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PROTOCOL SUMMARY

The impact of a telemetric chronic obstructive pulmonary disease monitoring service: randomised controlled trial with economic evaluation and nested qualitative study

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on behalf of the TELESCOT programme group

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Keywords telemetry, COPD, RCT, economic evaluation, qualitative study

The full trial protocol, together with Appendices, is available online at www.thepcrj.org. See linked editorial by McLean and Sheikh on pg 125

Introduction

Admissions for chronic obstructive pulmonary disease (COPD) are increasing, at considerable cost to healthcare systems, with many patients experiencing multiple admissions.[1] Such exacerbations reduce quality of life and drive disease progression.[2,3] There is good evidence that early identification of COPD exacerbations reduces the risk of hospital admission, improves quality of life and may slow disease progression.[4]

Telemetric-supported self-monitoring of COPD has the potential to engage the patient in their care, and enables timely response to deterioration. In addition, tele-monitoring may support 'Hospital-at-Home' and 'Early Supported Discharge' services, which are known to reduce admissions and bed-days in selected patients.[5] Pilot work has shown that tele-monitoring is feasible and acceptable to patients and professionals.[6,7]

This approach resonates with three key health service policies: the shift of care into the community;[8,9] the drive for technological solutions to healthcare problems;[10] and the importance of expert patients and self-management of long-term conditions.[11,12] While evidence can be gleaned both from international research into telemetric solutions for chronic disease management and UK pilot studies,[6,13,14] there remains a need for rigorous, multi-faceted evaluation of such interventions in UK NHS settings.

Our randomised controlled trial, incorporating quantitative and qualitative evaluations, will investigate the clinical and cost effectiveness and social and service impact of introducing telemetrically supported self-monitoring of COPD in primary care in Scotland.

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Research questions

1. In people with moderate to severe COPD, does tele-supported self-monitoring compared to usual care:

- reduce the time to re-admission?
- reduce the number and length of hospital admissions and exacerbations?
- improve disease-specific quality of life?
- reduce anxiety and depression?
- improve patient knowledge and self-efficacy?
- engage patients in self-care and improve compliance?
- represent a cost-effective use of NHS resources?

2. What are the experiences and opinions of people with COPD about this service (including impact on behaviour, mood, positive and negative experiences and change in relationship with their healthcare provider) and what are healthcare providers' experiences and opinions of this service?

Outcome measures

The primary outcome measure is the time until first hospital admission with a primary diagnosis of an exacerbation of COPD up to one year post-randomisation.

Other outcomes of interest include the number and duration of emergency admissions, the number of exacerbations and deaths from COPD, health-related quality of life using the St George's Respiratory Questionnaire,[15,16] Hospital Anxiety and Depression Scale,[17] Self-Efficacy for Managing Chronic Disease 6-item scale,[18] Lung Information Needs Questionnaire,[19] Medication Adherence Report Scale,[20] and use of healthcare resources, and cost-effectiveness measured as cost per Quality Adjusted Life Year (QALY).

Methods

Recruitment and randomisation

We will use hospital and community-based specialist respiratory services' records to identify patients registered with Lothian general practices who have been admitted with a primary diagnosis of an exacerbation of COPD in the previous six months. The only exclusion criteria are other respiratory conditions, or inability to use the technology or participate in the trial for over-riding clinical or social reasons.

With general practitioner (GP) agreement, potential participants will be invited to an assessment with a researcher to confirm eligibility, obtain consent and administer baseline questionnaires. Using telephone randomisation (undertaken by the Edinburgh Clinical Trials Unit) – which will conceal allocation until the treatment is assigned – all eligible participants will be randomised using blocks of varying size, stratified by the community service providing the clinical care.

Initial optimisation of care and self-management education

All patients will be seen by a COPD-trained healthcare professional who will optimise management in line with national guidelines,[21] and deliver COPD education specifically covering early recognition and self-management of exacerbations. Patients will be given a written management plan, and an emergency supply of antibiotics and steroids will be requested from their GP.

Intervention group: tele-monitoring

Patients in the intervention group will be given a modified "tablet" touch screen computer with video capability linked to a secure Internet connection. They will use the system to record daily symptoms (based on validated diary cards[22]) and use of medication, and monitor peak flow and oxygen saturation. The supervising clinical team will review the on-line data on a daily basis and contact patients if they have not sent information or if questionnaire responses and physiological parameters fall outside the expected range. The system incorporates a video link to enable remote consultation.

Control group

Patients allocated to the control group will receive the same clinical support, including a written management plan, the only difference being that they will access services via standard routes of communication, not the tele-monitoring system.

Data collection and management

Time to an admission with a primary diagnosis of COPD, and details of all admissions, will be extracted from the patients' clinical records at the end of the trial. Questionnaires will be administered at 12 months, and use of healthcare resources obtained by questionnaires posted to the patient quarterly. All trial data collection will be undertaken by a researcher blinded to allocation in order to reduce bias.

Sample size and quantitative analyses

To detect a difference in the primary outcome from a median of 200 days to readmission in the control group to 300 days in the intervention group,[13] (80% power, significance 5%) we will need 125 patients to complete in each arm (increased to 150 to allow for attrition).[23,24]

Using an intention-to-treat analysis, we will present survival data using Kaplan-Meier curves and, if appropriate, use Cox proportional hazards models, adjusting for potentially important confounders. The economic evaluation will estimate the incremental cost per QALY, including deterministic and probabilistic sensitivity analyses, from the perspective of the NHS.

Qualitative study

A maximum variation sample of up to 20 participants from the intervention group will be recruited for semi-structured interviews plus a further 10-12 people for two focus groups which will explore participants' views on the tele-monitoring system. Up to 20 professionals involved in delivering the service will be interviewed about their perceptions of the benefits (or otherwise) of the intervention, and experiences of

implementing and maintaining the service.

Analysis will use the Framework method;[25] data will be analysed from the theoretical perspective of relevant theory,[26,27] and reviewed by the wider research team to aid interpretation.

Timescale

The trial will be recruiting patients throughout 2009 and follow-up is for one year. We anticipate reporting results in 2011.

Funding

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The Chief Scientist Office of the Scottish Government Health Directorates funds the Health Economics Research Unit, Aberdeen.

The tele-monitoring equipment was provided by NHS Lothian and the Scottish Government.

Contributorship

BM is the TELESCOT programme lead, HP is the Principal Investigator for the COPD trial, JH led the development of the qualitative study, SL is the trial statistician and MV provided health economic advice. AS, WM, CP are members of the COPD trial group. All the authors have contributed to the development of the protocol and have read and approved the final documents.

Conflict of interest

None known.

