK TO PDF]. You can come back to this at any point. Remember that if you want to opt out at any time during the next 6 months you can do so via this link: https://forms.gle/N7jGrLjQeAeKQ9ee9	Thanks, [Name] [Practice]
Hi [name],	Please take 2 minutes to fill out the questionnaire below. This will help us to understand your COPD symptoms and how you're currently using your regular inhaler. If you do not complete this survey, you will not be able to take part in the study. Please complete this questionnaire: URL [COPD CAT Questionnaire] Any messages we send you over the next 6 months will relate to your regular inhaler (the one that is prescribed to be taken every day) NOT a reliever or rescue inhaler	Many thanks, [Name] [Practice]

	(one only prescribed to take as and when you need to). If you're unsure which inhaler is which, please get in touch with your local pharmacy or the practice.	
Good morning [name],	To make sure you're using your regular inhaler correctly and getting the maximum benefit from it, please take a few minutes to watch the relevant video on the Asthma + Lung UK website below. You can easily search for your inhaler type or name on this site. https://www.asthma.org.uk/advice/inhaler-videos/	Thanks, [Name] [Practice]
Hi [name],	It's important to take your regular inhaler every day, as prescribed, even if you think your COPD is okay. It works by opening your airways. Using the inhaler every day helps you to build up protection over time.	[Name] [Practice]
Hi [name],	This is just a gentle reminder to take your inhaler today to help you better control your COPD symptoms.	Thanks, [Name] [Practice]
Good morning [name],	There can be many benefits to taking your regular inhaler every day, such as preventing flare-ups, helping with breathlessness throughout the day and making it easier to carry out your daily activities. Together, these things can make a big difference to your quality of life. Please take your inhaler today if you haven't already.	Thanks, [Name] [Practice]
Hi [name],	We know that some patients were diagnosed with COPD many years ago. Have a look at this information on the British Lung Foundation website for a refresher on what COPD is. https://www.blf.org.uk/support-for-you/copd/what-is-copd	Many thanks, [Name] [Practice]
Hi [name],	Do you take your inhaler as part of a routine? Many patients find that incorporating it into their daily routine can help them remember to take it. If you think this might help you, you could try taking your inhaler before you brush your teeth every day.	Many thanks, [Name] [Practice]
Hi [name],	Just a quick reminder to use your inhaler today if you haven't already. By using your regular inhaler every day, you are helping better control your COPD symptoms.	[Name] [Practice]
Hi [name],	Last week we suggested you try and incorporate taking your preventer inhaler into your daily routine. Today, take a moment to reflect on how that is going. Have you remembered to take your inhaler more this week now that it is part of a routine?	[Name] [Practice]
Hi [name],	Remember to pick up a new prescription before your regular inhaler runs out. If you haven't already, you can arrange repeat prescriptions directly with the practice or through your local pharmacy to make things easier.	Thanks, [Name] [Practice]

