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PROTOCOL SUMMARY

The CYMPLA trial. Mobile phone-based structured intervention to achieve asthma control in patients with uncontrolled persistent asthma: a pragmatic randomised controlled trial

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The full trial protocol, together with Appendices, is available online at www.thepcrj.org

Introduction

Morbidity and mortality from asthma are major problems worldwide.[1] Despite effective treatments, studies continue to demonstrate that asthma is poorly controlled,[2,3] though marked variation in the control achieved in UK general practices suggests that improvement is possible for the vast majority of patients.[4,5]

There is a significant body of evidence which demonstrates that asthma education coupled with self-management improves control in terms of increased adherence to medication, fewer exacerbations of asthma and reduced hospital admissions.[6] However, despite self-management education, compliance with traditional diary monitoring can be as low as 6%,[7] and there is concern about fabrication of results.[8] Electronic recording may improve adherence to self-recording of biometric data,[9] with, for example, over two-thirds of potential readings recorded during a 72-week study using mobile phone technology.[10]

Increasingly pervasive throughout society, mobile phone technology provides a convenient, portable communications medium. Our recent qualitative study suggests that people with asthma perceive a role for mobile technology in aiding transition from clinician-supported management while control is gained, to effective self-management during maintenance phases.[11]

Our trial tests the hypothesis that, through engaging the patient in self-monitoring with timely biofeedback, mobile phone technology can improve asthma control compared to usual paper-based monitoring.

Research questions

In teenagers and adults with poorly controlled asthma, who are offered treatment according to the British Thoracic Society

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and Scottish Intercollegiate Guideline Network (BTS/SIGN) Asthma Guideline,[12] does the use of mobile phone-based lung function and symptom monitoring with feedback:

1. Improve asthma control achieved at six months compared to usual paper-based monitoring strategies?
2. Improve self-efficacy at six months compared to usual paper-based monitoring strategies?
3. Improve disease-specific quality of life?
4. Engage patients in self-care and improve compliance?
5. Represent a cost-effective use of NHS resources?

Outcome measures

The primary outcome measure is the change in asthma control between baseline and six months as measured by the Asthma Control Questionnaire (ACQ).[13] The ACQ measures clinical goals of asthma management on a scale of 0 (good control) to 6. It is responsive to change,[13] with an intra-individual minimum important difference (MID) of 0.5.[14] The 6-question version of the ACQ will be used for the primary analysis.

Self-efficacy will be measured as the mean difference in the Knowledge, Attitude and Self-Efficacy Asthma Questionnaire (KASE-AQ) scores between the intervention and control groups at six months.[15] Other outcomes of interest include mean difference in the ACQ scores, the mini Asthma Quality of Life Questionnaire (miniAQLQ),[16] the modified Patient Enablement Instrument (mPEI),[17] and the Aberdeen Asthma Questionnaire (AAQ).[18] Compliance with monitoring, use of medication, and defaults from clinical follow-up, will be used to gauge engagement with the process. We will also collect data on adverse events and use of healthcare resources from the records.

Methods

Recruitment and randomisation

We will search the computer of participating practices to identify patients over the age of twelve whose records suggest they may have poorly controlled asthma. The only exclusion criteria are: people with other significant lung disease; those under specialist care for severe/difficult asthma; those unable to communicate in English or use a mobile phone; and those with significant social/clinical problems.

With the agreement of the patient's general practitioner (GP), potential participants will be invited to a screening assessment at which eligibility will be confirmed, current asthma control assessed using the ACQ,[13] and suitability of their mobile phone for data transmission established. All consenting patients with poorly controlled asthma (defined as ACQ>1.5[19]) will be entered into the trial. Using telephone randomisation (provided by the University of Aberdeen's Health Services Research Unit) – which will conceal allocation until the treatment is assigned – all eligible participants will be randomised to mobile phone or paper-based monitoring using randomised blocks of varying size, and stratified by practice to ensure equal randomisation within each practice.

Intervention group: tele-monitoring

Patients in the intervention group will be issued with a Piko peak flow meter (nSpire Health, Hertford, UK) and the t+ Asthma software (t+ Medical, Abingdon, UK) will be loaded onto their mobile phone (or a loaned phone if their own is unsuitable). The participants will be asked to monitor symptoms, medication usage and peak flow rate twice a day and to submit the readings. The web-record will be available to both the patient and asthma nurse to aid assessment of control during routine reviews, and to the patient's GP in the event of an unscheduled asthma consultation.

Control group

Patients in the control group will be issued with a Piko meter, and asked to keep a paper diary for recording symptoms, medication usage and peak flow readings twice a day.

Clinical care and self-management education in both groups

Clinical care will be provided by the practices' asthma nurse(s) in accordance with the step-wise approach of the BTS/SIGN Guideline.[12] All patients will receive standardised asthma education, including information on asthma, asthma treatment, inhaler technique, monitoring, and when to seek urgent assistance. Patients will be reviewed monthly until control is achieved as judged by the nurse on the basis of clinical monitoring.