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TELESCOT

TELEmetric supported Self-monitoring of long-term COndiTions

Chronic Obstructive Pulmonary Disease: The impact of a telemetric COPD monitoring service

Randomised controlled trial with nested qualitative study

Tele-health programme

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COPD trial

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Contents

1. Introduction

1.1. Self-monitoring in long-term conditions

Long-term conditions are a major healthcare challenge.[1] As the population ages more people are living with long-term conditions rendering the current, clinician-centred models of management unsustainable in the longer-tem.[2] NHS policy increasingly encourages people to self-manage their condition with additional professional support for those at greatest risk.[3] Systematic reviews indicate that engaging patients in self-monitoring and management can improve clinical outcomes in asthma,[4] but the evidence in COPD is mixed.[5] There is, however, good evidence that early identification of exacerbations in COPD reduces hospital admission and may slow disease progression.[6]

Monitoring is, in itself, an intervention which alters 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.[7] This approach resonates with two key health service policies: the drive for technological solutions to healthcare problems;[8] and the importance of expert patients and self-management of long-term conditions.[9,10] While some evidence can be gleaned from international research into telemetric solutions for chronic disease management and the encouraging results from UK pilot studies,[11-15] there remains a pressing need to evaluate rigorously such interventions in a UK NHS setting.

Effective interventions need to reflect patients' needs, enable professionals to adapt their working practices and address organisational infrastructure.[16] Telemetric systems enabling patient self-monitoring and relay of information to clinicians can potentially improve integration between self-management and professional support, as well as facilitate intensive monitoring and aggressive intervention when needed.

The service model to be tested is shown in Appendix 1. The systems can work on a range of technology platforms and with multiple measuring devices, facilitating seamless care for patients with several co-morbidities. The tele-health research programme focuses on four disease areas which account for much long-term morbidity in the population, a high proportion of consultations in primary care and are major causes of hospitalisation, namely: COPD; hypertension; blood pressure reduction after stroke/transient ischaemic attack; diabetes and obesity.

1.2. The tele-health programme

Our programme of work sits within the MRC framework for the development and evaluation of complex interventions.[17,18] Building on existing literature,[14,15,19,20] and in an iterative process using insights from completed and on-going exploratory and pilot work,[21] we have designed Phase III randomised controlled trials.[22] These will evaluate how telemetry aided, supervised self-monitoring impacts on the management of long-term conditions in four different contexts (largely asymptomatic conditions; symptomatic, potentially unstable and progressive conditions; an older, more disabled group with challenging management targets; co-morbid conditions). Each will incorporate qualitative and quantitative process evaluations, which are increasingly recognised as being critical to the subsequent implementation.[23,24]

For each condition:

- A randomised controlled trial which aims to evaluate the clinical effectiveness of telemetrically supported self-monitoring
- A qualitative study, which aims to improve understanding of how these interventions impact on patients, carers and healthcare professionals, and explore the facilitative factors and barriers to implementation in patients and practices.
- Health economic analysis from the perspective of both the NHS and the patient, which will provide the evidence on cost-effectiveness needed to make decisions on the roll out of this model of service.

1.3. The COPD trial

Predicted to become a leading cause of morbidity and mortality by 2020,[25] COPD is already the third commonest long-term condition in Scotland,[1] with a prevalence of 1.8%,[26] nearly 30% greater than in England,[27] reflecting the known association between deprivation and smoking.[28,29] With increasing life expectancy, the number of COPD suffers in Scotland is projected to increase by 33% over the next two decades to 120,000.[1] There is evidence that the extensive needs of people with severe COPD are not adequately being met, with limited evidence of a strategic approach to provision of clinical and social care within the community,[1] justifying Audit Scotland's recent focus on the care of people with COPD.

Despite the policy to shift the balance of care into the community,[30] inpatient and day cases for COPD in Scotland have increased by 25% between 1996/7 and 2005/6 considerably exceeding the 3% increase for all illnesses.[1] Although the average length of stay for patients with COPD fell from 8.4 to 6.1 days over the same period, readmissions are increasing.[1] In 2003/04, a total of 10,214 COPD patients were admitted to hospital in Scotland, of whom 19% were admitted twice during the year and 16% were admitted three or more times.[1] This compares to the UK average of 34% readmission within 3 months,[31] and readmission rates of 50% over a year in patients admitted with respiratory failure.[32] Such exacerbations reduce quality of life[33] and drive disease progression.[34]

The direct cost of COPD to the NHS in Scotland was estimated at just over £98.5 million in 2004/05,[1] but this substantially underestimates the full socio-economic impact as both patients and their carers lose time from work.

Patient recognition of exacerbation symptoms and prompt treatment has been shown to improve exacerbation recovery, reduce risk of hospitalisation, and is associated with improved health-related quality of life.[6] However, current strategies for providing self-management education are inconclusive, with some evidence that written action plans can increase recognition (mean difference for recognition of a severe exacerbation was 2.50; 95%CI 1.04 to 3.96) and treatment (mean difference for self-action in severe exacerbations was 1.50; 95%CI 0.62 to 2.38, positive effect on the initiation of antibiotics (odds ratio (OR) 10.16; 95%CI 2.02 to 51.09) and/or oral steroids (OR 6.58; 95%CI 1.29 to 33.62), but no evidence of significant effects on healthcare utilisation, health-related quality of life, lung function, functional capacity, symptom scores, mortality, anxiety, or depression.[35] The Cochrane review of more extensive self-management programmes, however, showed a significant reduction in the probability of at least one hospital admission (OR 0.64; 95%CI 0.47 to 0.89). The Number Needed to Treat for patients with a 51% risk of exacerbation is 10 (95%CI 6 to 35) and 24 (95%CI 16 to 80) for patients with a 13% risk of exacerbation).[5]

Telemetric-supported self-monitoring of COPD based on symptom diary, spirometry, and pulse oximetry monitored by a call-centre linked to clinicians has the potential to engage the patient more fully in their care, and support timely response to deterioration. In addition, tele-monitoring may effectively support 'Hospital-at-Home' and 'Early Supported Discharge' services,[14] known to reduce admissions and bed-days in selected patients.[36]

Our hypothesis is supported by international pilot studies using similar technology which have shown between 20-36% fewer admissions,[15,19] and a 55% reduction in bed days.[15] A proportion of nursing visits may be replaced by telephone consultations informed by tele-monitoring further reducing costs.[37,38] Tele-monitoring has been shown to be feasible and acceptable to patients and professionals.[19,20]

In the trial using a tele-monitoring protocol similar to ours, at the 12 month follow-up the intervention group showed a lower hospitalisation rate (mean 1.5 admissions/year (SD 2.6) versus 2.1 admissions/year (SD 3.1) p=0.03. Hazard ratio (adjusted Cox analysis) was 0.55 (95% CI 0.35-0.88; p=0.01)) and a higher percentage of patients without re-admissions (49% versus 31%, p=0.03) than usual without differences in mortality (19% versus 16%, p=0.67).[14] This trial, however, randomised 155 patients in two centres which working within different healthcare services (dedicated specialist nurse-led team or individual GP-led care) and although both services showed benefit, there was a difference in the magnitude of the effect (Nurse-led service: hazard ratio 0.52 (95% CI 0.28-0.95); p=0.04 and GP-led service hazard ratio 0.35 (95% CI 0.15-0.80); p=0.01) though numbers in the GP-led service were small (n=42).