Hi [name],	Are you finding these messages useful? Let us know by answering two quick questions via the link below. Please complete this questionnaire: [GOOGLE FORM] If you no longer want to receive the messages, you can opt out at [link to opt out].	Many thanks, [Name] [Practice]
Hi [name],	You can reduce the risk of symptoms like wheezing, breathlessness and a tight chest by using your regular inhaler every day. Please use your inhaler today if you haven't already.	[Name] [Practice]
Good morning [name],	Have you taken your regular inhaler yet today? Please remember to take it if you haven't already.	Thanks, [Name] [Practice]
Hi [name],	COPD flare-ups can have a negative impact on your day-to-day life. Using your inhaler today - and every day - lets you gain greater control of your symptoms to help avoid these flare-ups. If you haven't already, please use your inhaler today.	[Name] [Practice]
Hi [name],	Some people tell us that they mean to use their inhaler every day but simply forget. If you struggle with this too, try keeping it somewhere where you'll see it every day, such as by your toothbrush, next to the kettle, or on your bedside table.	Thanks, [Name] [Practice]
Hi [name],	Hopefully you're finding that your COPD is better controlled now that you've been taking your regular inhaler more often. We know that many patients find it difficult to remember to take their regular inhaler when their symptoms improve, but please try to keep taking it as prescribed to help stop your symptoms getting worse and reduce the risk of a flare-up.	Thanks, [Name] [Practice]
Hi [name],	We've been sending you these messages for 3 months now, and we hope that you're finding them helpful. Please answer the short questionnaire below about your COPD to help us understand your symptoms and how you're using your regular inhaler. Please complete this questionnaire: florey.url CAT	Many thanks, [Name] [Practice]
Good morning [name],	Make sure your COPD is better controlled by using your regular inhaler today - and every day. Remember that if you no longer want to receive the messages, you can opt out at [link to opt out].	Thanks, [Name] [Practice]
Hi [name],	Remember that you need to take your regular inhaler every day. Taking your inhaler every day will reduce your risk of experiencing COPD symptoms.	Thanks, [Name] [Practice]
Hi [name],	Your regular inhaler is designed to prevent and improve COPD symptoms. It's important to use it every day, as prescribed, and not only when you experience symptoms. Please try to take it even when your COPD doesn't feel particularly bad.	[Name] [Practice]
Hi [name],	Please remember to take your inhaler today if you haven't taken it yet. By taking your regular inhaler today - and every day - you are helping to control your COPD symptoms.	Thanks, [Name] [Practice]

Good morning [name],	Don't forget to pick up a new prescription before your regular inhaler runs out. If you haven't already, you can arrange repeat prescriptions with your local pharmacy to make things easier.	Thanks, [Name] [Practice]
Good morning [name],	Just a quick reminder to take your inhaler today if you haven't already. Using your inhaler regularly helps us keep your COPD under control.	Thanks, [Name] [Practice]
Hi [name],	You've now received these messages for the past 6 months. Please let us know how you're feeling by answering the short questionnaire below about your COPD. It should only take you 3 minutes and it will really help us to understand whether these reminders benefit patients. Please complete this questionnaire: florey.url CAT	Many thanks, [Name] [Practice]
Hi [name],	Final step! Tell us how you found receiving messages from us at accuRx on behalf of your GP practice over the last 6 months. Please could you take 2 minutes to share your feedback through the anonymous survey link below? The deadline for completing the survey is [date]. [survey link] Thank you for taking part in this study. This is the last text message we'll be sending you as part of the study.	Thanks, Alex accuRx

23 APPENDIX 5 - Control group: text message schedule

Week	1							2							3							4						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔																											
Week	5							6							7							8						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message																												
Week	9							10							11							12						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message																												
Week	13							14							15							16						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message	✔																											
Week	17							18							19							20						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message																												
Week	21							22							23							24						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message																												
Week	25							26							27							28						
Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Message												✔																	

24 APPENDIX 6 - Control group: text message content

Asthma - control group		
Hi [name],	Thanks for signing up to take part in the study about your asthma. You'll receive your first message from us in the next few days. A copy of the information sheet is here: [INSERT LINK TO PDF]. You can come back to this at any point. Remember that if you want to opt out at any time during the next 6 months you can do so via this link: https://forms.gle/N7jGrLjQeAeKQ9ee9	Thanks, [Name] [Practice]
Hi [name],	Please take 2 minutes to fill out the questionnaire below. This will help us to understand your asthma symptoms and how you're currently using your preventer inhaler. If you do not complete this survey, you will not be able to take part in the study. Please complete this questionnaire: URL [Asthma ACT Questionnaire] Any messages we send you over the next 6 months will relate to your preventer inhaler (the one that is prescribed to be taken every day) NOT a reliever or rescue inhaler (one only prescribed to take as and when you need to). If you're unsure which inhaler is which, please get in touch with your local pharmacy or the practice.	Many thanks, [Name] [Practice]
Hi [name],	Please answer the short questionnaire below about your asthma to help us understand your symptoms and how you're using your preventer inhaler. Please complete this questionnaire: florey.url ACT/CAT	Many thanks, [Name] [Practice]
Hi [name],	Please let us know how you're feeling by answering the short questionnaire below about your asthma. It should only take you 3 minutes and it will really help us. Please complete this questionnaire: florey.url ACT/CAT Thank you for taking part in this study. This is the last text message we'll be sending you as part of the study.	Many thanks, [Name] [Practice]