Data collection and management

Questionnaires will be administered by the researcher (supervised self-completion) at baseline and at six months post randomisation. Interim questionnaires (at three months) will be administered by post. Use of healthcare resources will be extracted by the researcher from the primary care records at the end of the trial. Records of the patients' daily tele-monitoring submissions will be retrieved electronically at the end of the trial.

Sample size and analyses

Using an estimated standard deviation of change in ACQ score as 0.25,[19] a sample size of 125 per arm would have 90% power with a two sided 5% significance level to detect a difference in mean change in ACQ score of 0.1 or more between groups. A sample size of 29 in each arm will have 80% power with a two sided 5% significance level to detect a mean difference in KASE-AQ (SD 13.3[20]) score of 10 or more. Allowing for 20% attrition we will need to recruit a total of 312 patients.

As a pragmatic trial, an intention-to-treat analysis will be performed for the main analysis; a per protocol analysis will also be undertaken as a sensitivity analysis. Groups will be

described at baseline in terms of socio-demographic factors, asthma history, ACQ, miniAQLQ, KASE-AQ and mPEI scores. Repeated measures analysis of variance will be used to examine trends over time in forced expiratory volume in one second (FEV_1) levels, ACQ, mini AQLQ, KASE-AQ and mPEI scores both within and between groups.

The health economic analyses will assess the cost-effectiveness of the mobile phone monitoring compared to usual care from the perspective of the health service. Resource use estimates will be combined with unit costs obtained from standard sources.[21]

We will also undertake exploratory analysis of peak flow patterns – examining their variability, and correlation with temperature and other atmospheric conditions.

Timescale

The trial has been recruiting patients throughout 2008/2009 and follow-up is for six months. We anticipate reporting results in 2010.

Funding

Asthma UK. HP is supported by a Primary Care Research Career Award from the Chief Scientist's Office of the Scottish Government.

Contributorship

DR and HP are the Principal Investigators, AL is the trial statistician. DP, AS, LT, CP are grantholders. All the authors have contributed to the development of the protocol and have read and approved the final documents.

Conflict of interest declarations

LT is a non-executive director of, and holds shares in, t+ Medical.

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Appendix

The CYMPLA trial

Can Your Mobile Phone Help Your Asthma ?

A mobile phone based structured intervention to achieve asthma control in patients with uncontrolled persistent asthma: a pragmatic randomised controlled trial

Principal investigators	Dr Dermot Ryan
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Funder	Asthma UK

International Standard Randomized Controlled Trial Number: NCT00512837

Contents

1. Introduction

1.1. The burden of disease

Morbidity and mortality from asthma are major problems worldwide.[1] The World Health Organisation estimates that there are 300 million sufferers globally and asthma is thought to be responsible for in excess of a quarter of a million deaths annually.[2] Asthma is the commonest chronic disease of childhood.[2] With rates exceeding 15% of the population, the United Kingdom (UK) has one of the highest prevalence rates in the world.[3]

Data from UK general practice suggests that 5.8% of the population have 'active asthma' (defined as a diagnosis of asthma and a prescription for asthma treatment in the previous 12 months).[4] In 2004/5, there were 4.1 million consultations with general practitioners (GPs) for asthma, over 70,000 hospital admissions and about 1,400 deaths attributed to asthma.[5] The economic cost of providing asthma care was estimated at £2.3bn of which direct NHS costs were £899m.[6]

Despite effective treatments, studies continue to demonstrate that asthma is poorly controlled,[7,8] though marked variation in the control achieved in UK general practices suggests that improvement is possible for the vast majority of patients.[9,10] Psychosocial factors such as denial of illness, low outcome expectations,[11,12] and hectic lifestyles, exacerbated by limited knowledge, poor self-recognition of symptoms and discordant attitudes, influence patients' ability to engage in self-management with resultant poor concordance with monitoring and treatment.[13]

1.2. Self management in asthma

Self management of long-term conditions is underpinned by the concept that with appropriate skills, education and supported by regular professional reviews, a patient can be enabled to self-care effectively on a day to day basis in order to maintain good control.[14] This framework recognises the emotional challenges faced by the patient, including anger, fear and frustration.[14] There is a significant body of evidence which demonstrates that asthma education coupled with self management improves control in terms of reduced hospital admissions, fewer exacerbations of asthma and increased adherence to medication.[15,16] NHS policy reinforces the importance of self management of long term conditions with enhanced support for those at greatest risk.[17-19]

1.3. Self monitoring

A core component of self management is self monitoring. Monitoring in itself is an intervention which may alter behaviour. The theoretical model developed

by Glasziou *et al*. describes the complementary and evolving roles of periodic professional support and on-going patient self-monitoring.[20]

However, despite self-management education, compliance with traditional diary monitoring can be as low as 6%,[21] and results are often fabricated.[22] Electronic recording may improve adherence to self recording of biometric data,[23] with over two-thirds of potential readings recorded over a 72-week study.[24] Interventions involving biofeedback can address these barriers by objectively demonstrating symptom severity and the impact of medication compliance. Internet based schemes to promote self management have proved successful but are less accessible than a mobile phone.[25,26] Early work has demonstrated good compliance and high patient satisfaction with such systems.[24,27]

A solution which encompasses self monitoring coupled with a system which permits instantaneous feedback to the patient should thus permit the patient to feel both involved in, and in control of their asthma.