1.4. Preparatory work

1.4.1. Phases 0-II: theoretical, exploratory and pilot work

Key issues emerging from the literature and our previous work which have informed the development of our randomised trial include the:

- importance of an increase in symptoms as a marker of an impending exacerbation.[39]
- poor outcomes following hospital admission with exacerbations.[40,41]
- potential benefit of early intervention with antibiotics and/or oral steroids.[6]
- need to engage patients in the process of guided self-management.[7,42]

1.4.2. Phase II

Our on-going pilot work (funded by Intel and Tunstall) in 50 patients with COPD is using qualitative methods to explore important barriers/facilitators to implementation, contextual influences on the intervention and patient and provider experience, whilst quantitative methods will provide estimates of impact on clinical variables and utilisation (and cost) of health services. Of 28 patients who received the technology, 25 are still using the system after 6 months, an 11% attrition rate. 2 died and 1 returned the machine because of frequent technical problems. The results of this exploratory work are directly informing the development of our randomised control trial. Piloting the algorithms for the call centre responses has led to reconsideration of the thresholds for alerts.

2. Aims

To investigate the clinical effectiveness, and social and service impact of introducing telemetry-aided, supervised, self-monitoring for COPD in primary care.

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3. Research Questions

3.1. Randomised controlled trial

In people with moderate to severe COPD, does tele-supported self-monitoring compared to usual care:

1. Reduce the time to re-admission, and the number and length of hospital admissions and exacerbations?
2. Improve disease-specific quality of life
3. Reduce anxiety and depression?
4. Improve patient knowledge and self-efficacy?
5. Engage patients in self-care and improve compliance?
6. Represent a cost-effective use of NHS resources?

3.2. Qualitative study

1. What are people's with COPD experiences and opinions of this service including impact on behaviour, mood, positive and negative experiences and change in relationship with their healthcare provider?
2. What are healthcare providers' experiences and opinions of this service?

4. Outcome Measures

4.1. Primary outcome measure

∞ The time until first hospital admission with a primary diagnosis of an exacerbation of COPD up to one calendar year post-randomisation

4.1.1. Definitions:

An exacerbation is a sustained worsening of the patient's symptoms from his or her usual stable state that is beyond normal day-to-day variations, and is acute in onset. Commonly reported symptoms are worsening breathlessness, cough, increased sputum production and change in sputum colour. The change in these symptoms often necessitates a change in medication.[43]

An exacerbation is defined as being the 'primary diagnosis' if the presenting symptoms are consistent with, and the patient is treated for an acute exacerbation of COPD, and if no other disease was treated as a priority. This will be assessed by a trained research nurse from the GP records.

4.2. Secondary outcome measures

4.2.1. Exacerbations and admissions

∞ The time until first hospital admission with a primary diagnosis of an exacerbation of COPD or all-cause deaths up to calendar one year.
∞ The difference in mean number of bed-days for emergency admissions with a primary diagnosis of COPD during one calendar year.
∞ The number of hospital admissions with a primary diagnosis of COPD during one calendar year.
∞ The number and duration of admissions in which COPD is listed in the discharge letter as a factor in the admission (ie not necessarily the primary diagnosis) during one calendar year.

- The number of exacerbations (defined as a sustained worsening of the patient's symptoms necessitating a change in medication) during one calendar year.[44]
- Proportion of deaths at one year. Cause of death will be taken from the primary and/or secondary care clinical records

4.2.2. Quality of life,

- St George's Respiratory Questionnaire (SGRQ) at one year.[45-47] The SGRQ is a validated and widely used instrument which measures health impairment (symptoms, activities and impacts) in patients with COPD on a scale: 100 (greatest impairment) to 0, is responsive to change,[49,46] with a minimum important difference (MID) of 4.[47]
- Proportion of patients with an improvement of 4 or more units in the SGRQ at one year.[47]

4.2.3. Anxiety and depression

- Hospital Anxiety and Depression Scale (HADS) at one year. The HADS is a validated questionnaire with independent scales for anxiety and for depression (scores ≥11 indicate significant anxiety (or depression); scores ≤7 are normal).[48]

4.2.4. Patient knowledge and self-efficacy

- Self-Efficacy for Managing Chronic Disease 6-item scale (SECD6) at one year.[49] The SECD6 assesses confidence in ability to self-manage symptoms and impact on life on a scale of 1 (low self-efficacy) to 10 (high).[50] It has been used in a range of long-term conditions.[49]
- Lung Information Needs Questionnaire (LINQ) at one year.[51] The LINQ measures the information needs of people with COPD on a scale of 0 (low needs) to 25 (high).[51] Scores correlate with the healthcare services accessed.[51]

4.2.5. Engagement with process:

- Medication Adherence Report Scale *(MARS)* at one year.[52] MARS-5 is a 5-item reduction of the validated MARS scale which has good reliability and validity in populations with respiratory conditions, and other chronic diseases [Horne R, personal communication August 2008] It assesses adherence to medication on a 5-point scale: higher scores indicating higher levels of adherence.
- Compliance with monitoring and self-management will be assessed using the electronic record of symptoms and the action taken (or not).

4.2.6. Cost-effectiveness

- Cost per Quality Adjusted Life-Years (QALYs) at one year. QALYs are derived from responses to the EuroQoL-5D (EQ-5D).[53]
- Use of healthcare resources during one calendar year will be extracted from the patients' primary and secondary care records, supplemented by questions about use of healthcare resources asked at the initial and 12 month research visits and a short quarterly questionnaire at 3, 6 an 9 months.

5. Methods

5.1. Trial design

A one year researcher-blinded randomised controlled trial

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5.2. Setting

Primary and intermediate care in Lothian

5.3. Participants

5.3.1. Inclusion criteria

Patients registered with Lothian general practices admitted with an exacerbation of COPD as the primary diagnosis to one of the three acute hospitals in Lothian in the previous year.

5.3.2. Exclusion criteria

Patients with other significant lung disease, unable to consent, unable to use the technology (e.g. inability to use the technology, or complete the questionnaires), or at the GPs discretion for other more significant medical/social reasons.

5.4. Sample size

Recruiting 125 patients per arm will allow us to detect a difference in the primary outcome from a median of 200 days to readmission in the control group to 300 days in the intervention group, with 80% power, using a significance level of 5% (log-rank test). This is based on data from a trial of tele-health,[14] which showed an increase from a median of approximately 200 days to 400 days. As effectiveness in this trial varied between centres, we have opted for a conservative estimate of effect size. Increasing the sample size to 150 patients per arm will allow for withdrawals or non-compliance with the study intervention (10%) and the estimated number deaths that will occur prior to admission to hospital with COPD (7%).