COPD - control group		
Hi [name],	Thanks for signing up to take part in the study about your breathing condition - COPD. You'll receive your first message from us in the next few days. A copy of the information sheet is here: [INSERT LINK TO PDF]. You can come back to this at any point. Remember that if you want to opt out at any time during the next 6 months you can do so via this link: https://forms.gle/N7jGrLjQeAeKQ9ee9	Thanks, [Name] [Practice]

Hi [name],	Please take 2 minutes to fill out the questionnaire below. This will help us to understand your COPD symptoms and how you're currently using your regular inhaler. If you do not complete this survey, you will not be able to take part in the study. Please complete this questionnaire: URL [COPD CAT Questionnaire] Any messages we send you over the next 6 months will relate to your regular inhaler (the one that is prescribed to be taken every day) NOT a reliever or rescue inhaler (one only prescribed to take as and when you need to). If you're unsure which inhaler is which, please get in touch with your local pharmacy or the practice.	Many thanks, [Name] [Practice]
Hi [name],	Please answer the short questionnaire below about your COPD to help us understand your symptoms and how you're using your regular inhaler. Please complete this questionnaire: florey.url CAT	Many thanks, [Name] [Practice]
Hi [name],	Please let us know how you're feeling by answering the short questionnaire below about your COPD. It should only take you 3 minutes and it will really help us. Please complete this questionnaire: florey.url CAT Thank you for taking part in this study. This is the last text message we'll be sending you as part of the study.	Many thanks, [Name] [Practice]

25 APPENDIX 7 - Full survey questionnaire for (1) asthma and (2) COPD patients, including symptom control, medication adherence and NHS utilisation questions

Complete questionnaire for asthma patients

1. During the past 4 weeks, how often did your asthma prevent you from getting as much done at work, school or home?
    a. All of time time
    b. Most of the time
    c. Some of the time
    d. A little of the time
    e. None of the time
2. During the past 4 weeks, how often have you had shortness of breath?
    a. More than once a day
    b. Once a day
    c. 3 to 6 times a week
    d. Once or twice a week
    e. Not at all
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
    a. 4 of more nights a week
    b. 2 to 3 nights a week
    c. Once a week
    d. Once or twice
    e. Not at all
4. During the past 4 weeks, how often have you used your reliever inhaler (usually the blue inhaler) or nebuliser medication?
    a. 3 or more times per day
    b. 1 or 2 times per day
    c. 2 or 3 times per week
    d. Once a week or less
    e. Not at all

5. How would you rate your asthma control during the past 4 weeks?
    a. Not controlled at all
    b. Poorly controlled
    c. Somewhat controlled
    d. Well controlled
    e. Completely controlled
6. During the past 2 weeks, how often did you forget to take your preventer inhaler?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
7. During the past 2 weeks, how often did you alter the dose of your preventer inhaler?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
8. During the past 2 weeks, how often did you stop taking your preventer inhaler for a while?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
9. During the past 2 weeks, how often did you miss out a dose?
    a. Always
    b. Often
    c. Sometimes

d. Rarely

e. Never

10. During the past 2 weeks, how often did you take less preventer inhaler than instructed?

    a. Always

    b. Often

    c. Sometimes

    d. Rarely

    e. Never

11. Roughly how many times have you stayed in hospital in relation to your asthma over the past 3 months, if at all?

    Put '0' if you haven't had to stay in hospital at all in relation to your COPD over the past 3 months. If you don't remember the exact number, please just put your best guess.

    a. Free text box

12. Roughly how many times have you attended an emergency GP appointment with your own GP or a walk-in centre in relation to your asthma over the past 3 months, if at all?