1.4. The potential of mobile technology

Increasingly pervasive throughout society, mobile phone technology provides a convenient, portable communications medium. In the UK, about 80% of the population own a mobile phone,[28] with estimates rising to 96% in the under 50s.[29] With more than three billion owners globally, mobile phones are now used by about half of the world's population.[30]

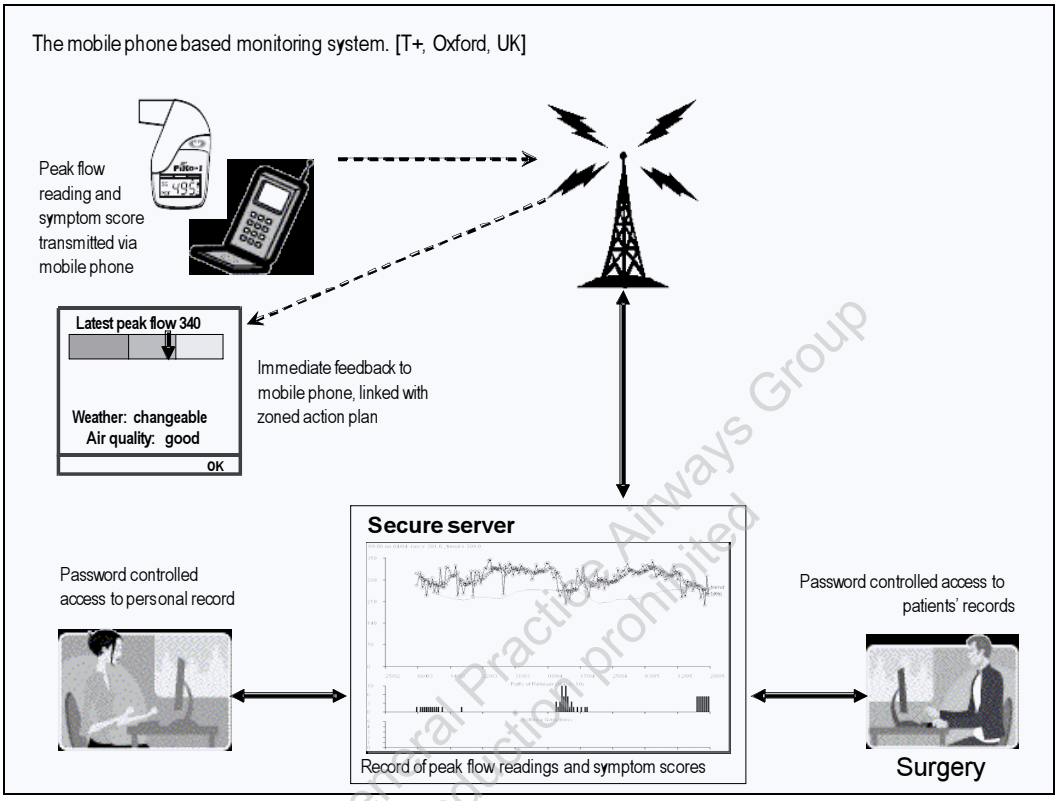
Our recent qualitative study suggests that people with asthma perceive a role for mobile technology in aiding transition from clinician-supported management while control is gained, to effective self-management during maintenance phases.[31] This approach resonates with two key health service policies: the drive for technological solutions to healthcare problems;[32] and the importance of expert patients and self-management of long-term conditions.[17-19,33]

Our randomised controlled trial (RCT) tests the hypothesis that through engaging the patient in self-monitoring with timely biofeedback, mobile phone technology can improve asthma control compared to usual paper-based monitoring.

1.5. Description of the mobile phone-based monitoring system

The t+ Asthma software (t+ Medical, Abingdon, UK) can be loaded onto many web-enabled mobile phones. It permits recording of symptoms, medication usage and lung function. Measurements are made with a Piko meter (a prescribable electronic meter which records both forced expiratory volume (FEV_1) and peak expiratory flow (PEF)). Patients are asked to record peak flow readings twice daily. Data transmitted to a remote server are analysed

and the latest reading returned to the mobile phone, compared with the preceding week's recordings and a prompt for using 'preventer' medication. In addition, the patient and their clinician can access the record via a password-protected website.