5.4.1. Deaths

We anticipate that 10-15% of patients whom we recruit will die during the course of the trial.[14,32,54,55] About a third of deaths will be due to an exacerbation of COPD (two thirds of whom will be admitted and die in hospital),[56] about a third from cardiovascular causes with other co-morbidity (including lung cancer) accounting for the remaining deaths.[54] We estimate that approximately 7% of patients will die prior to admission to hospital with COPD. We do not anticipate that our intervention will have a significant effect on mortality.[54]

5.4.2. Losses to follow up

Trials of tele-monitoring in COPD have reported withdrawal rates ranging from 8% to 31%, the latter because of some major technical problems.[14,57] Our pilot work suggests that withdrawal because of dissatisfaction with the system will be rare, so that attrition is likely to be in the region of 10%. We will endeavour to collect data from patients from patients regardless of compliance with the study intervention, and 10% loss to follow up is a conservative estimate for our primary outcome. However, if it is apparent that our withdrawal rate substantially exceeds our projection we will review our sample size during the course of the trial

5.5. Recruitment

Working with secondary care respiratory teams, we will use hospital records to identify patients registered with Lothian general practices who have been admitted with an exacerbation of COPD as the primary diagnosis to the three acute hospitals in Lothian (Royal Infirmary of Edinburgh [RIE], Western General Hospital [WGH] and St John's Hospital at Howden [StJ],) in the previous year. These hospitals admit around 1,300 patients with exacerbation of COPD each year. Data from

Information Services Division (ISD) demonstrate that these patients have a 60% risk of re-admission for any condition and 34% risk for COPD in the following year.

The secondary care team will write to the GPs of potentially eligible patients to check if they are still alive, and to determine if they have any exclusion criteria. With the GPs agreement, trial information will be sent to all eligible patients inviting them to participate in the trial. We will stagger the recruitment over six months for practical reasons and so as to avoid overloading clinical services.

5.6. Confirmation of eligibility and consent

Potential participants will be invited, with one reminder, to a baseline assessment with a research nurse at the practice or other venue convenient to the patient, or in their home, at least six weeks after the most recent exacerbation. The researcher will provide further information about the trial and obtain consent. The diagnosis of COPD will be confirmed by a history of exposure to risk factors (normally smoking) and the presence of airflow obstruction on spirometry. It is anticipated that this group will have moderate to severe COPD (post-bronchodilator FEV_1 < 50% predicted, FEV_1/ FVC <70% predicted). Spirometry undertaken by a specialist respiratory service within the previous three months will be accepted.

5.7. Baseline measurements

Eligible, consenting patients will have a baseline assessment including current smoking status, MRC Dyspnoea score, presence of co-morbidity and baseline questionnaires (SGRQ,[45-47] HADS,[48] SECD6,[49] LINQ,[51] MARS-5[52] EQ-5D,[53]) will be administered.

5.8. Initial optimisation of care and self-management education

All patients will be seen by a healthcare professional (usually a physiotherapist or nurse) trained in the management of COPD who will assess current control, and optimise management in line with national guidelines [43] and Lothian COPD protocols (liaising with GPs as necessary for prescriptions), and deliver a one-to-one standardised COPD education session specifically covering early recognition and self-management of exacerbations.

5.9. Randomisation

All eligible participants will be randomised using randomised blocks of varying size, stratified by the service who will providing their clinical care (i.e. Edinburgh respiratory physiotherapy service, Mid-Lothian Chronic Disease nursing team) to either control or intervention. This will be managed by the telephone randomisation service of the Edinburgh Clinical Trials Unit who will generate the randomisation sequence. The research nurse will phone the randomisation service and inform the patient of the allocation. Arrangements will then be made for installation of the telemetric equipment. All allocated patients will be included in the intention-to-treat analysis.

5.10. Protection against bias

Baseline data and optimisation of care will take place prior to randomisation and allocation which will be carried out remotely at the Clinical Trials Unit 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 (admissions, validated questionnaires) will also reduce the possibility of bias.

5.11. Trial interventions

5.11.1. Intervention group: Telemedicine monitoring

Patients in the intervention group will be given a modified "tablet" touch screen computer with video capability which is linked by broadband to a secure N3 connection to the internet. Shortly after the tele-monitoring equipment has been installed in their homes, patients allocated to the intervention group will be visited at home by the clinical team responsible for care to instruct them in its use. They will be given a written management plan and an emergency supply of antibiotics and steroids will be requested from the patients' own GP.

Daily (normally mornings) the patient will use the telemonitoring system to record symptoms and use of medication using a touch screen questionnaire and monitor peak flow and oxygen saturation using linked validated instruments. The symptom monitoring is based on the diary cards used by Wedzicha ***et al***,[39] to define an exacerbation as an increase in symptoms (dyspnoea, sputum purulence and volume, wheeze, cough and upper respiratory tract symptoms) which increase in the prodroma to an exacerbation (see Appendix 2). This information will be sent by the secure internet connection to an NHS server which is accessible via a high level password to the specialist respiratory clinicians involved in the care of the patients. A symptom score of four sustained for two days or a single score of five defines an early exacerbation and will trigger direct contact with the patient. Although unlikely to be helpful in predicting an exacerbation, the peak flow and oxygen saturation will be available to the advising clinician to aid clinical assessment of severity, who will also have the benefit of a video link to observe any respiratory distress (tachypnoea, use of accessory muscles of respiration).

Questions about use of medication will track patients' response to the deterioration. This information will be initially forwarded to an NHS secure server. The specialist respiratory team will routinely survey the on-line data every day and remind patients if they have not sent information or contact them if questionnaire responses and physiological parameters fall outside the expected range. Following discussion with the patient and repeat of physiological measurements (if required) appropriate clinical management will be instituted.(see Appendix 2 for response flow chart).

Patients will have access to technological advice and support throughout the trial, but this will be enhanced in the initial two weeks to ensure that they gain confidence in using the equipment.

5.11.2. Control group: paper-based monitoring

Patients allocated to the control group will receive the same written management plan and will be instructed in its use. An emergency supply of antibiotics and steroids will be arranged with the patients' own GP. Specialist respiratory nurses/physiotherapists will provide comparable care for the control patients as for the intervention group, accessed though via the standard routes of communication, the only difference being that control group patients will not use the tele-monitoring system.

5.11.3. Clinical care

Throughout the trial, patients will be reviewed according to clinical need by their normal clinical advisors. Clinical care in both groups will be in accordance with the Lothian protocols which will be based on the recommendations of national and international guidelines.[43,58]

5.12. Duration of intervention

One calendar year

5.13. Data collection and management

- Data on the primary outcome measure (time to an admission with a primary diagnosis of COPD) will be extracted by a researcher, blinded to allocation, from the patients' primary care records at the end of the trial.
- Number and duration of admissions with a primary diagnosis of COPD (including any time spent in intensive therapy units which will be confirmed by scrutiny of the hospital records), number of admissions in which COPD is listed as a factor in the admission, number of exacerbations treated with antibiotics and/or oral steroids will be extracted by a researcher, blinded to allocation, from the patients' primary care records at the end of the trial.
- Adverse events will be recorded the patients' primary care records at the end of the trial
- Use of healthcare resources for the health economic analysis (including, in addition to data about admissions, practice and out-of-hours consultations for COPD, routine reviews for COPD, prescriptions for respiratory drugs,) will be extracted by the researcher from the primary care records at the end of the trial.
- Questionnaires will be administered by the researcher (supervised self-completion) at baseline and at 12 months. Arrangements will be made for completion at the patient's surgery, home or other suitable location convenient to the patient. Baseline and follow up questionnaires will be mailed to the patient's home prior to the supervised self completion to allow patients enough time to read through the questionnaires prior to completion.
- Use of healthcare resources questionnaires will be mailed to patients' homes for self completion at 3, 6 and 9 months following randomisation. One reminder will be sent for questinnaires which are not returned. Where questionnaires are incomplete or answers unclear, patients will be telephoned at home by the researcher to clarify responses.
- The records of the patients' daily tele-monitoring submissions will be retrieved at the end of the trial and analysed for compliance with monitoring, time interval between exacerbation and onset of treatment, exacerbations not reported to clinicians.