    Put '0' if you haven't had to use this service at all in relation to your asthma over the past 3 months. If you don't remember the exact number, please just put your best guess.

    a. Free text box

13. Roughly how many times have you called the NHS 111 helpline in relation to your asthma over the past 3 months, if at all?

    Put '0' if you haven't had to use this service at all in relation to your asthma over the past 3 months. If you don't remember the exact number, please just put your best guess.

    a. Free text box

14. Roughly how many times have you visited an Urgent Care Centre in relation to your asthma over the past 3 months, if at all?

    Put '0' if you haven't had to use this service at all in relation to your asthma over the past 3 months. If you don't remember the exact number, please just put your best guess.

    a. Free text box

15. Roughly how many times have you visited Accident & Emergency (A&E) in relation to your asthma over the past 3 months, if at all?

    Put '0' if you haven't had to use this service at all in relation to your asthma over the past 3 months. If you don't remember the exact number, please just put your best guess.

    a. Free text box

Complete questionnaire for COPD patients

1. How often do you cough?
    a. 0 - I never cough
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5 - I cough all the time
2. How much phlegm (mucus) do you feel you have on your chest?
    a. 0 - I have no phlegm (mucus) on my chest at all
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5 - My chest is completely full of phlegm (mucus)
3. How tight is your chest?
    a. 0 - My chest does not feel tight at all
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5 - My chest feels very tight
4. When do you get out of breath?
    a. 0 - When I walk up a hill or one flight of stairs I am not breathless
    b. 1
    c. 2

d. 3

e. 4

f. 5 - When I walk up a hill or flight of stairs I am completely out of breath

5. How much are you limited by your COPD when at home?

    a. 0 - I am not limited doing any activities at home

    b. 1

    c. 2

    d. 3

    e. 4

    f. 5 - I am very limited doing activities at home

6. How confident do you feel leaving your home?

    a. 0 - I am confident leaving my home despite my lung condition

    b. 1

    c. 2

    d. 3

    e. 4

    f. 5 - I am not confident leaving my home at all because of my lung condition

7. How well do you sleep?

    a. 0 - I sleep soundly at night

    b. 1

    c. 2

    d. 3

    e. 4

    f. 5 - I do not sleep soundly because of my lung condition

8. How much energy do you have?

    a. 0 - I have lots of energy

    b. 1

    c. 2

d. 3

e. 4

f. 5 - I have no energy at all

9. During the past 2 weeks, how often did you forget to take your regular inhaler?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
10. During the past 2 weeks, how often did you alter the dose of your regular inhaler?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
11. During the past 2 weeks, how often did you stop taking your regular inhaler for a while?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never
12. During the past 2 weeks, how often did you miss out a dose?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never

13. During the past 2 weeks, how often did you take less regular inhaler than instructed?
    a. Always
    b. Often
    c. Sometimes
    d. Rarely
    e. Never

14. Roughly how many times have you stayed in hospital in relation to your COPD over the past 3 months, if at all?

    Put ‘0’ if you haven’t had to stay in hospital at all in relation to your COPD over the past 3 months. If you don’t remember the exact number, please just put your best guess.

    a. Free text box

15. Roughly how many times have you attended an emergency GP appointment with your own GP or a walk-in centre in relation to your COPD over the past 3 months, if at all?

    Put ‘0’ if you haven’t had to use this service at all in relation to your asthma over the past 3 months. If you don’t remember the exact number, please just put your best guess.

    a. Free text box

16. Roughly how many times have you called the NHS 111 helpline in relation to your COPD over the past 3 months, if at all?

    Put ‘0’ if you haven’t had to use this service at all in relation to your asthma over the past 3 months. If you don’t remember the exact number, please just put your best guess.

    a. Free text box

17. Roughly how many times have you visited an Urgent Care Centre in relation to your COPD over the past 3 months, if at all?

    Put ‘0’ if you haven’t had to use this service at all in relation to your asthma over the past 3 months. If you don’t remember the exact number, please just put your best guess.

    a. Free text box

18. Roughly how many times have you visited Accident & Emergency (A&E) in relation to your COPD over the past 3 months, if at all?