2. Hypothesis

Our RCT trial tests the hypothesis that in teenagers and adults with poorly controlled asthma offered treatment according to the British Thoracic Society / Scottish Intercollegiate Guideline Network (BTS-SIGN) asthma guideline,[34] the use of mobile phone-based lung function and symptom monitoring with patient feedback will improve the asthma control achieved and patient self-efficacy at six-months compared to usual paper-based monitoring strategies.

3. Research questions

In teenagers and adults with poorly controlled asthma, offered treatment according to BTS-SIGN Asthma Guideline, does the use of mobile phone-based lung function and symptom monitoring with feedback:

1. Improve asthma control achieved at six months compared to usual paper-based monitoring strategies?

2. Improve self-efficacy at six months compared to usual paper-based monitoring strategies?
3. Improve disease-specific quality of life
4. Engage patients in self-care and improve compliance?
5. Represent a cost-effective use of NHS resources?

4. Outcome measures

4.1. Primary outcome measures

4.1.1. Asthma Control Questionnaire (ACQ)

The primary outcome measure is the change in asthma control between baseline and six months as measured by ACQ (six-question version),[35] The ACQ measures clinical goals of asthma management on a scale: 0 (good control) to 6 (poor control), is responsive to change,[35] and has an intra-individual minimum important difference (MID) of 0.5.[36] Postal administration of the six-question version gives comparable results to supervised completion.[37,38] The six question version of the ACQ will be used in the primary analysis.

4.1.2. Knowledge, Attitude and Self-efficacy Asthma Questionnaire (KASE-AQ)

Self-efficacy will be measured as the mean difference in KASE-AQ between Intervention and control group at six months. The KASE-AQ has three independently-scored subscales of 20 items.[39] The 'self-efficacy' scale which measures perceived ability to control asthma, and the 'attitude to asthma' scales: 20 (minimum score) to 100, are responsive to change.[40] We omitted the knowledge subscale as it was outdated, and heavily oriented to United States practice.

4.2. Secondary outcome measures

4.2.1. Morbidity measures

- Mean difference in ACQ score at 3 and 6 months.[35,36]
- The proportion of patients with an ACQ<0.75 at three and six months.[41]
- Mean difference in the mini Asthma Quality of Life Questionnaire (mini-AQLQ) which measures the physical/emotional impact of asthma on a scale: 1 (greatest impairment) to 7, is responsive to change,[42] with a MID of 0.5,[36] and is validated for postal administration.[38]
- Adverse occurrences (including unscheduled asthma consultations, hospital admissions) will be obtained from the practice records.

4.2.2. Self-efficacy/enablement

- Mean difference in the modified Patient Enablement Instrument (mPEI). The mPEI is a six item measure which reflects enablement in asthma on a scale of 0 to 12.[43] A difference of 0.8 has been regarded as significant when used to assess the impact of a single consultation,[43] and an asthma self-management programme.[44]
- Mean difference in the Aberdeen Asthma Questionnaire (AAQ), a disease specific instrument which measures enablement. The AAQ is a 13 item measure, scoring 0-6 for each item.[45] It seeks to capture an individual with asthma's capacity for self-efficacy, participation in their own health care, enablement or empowerment. It was developed through extensive consultation with people with asthma and through statistical data reduction techniques.

4.2.3. Engagement with process:

- Compliance with monitoring will be assessed using the electronic record of peak flow readings on the Piko meter.
- Proportion of patients defaulting from clinical follow-up appointments in each group will be quantified.

4.2.4. Cost-effectiveness

- Use of healthcare resources during the 6-month trial will be extracted from the patients' primary care records.

5. Methods

5.1. Trial design

A six month single-blinded randomised controlled trial. A CONSORT diagram is included in the appendices: section 15.1

5.2. Setting

The RCT will be based in UK general practices

5.3. Participants

5.3.1. Inclusion criteria

Patients over the age of twelve years who are registered with participating practices and who have poorly controlled asthma (defined as an ACQ score >1.5 [41]) who have, or are willing to borrow, a compatible mobile phone hand set and a contract with a compatible network.

5.3.2. Exclusion criteria

Patients with other significant lung disease, under specialist care for severe/difficult asthma, unable to communicate in English or use a mobile phone and at the request of the GP for other significant social/clinical problems.

5.4. Sample size

5.1.1. ACQ

Using an estimated standard deviation of change in ACQ score as 0.25,[46] a sample size of 125 per arm will have 90% power with a two sided 5% significance level to detect a difference in mean change in ACQ score of 0.1 or more between groups. In the absence of published MID for between-group differences in ACQ score we have powered the study for a relatively small difference of 0.1 (though clearly we will have sufficient power to also detect larger differences).