Data will be entered from questionnaires and paper records by the trial manager, with 10% checked for accuracy. If we detect systematic errors we will re-enter all the data.

5.14. Statistical analysis

All patients who are randomised will be followed up and included in the analysis in their allocated treatment groups regardless of the treatment actually received (intention-to-treat analysis). Survival data will be presented using Kaplan-Meier curves, and if appropriate, will be analysed using Cox proportional hazards models

adjusting for service (stratification variable), age, gender, severity (FEV_1 %predicted), current smoking status, presence of co-morbidity, HADS, SGRQ, social class(determined using post-code and the Scottish Index of Multiple Deprivation), and previous admission history (potentially important confounders). Binary outcomes will be analysed using logistic regression and continuous outcomes (if appropriately distributed) will be analysed using linear regression, adjusting for the stratification variable and potential confounders. Unadjusted analyses will also be performed. Adjustments will be made for baseline measurements using analysis of covariance.

Patients with missing data will be omitted from the analyses (we have increased the sample size to allow for this). The impact of this will be assessed using sensitivity analysis. Patients who die without having had an admission (approximately 7% of patients [14,56]) with a primary diagnosis of COPD will be censored in the final analysis

5.14.1. Subgroup analyses

For the primary outcome, subgroup analyses will be performed based on age, sex severity, presence of co-morbidity, SGRQ and HAD score. These factors may all reasonably be hypothesised to affect the impact of the intervention.[59] Subgroup analyses will be performed by adding the interaction between these factors and treatment into the survival analysis model and observing whether the fit of the model is statistically significantly improved.

5.14.2. Health economic analyses

The health economic analyses will assess the cost-effectiveness of the tele-supported self-monitoring compared to usual care. A cost-utility analysis (incremental cost per QALY) will be performed. The perspective will be the NHS. The benefits will include health outcomes measured in terms of QALYs which will be derived from the responses to the EQ-5D.[53] 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. Questionnaires recording the variable costs of the tele-supported self-monitoring will be completed by call centre staff and clinicians. The costs of the tele-monitoring equipment and the set-up costs will be estimated. Resource use estimates will be combined with unit costs obtained from standard sources or study specific estimates (e.g. the time taken to survey monitoring data each day, or undertake monitoring telephone calls will be estimated by timing a sample of these tasks.[60] 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.

5.15. Qualitative study

5.15.1. Patients

A sub sample of participants in the randomised controlled trial and screening study will be recruited to the nested qualitative study. Up to 20 participants from the intervention group will be recruited for semi-structured interviews plus a further 10-12 for two focus groups. The purpose of the focus groups will be to allow the group to explore shared ideas and experiences relating to COPD and their experiences in managing it. The interviews with individuals will cover similar subjects but will allow private discussion of issues such as not using medication in

the prescribed way (which people may not be willing to discuss in a public situation). A maximum variation sample in relation to age, social class, ethnicity (if ethnicity varies sufficiently between participants) and severity of COPD and number of admissions at recruitment, plus level of use of the system will be sought.

5.15.2. Healthcare Professionals

Up to 20 professionals participating in the trial will be interviewed (face-to-face or by telephone according to the preference of the clinician). This will include the specialist respiratory physiotherapists/nurses providing the support services, long-term condition nurses, early discharge nurses and representatives of primary and secondary care services

5.15.3. Topic guides

The initial guide for semi-structured interviews with patients will be based on the themes identified from the literature and the on-going pilot studies, but the guide will be reviewed and refined iteratively as data are gathered and analysed and new themes arise. Participants will therefore be encouraged to give their views on the usefulness of the systems in general and then tell their own story about managing their own long-term conditions and the impact of the systems.

Interviews with professionals will seek to investigate perceptions of the benefits (or otherwise) of the intervention, experiences of implementing and maintaining it and the barriers and facilitators they have experienced.

5.15.4. Analysis

The interviews and focus groups will be fully transcribed. The Framework method will be used to classify and organise data according to key themes, concepts and emergent categories.[61] Data will be analysed from the theoretical perspective of the diffusion of innovations literature and the behaviour change literature, underpinned by social learning theory, which emphasise the importance of people's perceptions in understanding their behaviour in relation to an innovation.[62-66]

Initial coding will be carried out by the qualitative researcher with reference to the transcripts and voice recordings and the analysis recorded using NVivo 7. Constant comparison (checking experiences against those of others in the sample) will ensure that the thematic analysis represents all perspectives and negative cases will be sought. The analysis will then be reviewed by the wider research team to aid interpretation. Validity checking of the analysis will include recoding of some interviews by an independent researcher and coding review of some of the data by a patient reference group.

6. Exit Strategy

The equipment used in this trial has been purchased by NHS Lothian who (if the intervention proves to be clinically and cost effective) hope to make the tele-monitoring system available after the end of the trial to all participants (i.e both patients in the intervention and the control group.

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, home monitoring, inappropriate response to an emergency, and excess clinical workload.

8.1. Data security within the telemetry system

The clinical data collection system will make use of NHS secure N3 system. All identifiable data are encrypted before being dispatched and will be held in a secure server behind the NHS firewall. 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. Information is regularly backed up according to NHS policy.

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 forms of contamination identified.

Patients in both groups will have their care optimised at baseline, and will receive self-management education including the provision of antibiotics and steroids. Whilst this is recommended by guidelines as good care, it probably represents a higher standard than is usual.

In addition, practitioners may become more familiar with the concept of COPD self-management and modify their management of patients in the control group. As most GPs (who will be responsible for prescribing emergency supplies of antibiotics and steroids) will only have one or two patients in the trial, this is unlikely to affect their management of COPD generally. Intermediate care nurses or physiotherapists are more likely to be influenced by the experience of working with patients in the intervention group. However, we anticipate that the 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.

These issues will be specifically explored in the qualitative interviews with professionals.

8.3. Inappropriate response to an emergency

The intervention is monitoring for the early symptoms of an exacerbation of COPD. There is a risk that a patient may fail to respond to potentially life-threatening symptoms that arise outwith their set self-monitoring periods (for example, chest pain, or rapid deterioration in breathing after the day's readings have been submitted), thinking that they can seek help when the following day's recordings

are made. Patients will be carefully warned about this risk (verbally and in writing). It will be explained that the tele-monitoring screens for early warning of exacerbations and is not designed to detect any other emergencies or clinical situations. They should seek help in the usual way if they are concerned about their health.