    Put ‘0’ if you haven’t had to use this service at all in relation to your asthma over the past 3 months. If you don’t remember the exact number, please just put your best guess.

    a. Free text box

Protocol Title: A randomised controlled trial to evaluate the impact of supportive text messages from GP practices on self-reported symptoms and inhaler adherence in patients with asthma and/or chronic obstructive pulmonary disease (COPD) who have been prescribed a preventer (daily) inhaler (Inhaler Trial)

Protocol no: Accurx-001

COMMERCIAL PARTICIPANT IDENTIFICATION CENTRE AGREEMENT

Between

Accurx Ltd, 7 Curtain Rd, London, EC2A 3LT

"Participating Organisation"

AND

GP Practice as detailed in the "Principal Investigator and Service Agreement for the Protocol" (Inhaler Trial protocol, page 2).

"Participant Identification Centre (PIC)"

Each of which shall be a **"Party"** and collectively the **"Parties"**

Whereas

A. The Sponsor is a technology company involved in the research, development, manufacture and sale of technology for the use in life science;

B. The Participating Organisation is contracted to act as the Processor of the Sponsor (as Controller) for Personal Data Processed for the purpose of the Clinical Trial;

C. The Participating Organisation wishes to sub-contract with the PIC to undertake Data Processing for the purpose of identifying potential Clinical Trial Subjects for the Clinical Trial.

It is therefore, agreed that the following terms and conditions shall apply to the conduct of the Data Processing undertaken by the PIC for the purpose of the Clinical Trial (as further defined below):

1. Definitions

1.1 In this Agreement, the following words shall have the following meanings:

- **Affiliate**

means any business entity that controls, is controlled by or is under the common control with the Sponsor, save where there are contractual arrangements in place to exclude such affiliate. For the purposes of this definition, a business entity shall be deemed to control another business entity if it owns, directly or indirectly, in excess of 50% of the voting interest in such business entity or the power to direct the management of such business entity;

- **Agent**

shall include but is not limited to, any person (including any nurse or other healthcare professional) providing services to the PIC under a contract for services (commonly known as an honorary contract) or otherwise any such person's principal employer in the event that it is not the PIG and/or any contracted third party providing services to a Party under a contract for services or otherwise;

- **Agreement**

means this Agreement comprising its clauses, schedules and any appendices attached to it;

- **Clinical Trial**

means the investigation to be conducted at the Site in accordance with the Protocol;

- **Clinical Trial Subject**

means a person enrolled to participate in the Clinical Trial according to criteria detailed in the Protocol;

- **Controller**

shall have the meaning set out in the Data Protection Laws and Guidance;

- **Data Protection Laws and Guidance**

means the GDPR, the Data Protection Act 2018, the Privacy and Electronic Communications (EC Directive) Regulations 2003, as well as any legally enforceable NHS requirements, Codes of Practice or Guidance issued by the Information Commissioner's Office, in each case in force from time to time in England, Northern Ireland, Scotland and/or Wales; and, pending a favourable decision from the competent authorities of the EU on the adequacy of the UK data protection regime will include the requirements set out or referenced in Part Three, Title VII, Article 71(1) of the Withdrawal Agreement signed by the UK and the EU in December 2019;

- **Data Subject**

shall have the meaning set out in the Data Protection Laws and Guidance;

- **EEA**

means the European Economic Area comprising the countries of the European Union as well as Iceland, Liechtenstein and Norway;

- **GDPR**

means Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, as it forms part of the law of England and Wales, Scotland and Northern Ireland by virtue of Section 3 of the European Union (Withdrawal) Act 2018 and as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations 2019;

- **Personal Data**

means any and all information, data and material of any nature received or obtained by any Party in connection with this Agreement which is personal data as defined in the Data Protection Laws and Guidance and which relates to a Clinical Trial Subject (or potential Clinical Trial Subject) and/or their treatment or medical history;