5.1.2. KASE-AQ

Using a standard deviation of 13.3,[40] a sample size of 29 in each arm will have 80% power with a two sided 5% significance level to detect a mean difference in KASE-AQ (self-efficacy scale) score of 10 or more between groups.

5.1.3. Recruitment estimate

Allowing for 20% attrition we will need to recruit 312 patients to ensure that 125 complete in each arm. If a third of the patients approached agree to participate,[47] we will need to invite 930 patients. The prevalence of 'active asthma' in England is 5.8%,[4] of whom about 45% will be poorly controlled.[7-9,11] If only half have web-enabled mobile phones, to identify 930 potentially eligible patients we will need to recruit practices with a total list size of 72,000 patients (about 6-8 practices).

5.5. Recruitment

5.5.1. Practice recruitment

We will recruit practices initially from the Norfolk, Great Yarmouth and Waveney PCT area, extending to other areas as necessary to achieve our recruitment target. Eligible practices will have an asthma-trained nurse able to commit to the additional clinical workload.

5.5.2. Participant identification

Practices computer database will be interrogated to identify patients over the age of twelve who have been prescribed a bronchodilator within the last year.

Where possible the search will be refined to identify patients with poorly controlled asthma (e.g. record of an exacerbation, recorded unscheduled appointments, presence of symptoms). Potential eligibility will be confirmed from the computer records and by the GP who will screen the list and exclude patients with other significant lung disease, under specialist care for severe/difficult asthma, unable to communicate in English or use a mobile phone and for other significant social/clinical problems. The practice will invite all potentially eligible patients by post to participate. Failure to respond to the first invitation will generate one more invitation.

5.5.3. Pre screening

Patients expressing an interest in participating will be pre-screened by telephone to determine whether they fulfil the criterion of poorly controlled asthma (ACQ score >1.5[41]) and that they have a contract with a compatible mobile phone network, and a compatible hand set. Those whose hand set is incompatible but who subscribe to a compatible network will be offered the opportunity of borrowing a hand set for the duration of the trial.

5.6. Confirmation of eligibility and consent

Potential participants will attend a screening assessment (normally in their own GP practice) at which eligibility will be confirmed, their current asthma control assessed using the ACQ,[35,41] and suitability of their mobile phone established. The researcher will provide further information about the trial and obtain consent. All consenting patients with poorly controlled asthma (defined as ACQ>1.5 [41]) will be entered in the trial.

5.7. Baseline measurements

Eligible, consenting patients will have a baseline assessment performed by the researcher. This will comprise asthma history, current smoking status, presence of co-morbidity, forced expiratory volume in one second (FEV_1) and baseline questionnaires (ACQ,[35] KASE-AQ,[39] miniAQLQ,[42] mPEI,[43] AAQ,[45] will be administered. We will use the Piko meter [nSpire Health,Hertford UK] to record FEV_1 as the correlation between Piko and spirometry FEV_1 is excellent (r=0.98).[48,49] The use of the Piko meter to record peak flows will be demonstrated and a meter given to the patient for them to use throughout the trial.

5.8. Randomisation

The University of Aberdeen's Health Services Research Unit (HSRU) will provide a 24hr telephone centralised randomisation service. Patients will be allocated, using random blocks of two or four and stratified by practice, to mobile phone or paper-based monitoring. The practice nurse will phone the

randomisation service (in order to ensure that the allocation is concealed from the researcher) and inform the patient of the allocation. All allocated patients will be included in the intention-to-treat analysis

5.9. Protection against bias

Baseline data collection will take place prior to randomisation and allocation which will be carried out remotely by the Aberdeen's HSRU to ensure adequate concealment. It is not possible to blind clinicians or patients to allocation thus potentially introducing bias in subsequent care. However, all trial data collection will be undertaken by the researcher, blinded to allocation. Patients will be requested not to reveal their allocation, although we recognise that inadvertent references by the patients or in their primary care record may reveal allocation. The use of objective outcomes (validated questionnaires) will also reduce the possibility of bias.

5.10. Trial interventions

5.10.1. Intervention group: Mobile phone based monitoring

Patients in the intervention group will be issued with a Piko meter and the t+ Asthma software will be loaded onto their (or a loaned) mobile phone. Contact details will be forwarded to t+ Asthma who will contact the patient at a time convenient to them, download the software to their phone, test its functionality, give details of web access, and follow up with a technical support call after one week. The participant will be asked to monitor symptoms, medication usage and peak flow rate twice a day and submit the readings. The web-record will be available to patient and asthma nurse to aid assessment of control during routine reviews, and to the patients' GP in the event of an unscheduled asthma consultation.

5.10.2. Control group: paper-based monitoring

Patients in the control group will be issued with a Piko meter, and asked to keep a paper diary, recording symptoms, medication usage and peak flow readings twice a day.

5.10.3. Clinical care and self-management education in both groups

Structured care will be provided by the practices' asthma nurse(s), trained in all aspects of the trial.