8.4. Excess workload

Tele-monitoring is likely to generate more alerts than requests for professional advice in the usual care group. However, the monitoring (including clinical measures such as serial peak flow and oxygen saturation) will probably facilitate telephone management in many cases. In addition, monitoring of the recovery phase should require fewer home visits than in normal care so that overall workload, therefore may not be significantly affected. All the participants will have had a recent hospital admission and will therefore be eligible for intermediate care support.

9. Project Team and Task Allocation

- Dr Hilary Pinnock is the Principal Investigator and will lead the research team.
- Dr Brian McKinstry leads the Lothian tele-health evaluation programme, and has been leading the ongoing pilot study.
- The qualitative study will be led by Dr Janet Hanley aided by Dr Claudia Pagliari both experienced qualitative researchers with nursing and psychology backgrounds, and advised by Professor Aziz Sheikh.
- The COPD trial group will include Professor William MacNee, supported by the trial collaborators: Sr Joyce Barr a respiratory specialist nurse responsible for nurse training in Lothian, Professor Wisia Wedzicha an expert in the causes, mechanisms and impact of COPD exacerbations and Professor Josep Roca an expert in telemetry in COPD. We will invite a member of the British Lung Foundation (Scotland) to provide a lay perspective to the trial.
- Health economic support will be provided by Dr Marjon van der Pol a Senior Research Fellow at the Health Economics Research Unit (HERU) in Aberdeen.
- Edinburgh Clinical Trials led by Anne Langston will co-ordinate the trials and statistical support from Stephanie Lewis a senior statistician with extensive trial experience
- We will appoint a trials manager, affiliated to Edinburgh Clinical Trials unit who will be responsible for research approvals, finance management, staff recruitment and management, progress reporting, co-ordinating data collection, data management and reporting.
- A clinical co-ordinator will be responsible for clinical liaison and training practices and call centre staff in the skill needed to work to the research protocols, plus clinical data and qualitative data collection and analysis as required.
- Wellcome Trust Clinical Research Facility research nurses will carry out the clinical data collection
- A qualitative researcher will be responsible for the qualitative studies including data collection and analysis.

10. Project Management and Quality Assurance

- The project team, consisting of grantholders and research staff, will meet monthly.

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- There will be a weekly meeting between the lead researchers and Edinburgh Clinical trials to discuss the progress of the whole programme, including the COPD trial study
- We will set up an independent trial steering committee (ITSC), for the tele-health programme which will comprise the chief investigator; an independent chairperson; the applicants, trial staff and representatives of the funding body; and a patient representative (if possible). Three experienced trialists have agreed to oversee the individual RCTs; Professor Chris Griffiths (COPD trial) Professor Lewis Richie (hypertension and stroke), and Anne-Louise Kinmonth (diabetes). Meetings of the ITSC will be held prior to the start of each trial, and thereafter annually 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); report to the sponsors on progress of the trial, and to the CSO as funder; advise CI, sponsor and CSO as funder on publicity and the presentation of all aspects of the trial. 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 the 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 and management approval from NHS Lothian.
- Research governance will be managed by the Edinburgh Clinical Trials Unit and NHS Lothian Research Governance Committee
- The trial will be co-sponsored by NHS Lothian and the University of Edinburgh.
- Indemnity will be provided by the NHS indemnity scheme, the University of Edinburgh

11. Timescale

Start of trial: April 2008

Month	Task
0-9	Ethics / approvals Fine tune intervention Recruitment of researchers Training for nurses and other staff
9-18	Identify eligible patients Recruit patients Baseline measures Randomisation
18-24	Management according to allocation Qualitative data collection
24-33	End-point measures Health economic data collection
33-39	Data analysis Report writing

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. Existing resources

The major costs of setting up telemetric supported home monitoring services will be met by NHS Lothian via their e-health initiative. The pilot/service development phase has been funded by Intel.

13.2. Project grant

- The trial is funded by the Chief Scientist's Office, NHS Applied Research Programme Grant
- The funding is managed by NHS Lothian
- There will be service level agreements between NHS Lothian and the appropriate academic institutions to cover agreed costs

13.3. NHS support costs

Support for Science costs will be sought from NHS Lothian 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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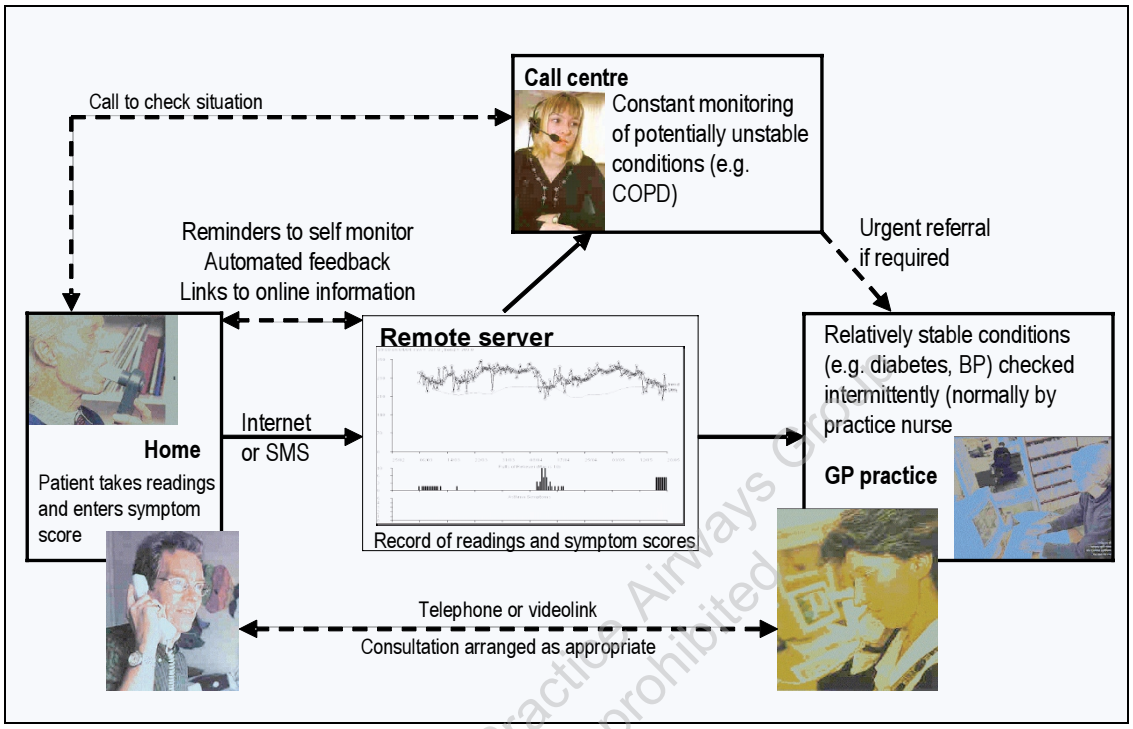
15. Appendices

15.1. Model of telemetry supported self care



This model illustrates an overview of tele-monitoring. Two models are under consideration in our programme.