- **Personal Data Breach**

means a breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted or otherwise processed;

- **Personnel**

means the persons who will undertake the activities specified at Clause 2.5 on behalf of the PIC;

- **Participant Identification Centre (PIC)**

means the organisation named on page one of this Agreement, being an organisation sub-contracted by the Participating Organisation to Process Personal Data on behalf of the Sponsor to identify potential Clinical Trial Subjects for the Clinical Trial;

- **Process**

shall have the meaning set out in the Data Protection Laws and Guidance (and "process" and "processed" shall be construed accordingly);

- **Processor**

shall have the meaning set out in the Data Protection Laws and Guidance;

- **Protocol**

means the full description of the Clinical Trial with the reference number set out on the front page of this Agreement and incorporated into this Agreement by reference;

- **Pseudonymised Data**

means individual-level data relating to a natural person (as opposed to aggregated data) who is made no longer identified or identifiable from that data by virtue of the replacement of personal identifiers with a code, or equivalent, and which is safeguarded as non-identifiable in accordance with this agreement;

- **Site**

means the physical location(s) where the Clinical Trial will be conducted within the Participating Organisation;

- **Sub-Processor**

means the PIC contracted by the Participating Organisation to Process Personal Data on behalf of the Sponsor (as per GDPR Article 28 (2)).

2. General

2.1 Any reference to a statutory provision, code or guidance shall be deemed to include reference to any subsequent modification or re-enactment of it.

2.2 The headings to clauses are inserted for convenience only and shall not affect the interpretation or construction of this Agreement.

2.3 Where appropriate, words denoting the singular shall include the plural and vice versa and words denoting any gender shall include all genders.

2.4 A reference to this Agreement or to any other agreement or document referred to in this Agreement is a reference to this Agreement or such other agreement or document as amended, varied or novated (in each case other than in breach of the provisions of this Agreement) from time to time.

2.5 The PIC will Process Personal Data to identify potential Clinical Trial Subjects as follows:

2.5.1 The PIC will forward an invite via the Accurx Batch Messaging Feature for potential Participants meeting the following criteria:

Inclusion criteria:

Participants eligible for enrollment in the study must meet all the following criteria:

1. Willing and able to provide informed consent and to comply with the study instructions

2. Male and females age 18 or older

3. Confirmed diagnosis of asthma and/or COPD as recorded in the patient's GP medical record
4. Currently prescribed a preventer inhaler
5. Access to a mobile phone
6. Ability to check text messages on phone
7. Ability to read

Exclusion criteria:

1. Inability to understand the study procedures
2. Inability or reluctance to provide responses to the study questionnaires
3. Inability to receive and respond to text messages

2.5.2 The PIC will be provided with the following information to provide to potential participants:

a. Study invitation

2.6 Where the PIC is constituted in England then this Agreement shall be governed and construed in accordance with the laws of England and Wales and the Courts of England and Wales shall have exclusive jurisdiction to hear any dispute relating to this Agreement.

Where the PIC is constituted in Wales then this Agreement shall be governed and construed in accordance with the laws of England and Wales as applied in Wales and the Courts of England and Wales shall have exclusive jurisdiction to hear any dispute relating to this Agreement.

Where the PIC is constituted in Scotland, this Agreement shall be governed and construed in accordance with the laws of Scotland and the Courts of Scotland shall have exclusive jurisdiction to hear any dispute relating to this Agreement.

Where the PIC is constituted in Northern Ireland, then this Agreement shall be governed and construed in accordance with the laws of Northern Ireland and the Courts of Northern Ireland shall have exclusive jurisdiction to hear any dispute relating to this Agreement.

3. Confidentiality and Data Protection Data Protection

3.1 The Parties agree:

3.1.1 To comply with all Data Protection Laws and Guidance in processing the Personal Data of Clinical Trial Subjects. This Clause 3 is in addition to and does not replace, relieve or remove a Party's obligations or rights under the Data Protection Laws and Guidance.