Clinical care in both groups will be in accordance with the step-wise approach of the BTS-SIGN Guideline.[34] Patients will be reviewed monthly until control is achieved as judged by the nurse on the basis of clinical monitoring.

All patients will receive a one-to-one standardised asthma education session, including information on asthma, asthma treatment, inhaler technique, monitoring and when to seek urgent assistance.

5.11. Duration of intervention

The intervention will run for six months.

5.12. Data collection and management

The table in the Appendix: section 15.2 summarises the trial procedure.

- Questionnaires will be administered by the researcher (supervised self-completion) at baseline and at 6 months. Three month questionnaires will be administered by post. In order to maximise response at 6 months, participants who do not attend for the final data collection will be sent postal versions of the questionnaires.

- Use of healthcare resources for the health economic analysis (including, in addition to data about admissions, practice and out-of-hours consultations for asthma, prescriptions for respiratory drugs) will be extracted by the researcher from the primary care records at the end of the trial.

- Data from records and other trial data will be entered on the trial database from the paper data collection sheets, with 10% checked for accuracy. If we detect systematic errors we will re-enter all the data.

- Adverse events will be recorded the patients' primary care records at the end of the trial

- The records of the patients' daily tele-monitoring submissions will be retrieved electronically at the end of the trial.

5.13. Statistical analysis

As a pragmatic trial, an intention-to-treat analysis will be performed for the main analysis; a per protocol analysis will also be undertaken as a sensitivity analyses. Non-responding subjects at the three month or final assessment will be assumed not to have improved their control and the previous ACQ carried forward. There will be no interim analysis.

Groups will be described at baseline in terms of socio-demographic factors, asthma history, ACQ, miniAQLQ, KASE-AQ and mPEI scores. Repeated measures analysis of variance will be used to examine trends over time in FEV_1 levels, ACQ, miniAQLQ, KASE-AQ and mPEI scores both within and between groups. Pre-specified between-group changes from baseline in

patient outcome measures will be compared using appropriate univariate and multivariate techniques (t-test, Mann-Whitney test, analysis of covariance etc). Since multiple practices are involved, multilevel modelling will be used to examine each of the primary and secondary outcomes before and after adjustment for potential confounders such as age group, sex and other socio-demographic factors.

5.13.1. Additional analyses

We will undertake exploratory analysis of peak flow patterns, correlated with temperature and other atmospheric conditions.[50] To examine if environmental factors have a quantifiable and predictable effect on the asthma of the patients, irritants will be considered which have been identified previously as likely to cause asthma exacerbations. These irritants can be grouped into three categories: weather, pollutant, and pollen. Each of these will be examined as a possible explanatory variable for the global dataset, and then for each individual patient.

We will examine variability and long term correlations in the data for differences between individuals and groups as these have been proposed as measures of control in one other study.[51]

5.13.2. Health economic analyses

The health economic analyses will assess the cost-effectiveness of the mobile phone monitoring compared to usual care from the perspective of the NHS. Health service (GP/nurse consultations, telephone consultations, home visits, accident and emergency attendances, out-patient consultations, hospitalisations) and drug use over the trial period will be abstracted from practice records. The costs of the t+ Asthma monitoring service, including set-up costs, will be estimated. Resource use estimates will be combined with unit costs obtained from standard sources.[52] The results of the economic evaluation will be presented as an incremental cost-effectiveness ratio (cost-utility analysis). The evaluation will include both deterministic and probabilistic sensitivity analysis.

6. Exit Strategy

Core components of the t+ Asthma system used in this trial will continue to be available after the end of the trial to all participants (i.e. both patients in the intervention and the control group) who have a compatible mobile phone and who are registered with a compatible network. The automated messages and web-records will continue to be available to both the patient and their clinicians, but the t+ Asthma nurse-led monitoring service will no longer be provided.

7. Publication Strategy

The findings of this trial will be published in peer-reviewed journals, presented as abstracts at national and international conferences and disseminated via the co-applicants contacts with professional and policy bodies.

8. Risk Management Strategy

The main risks associated with this study are data security within the telemetry system, contamination between the intervention and control groups, and inappropriate response to an emergency.

8.1. Data security within the telemetry system

Data captured by the mobile phone will be held on a secure data base by t+ Asthma in accordance with their normal practice which meets BS7799 standards (ISO 27001) and is fully compliant with the Data Protection Act 1998. This may be accessed by the patient using normal internet, at any time using an individual personal identification number (PIN). The data is time stamped and tamperproof. The researchers will have access to these data for the duration of the trial.

The storage of data and its access to the participant and to their nominated healthcare professionals and research team will be provided in a secure manner.

All person identifiable data will be encrypted. Access to the data will be by personal high-level user-name and password. Access will be limited to the clinicians managing the patient and restricted members of the research team (with the patients' permission). A permanent audit trail of access will be kept.