3.1.2 When one Party is Processing Personal Data, as Controller, for which the other Party is at that time a separate and independent Controller, to promptly and without undue delay, notify and inform that other Party in the event of any Personal Data Breach that relates to that Personal Data.

3.2 **Processing of Clinical Trial Subject Personal Data**

3.2.1 For the purpose of the Data Protection Laws and Guidance, the Sponsor is the Controller, the Participating Organisation is the Processor and the PIC is the Sub-Processor of the Participating Organisation in relation to the Processing of Personal Data for the purpose of the Clinical Trial.

3.2.2 The PIG's Processing of Personal Data, as a Sub-Processor of the Participating Organisation, shall be governed by this Agreement, including the Protocol, which sets out the subject matter, duration, nature, and purpose of the Processing, type of Personal Data and categories of data subjects, and obligations and rights of Sponsor as Controller and Participating Organisation as Sub-Processor.

3.2.3 The PIC is the Controller of Personal Data that it processes for purposes other than the Clinical Trial, e.g. the provision of medical care.

3.2.4 The PIC, in its role as Processor of the Personal Data under Clause 3.2.1, agrees to only Process Personal Data for and on behalf of the Sponsor in accordance with the documented instructions of the Sponsor and/or Participating Organisation, including with regard to transfers of personal data to a third country or an international organisation. If the PIC is required by law to otherwise Process the Personal Data, the PIC shall notify the Participating Organisation before undertaking the Processing, unless such notification is prohibited on important grounds of public interest in accordance with GDPR Article 28(3)(a). In the case of such prohibition, the PIC shall notify the Participating Organisation as soon as possible once the prohibition is lifted, if it is lifted.

3.2.5 The PIC agrees to comply with the obligations applicable to Processors described by Article 28 of the GDPR, as well as those additional obligations required by Participating Organisation pursuant to this Agreement, including but not limited to the following:

a. implementing and maintaining appropriate technical and organisational security measures for Personal Data Processed in its systems, in keeping with its

obligations as an NHS organisation, thereby providing guarantee to the Sponsor pursuant to GDPR Article 28(1);

b. ensuring that Personnel authorised to Process Personal Data have committed themselves to confidentiality or are under an appropriate statutory obligation of confidentiality (Article 28(3)(b));

c. taking all measures required by GDPR Article 32 in relation to the security of processing (GDPR Article 28(3c));

d. complying with the conditions described in GDPR Article 28(2) and (4) for engaging another Processor (GDPR Article 28(3d));

e. taking into account the nature of the Processing, assist the Sponsor and/or the Participating Organisation, by appropriate technical and organisational measures, insofar as this is possible, to respond to requests for exercising Data Subjects' rights (GDPR Article 28(3e));

f. assisting the Controller, to ensure compliance with the obligations pursuant to GDPR Articles 32 to 36, taking into account the nature of the Processing and the information available to the PIC (GDPR Article 28(3f));

g. maintaining a record to demonstrate compliance with this Clause and Data Protection Laws and Guidance, including the records required pursuant to GDPR Article 30(2);

h. in the event of any Personal Data Breach by the PIC as a Sub- Processor of the Participating Organisation, the PIC shall: (i) promptly and without undue delay following discovery of such Personal Data Breach, send written notice of the incident via e-mail to research@accurx.com (ii) not make any statements or notifications about the Personal Data Breach, as it relates to the Processing for the purpose of the Clinical Trial, to any individual affected by the incident, the public or any third party without Sponsor or Participating Organisations prior written approval; and (iii) immediately take steps to investigate and mitigate the Personal Data Breach and reasonably cooperate with Sponsor and the Participating Organisation.

3.2.6 In furtherance of its obligations under Article 28 GDPR, the PIC agrees that it will not engage another Processor for the purpose of the Clinical Trial without the prior written authorisation of the Sponsor or Participating Organisation (GDPR Article 28(2)).