Research data will be stored on secure, password-protected university computers with access limited to the named research team.

8.2. Contamination between the intervention and control groups

The decision to randomise at the patient rather than the practice or service level avoids the methodological issues associated with cluster randomisation, but raises the possibility of contamination (i.e. the research also affecting the way patients in the control group are treated). This has been considered carefully and two potential sources of contamination identified.

Patients in both groups will receive self-management education including self monitoring and regular review until asthma control is deemed to have been achieved. Whilst this is recommended by guidelines as good care,[34] it probably represents a higher standard than is usual.

Asthma nurses may be influenced by the experience of working with patients in the intervention group, increasing their familiarity with using specific morbidity questions and heightening their awareness of poor control. However, we anticipate that a key impact of the intervention will be on patients' engagement with their care as a result of the tele-monitoring rather than changing professional management.

8.3. Inappropriate response to a deterioration or emergency

The intervention is monitoring for the early symptoms of an exacerbation of asthma and despite the provision of a self management plan with specific instructions as to when they should seek urgent medical care, there is a risk that a patient may fail to respond to deteriorating symptoms that arise. Patients will be advised that if they are concerned about their health, they should seek help in the usual way.

For those patients in the intervention group, an 'alert' triggered by a deterioration in symptoms of peak flow, will be followed up by a phone call from a t+ Asthma nurse to determine as far as possible, what triggered the fall in lung function, whether the patient has recovered and what steps did the participant take, what if any lessons have been learnt. If the t+ Asthma nurse recognises that the patients plan has not been followed or understood then the participant is instructed to contact their asthma nurse for clarification of the plan. A log of these interventions will be kept.

9. Project Team and Task Allocation

- Dr Dermot Ryan is the Principal Investigator and will lead the research team.
- Dr Hilary Pinnock is co-principal investigator.
- Professor Amanda Lee, University of Aberdeen will be responsible for writing the data analysis plan and for supervising a member of the Medical Statistics Team to perform the statistical analysis.
- Experienced researcher(s) appointed to the trial will undertake the day to day running of the trial, including recruitment of practices and participants, undertaking data collection and management and reporting.

10. Project Management and Quality Assurance

- The project team, consisting of grantholders and research staff, will meet regularly.
- We will set up an independent trial steering committee (ITSC), for the CYMPLA trial which will comprise an independent chairperson (Dr Andrew Wilson, University of East Anglia), the principal investigators and the

senior researcher. Meetings of the ITSC will be held prior to the start of the trial and then six monthly or more frequently if required. The ITSC will monitor and supervise the progress of the programme of trials towards its overall objectives; review at regular intervals relevant information from other sources (eg, other related trials). In particular the ITSC will review safety. Adverse events will be analysed on regular basis and where necessary the ITSC will be empowered to terminate the study should there be any safety concerns or if recruitment falls below a level expected to deliver useful results. If examination of unblinded data is required to make a decision about the continuation of the study for any reason then an experienced independent trial statistician will be appointed to review the data and advise the committee.

- The study will be carried out to Good Clinical Practice standards and managed within the Research Governance Framework. Ethical approval will be sought via the National Research Ethics Service.
- Research governance will be managed by the local Research Governance Committees as appropriate.
- The trial will be sponsored by the University of Aberdeen.
- Indemnity will be provided by the NHS indemnity scheme, and the University of Aberdeen.

11. Timescale

Start of trial: October 2007

Month	Activity
Pre-start date	Ethics approval, research governance approval, Staff recruitment, honorary contracts.
1-3	Practice recruitment, Practice nurse training Baseline computer searches, identification of patients.
3-9	Patient recruitment, baseline assessment Randomisation Teaching monitoring; initial clinical consultation
10-15	Clinical care with monitoring according to allocation Assessment visits at 3-months and 6-months
16–21	Data analysis Preparation of reports and publications

12. Reporting

Six monthly progress reports and a final report will be provided to the funder in the format required. Reports will also be provided as required for the programme management group, steering group and data monitoring committee.

13. Finance

13.1. Project grant

The trial is funded by a research grant from Asthma UK. The funding is managed by the University of Aberdeen.

13.2. NHS service support costs

NHS service support costs will be used to recompense GP practices for time involved in the trial, including approving mailshots to potential participants and arranging collection of data from records.

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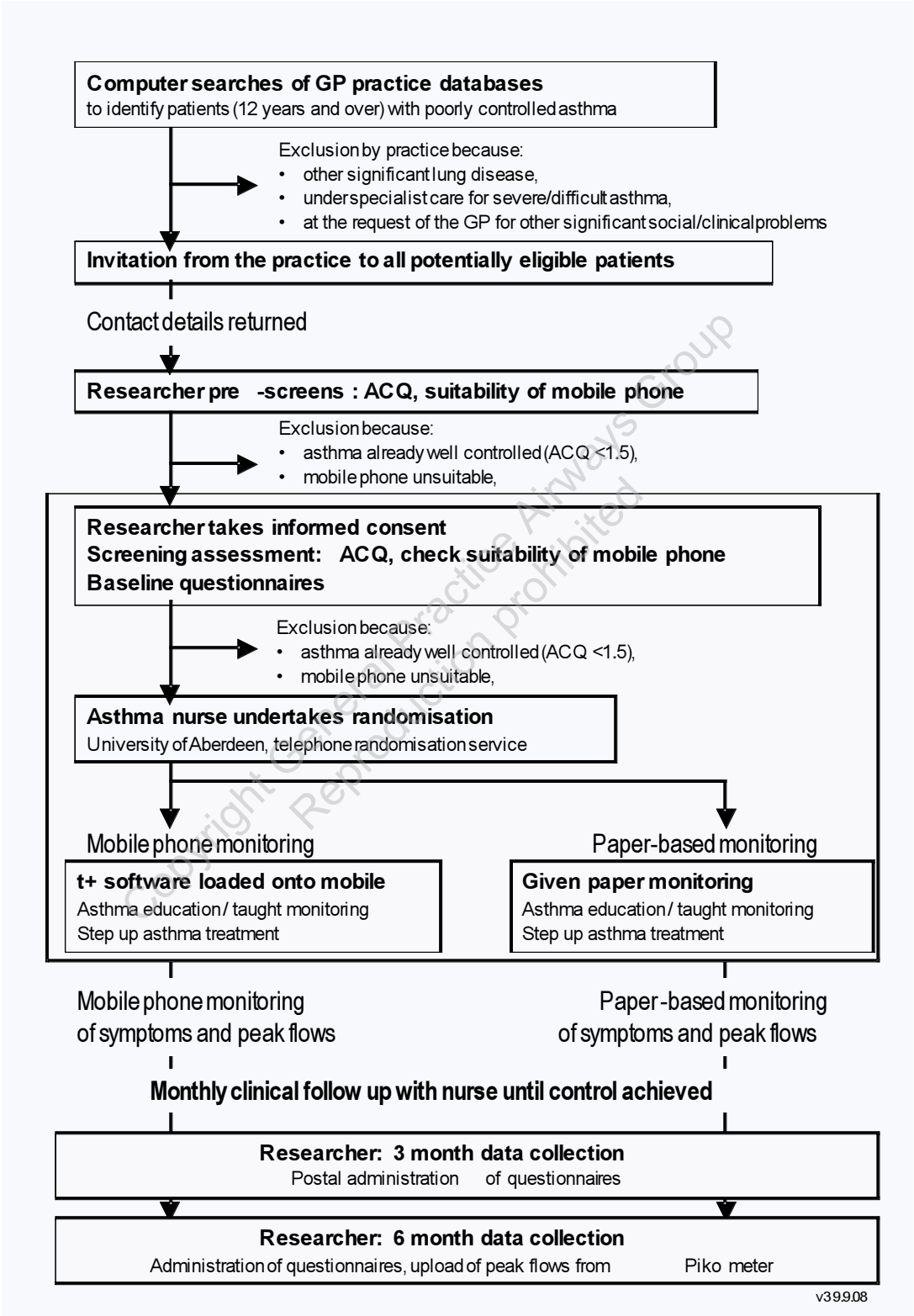
15. Appendices

15.1. CONSORT diagram



15.2. Summary of trial procedures

Visit	Professional	Function	Procedure
		Identify potential patients Confirm potential eligibility Invitation	MAAT interrogation of practice database,[3] Check for inclusion/exclusion criteria Postal invitation to all potential participants
Visit 1 Baseline assessment	Researcher	Confirm poor control Baseline assessment	ACQ >1.5,[41] Demographics, asthma history miniAQLQ,[42] KASE-AQ,[39] mPEI,[43] AAQ,[45] FEV_1 .
Randomisation	Practice nurse		Telephone randomisation
Clinical care	Practice nurse	Teach monitoring according to allocation Asthma education Clinical management	Intervention group: mobile-phone based monitoring with immediate feedback and access to web-based records. Control: paper-based diaries Standardised education According to BTS-SIGN steps,[34]
Monthly clinical follow-up until controlled	Practice nurse	Assess control Clinical management	Clinical assessment and monitoring data. Treatment according to BTS-SIGN steps,[34]
Postal 3-month data collection	Postal administration	3-month assessment	ACQ,[35] miniAQLQ,[42] KASE-AQ,[39] mPEI,[43] AAQ,[45]
Visit 3 6-month data collection	Researcher	Final assessment	ACQ,[35] miniAQLQ,[42] KASE-AQ,[39] mPEI,[43] AAQ,[45] FEV_1 Upload readings from Piko meter
	Researcher	Data from records	Medication use Unscheduled asthma consultations Adverse events