3.2.7 At the expiry or lapse of this Agreement, the PIC shall, at the choice of the Participating Organisation, destroy or return all Personal Data to the Sponsor or Participating Organisation unless there is a legal requirement for retention and storage

(GDPR Article 28(3g)) and/or where that Personal Data is held by the PIC as Controller for its own purpose(s).

3.2.8 The PIC will:

a. ensure that its Personnel do not Process Personal Data except in accordance with the Protocol and this Agreement;

b. take all reasonable steps to ensure the reliability and integrity of any of its Personnel who have access to the Personal Data and ensure that the Personnel:
   (i) are aware and comply with the PIG's duties under this Clause 3 (Confidentiality and Data Protection);
   (ii) are subject to mandatory training in their information governance responsibilities and have appropriate contracts, including sanctions, including for breach of confidence or misuse of Personal Data; and
   (iii) are informed of the confidential nature of the Personal Data and understand their responsibilities for information governance, including their obligation to Process Personal Data securely and to only disseminate or disclose it for lawful and appropriate purposes.

3.2.9 The PIC agrees to:

a. provide the Sponsor and/or the Participating Organisation with evidence of its compliance with the obligations set out in this Agreement, or, at the Sponsor and/or Participating Organisation's discretion and on reasonable notice, to allow the Sponsor, Participating Organisation or a third party appointed by the Sponsor or Participating Organisation, to audit the PIG's compliance with the obligations described in this Agreement, Data Protection Legislation and Guidance (including but not limited to Article 28 GDPR), subject to the Sponsor, Participating Organisation or appointed third party, complying with all relevant health and safety and security policies of the PIC;

b. obtain prior written agreement of the Sponsor or Participating Organisation to Process Personal Data outside of the UK and the EEA.

3.2.10 In addition to the PIG's obligations under Clause 3.2.9.b, where the PIG, acting as the Participating Organisation's Sub-Processor, Processes Personal Data outside of the UK and the EEA, the PIC warrants that it does so in compliance with the Data Protection Laws and Guidance.

4. Intellectual Property

4.1 All Intellectual Property Rights and Know-How owned by or licensed to the Sponsor, Participating Organisation or Affiliate(s) prior to and after the date of this Agreement, other than any Intellectual Property Rights and Know-How arising from the Clinical Trial, are and shall remain the property of the Sponsor, Participating Organisation or Affiliate(s), as the case may be.

4.2 All Intellectual Property Rights and Know-How owned by or licensed to the PIC prior to and after the date of this Agreement, other than any Intellectual Property Rights and Know-How arising from the Clinical Trial, are and shall remain the property of the PIC.

4.3 All Intellectual Property Rights and Know-How arising from and relating to the Clinical Trial, the IMP (including but not limited to its formulation and use alone or in combination with other drugs), and/or the Protocol, but excluding any clinical procedure and improvements thereto that are clinical procedures of the PIC, shall vest in the Sponsor in accordance with Clauses 4.4 and 4.5 of this Agreement.

4.4 In accordance with Clause 4.3, the PIC hereby assigns, and shall procure that its Agents assign, its rights in relation to all Intellectual Property Rights and Know- How, falling within Clause 4.3, to the Sponsor or its nominee. At the request and expense of the Sponsor, the PIC shall execute, and shall procure that its Agents shall execute, all such documents and do all such other acts as the Sponsor may reasonably require in order to vest fully and effectively all such Intellectual Property Rights and Know-How in the Sponsor or its nominee.

4.5 PIC shall and will ensure that the Personnel promptly disclose to the Participating Organisation any Know-How generated pursuant to this Agreement and falling within Clause 4.3 and undertakes not to use or disclose such Know-How other than for the purposes of this Agreement.

4.6 Nothing in this Clause 4 shall be construed so as to prevent or hinder the PIC from using its Know-How generated during the performance of the Clinical Trial in the furtherance of its normal activities, to the extent that such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Intellectual Property Right or Know-How of the Sponsor or Participating Organisation.

5. Sign Off

Refer to page 2 "Principal Investigator and Service Agreement for the Protocol" of the Inhaler Trial (IRAS 316452) protocol.