- In COPD (a potentially unstable condition) patients daily symptoms scores are scrutinised by a call-centre team who will contact the patient when responses to symptom questionnaire fall outside expected parameters or if readings are not transmitted. According to protocol, they will observed the following day, or referral made to a clinician who will be able to consult with the patient (either face-to-face or remotely via telephone or video-link) and arrange treatment as necessary.
- In the other models automatic responses to readings will be fed back to patients advising them if they need to contact their clinician (based on mean average of their results) or reminding them to take readings. Clinicians will view the patient record at regular intervals and contact patients by phone, email or text to give advice. Patients can also view results on line.

15.2. The daily symptom questionnaire

Each day, please record any WORSENING of symptoms from your usual daily level. The symptoms we are interested in are listed below, just tick yes or no in the box beside each symptom:

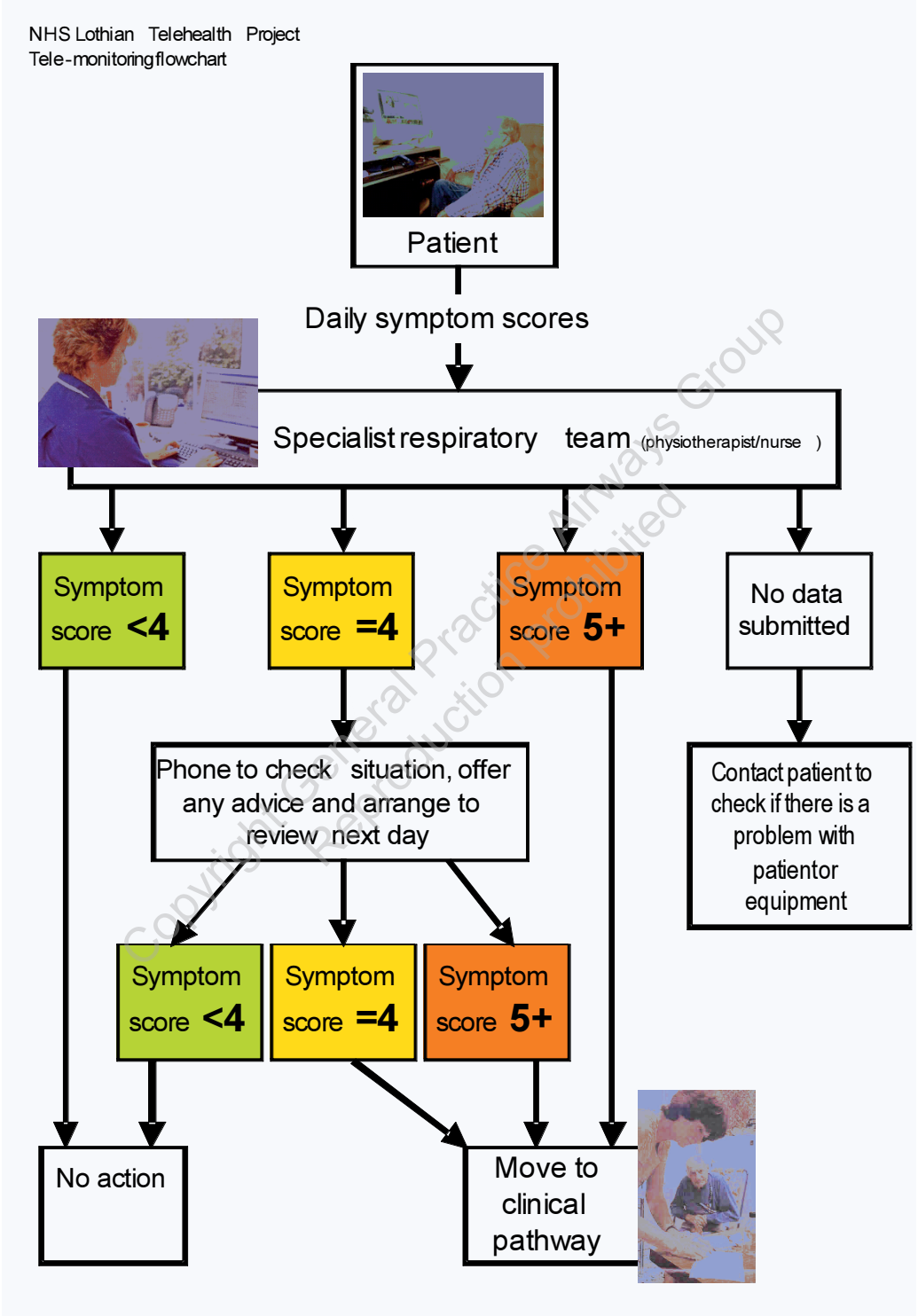
Symptom:	Yes	No
I am more breathless than usual		
My sputum has increased in colour		
My sputum has increased in amount		
I have a cold (such as runny or blocked nose)		
I have increased wheeze or chest tightness		
I have a sore throat		
I have an increased cough		
I have a fever		

Please record any CHANGE to your usual treatment by ticking either yes or no next to each of the following:

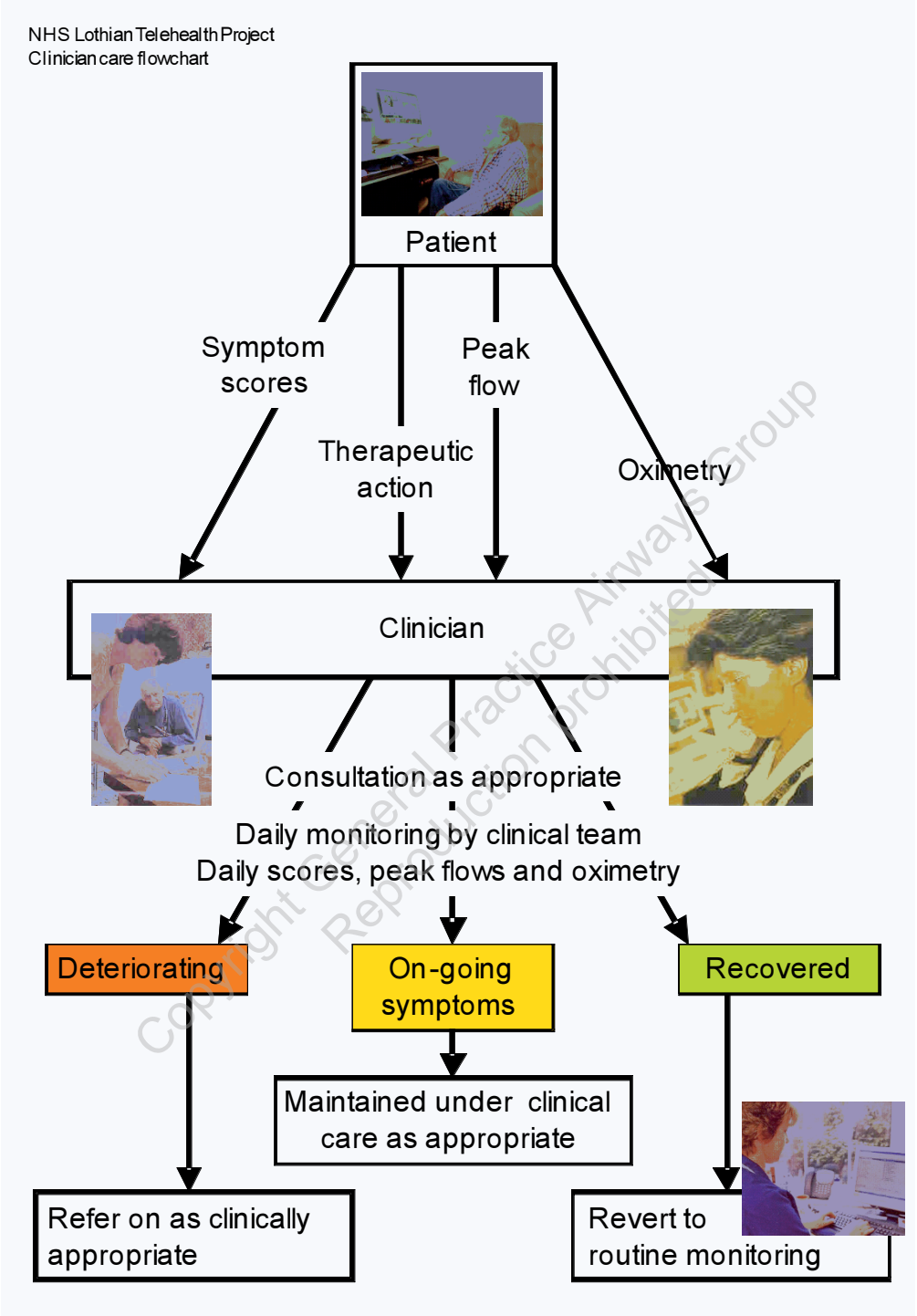
Medication	Yes	No
I am taking more of my inhaled steroid than normal		
I need to take more of my reliever than normal		
I am taking steroid (prednisolone) tablets		
I am taking antibiotic tablets		

15.3. Intervention flow diagrams

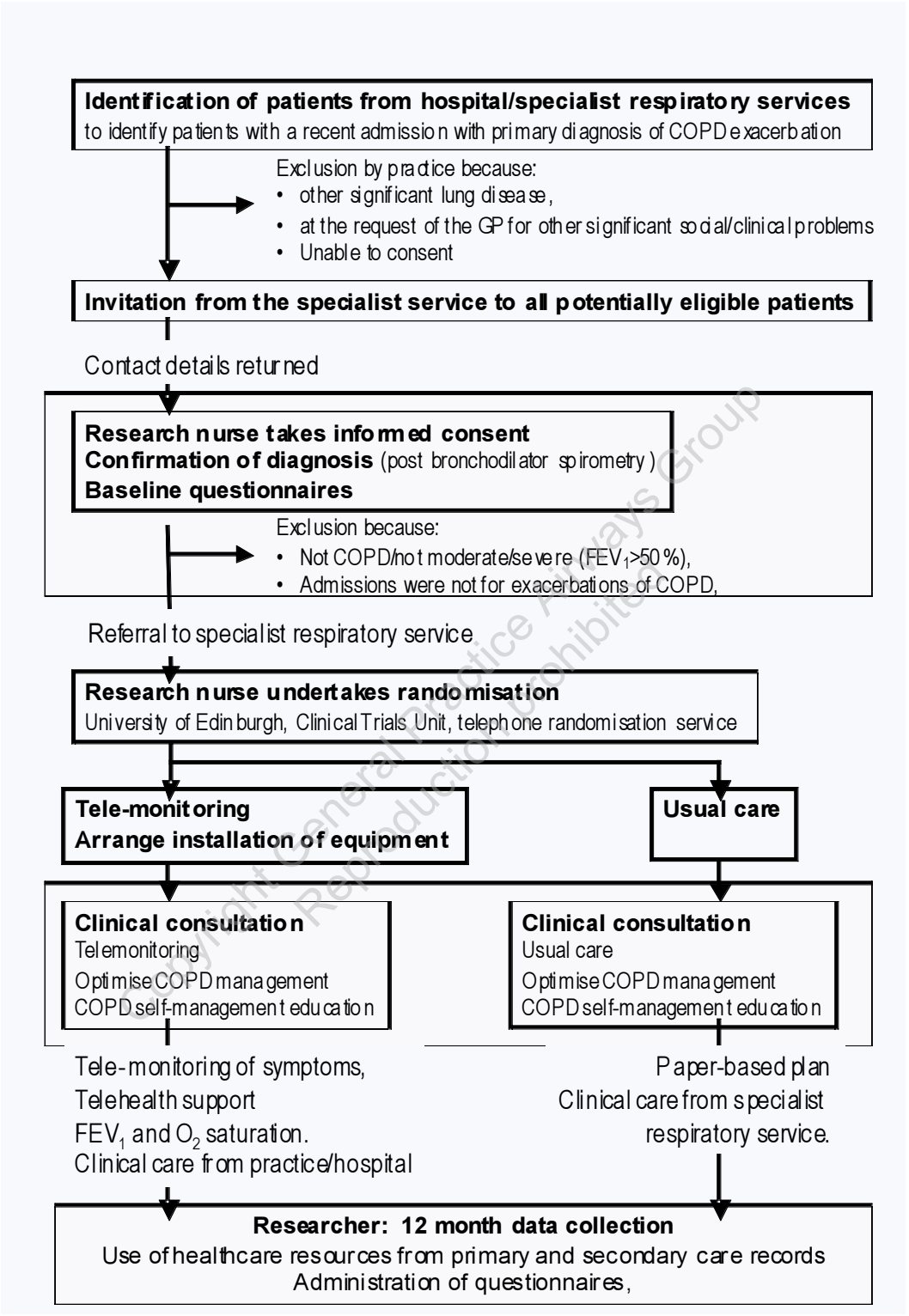
15.3.1. The tele-monitoring response flow diagram



15.3.2. The clinical flow diagram



15.4. The trial consort diagram



15.5. Theoretical framework for telehealth studies

The technologies being trialled in this programme enable frequent self monitoring, organisation of the resultant data, and sharing of the data between patients and healthcare professionals in a way which has not been previously available in Primary Care. This is a complex intervention involving the following elements:

- Self monitoring. Although everyone monitors their own health, for most of the patients involved in this trial, formal measurement of symptoms and vital signs will be new to them – it was previously the responsibility of healthcare professionals. The exceptions will be blood glucose measurement for the diabetic patients and blood pressure monitoring for the 30% of patients that our pilot work suggests already own their own home monitors.
- The information itself. In most cases the parameters of interest have not been routinely and frequently monitored so the data, in conjunction with the way in which it is organised and shared, provides novel information about the condition and its control to the patients and their healthcare professionals.
- The organisation of the data. The systems used in these trials are able to organise and display the data provided in different ways eg an average blood pressure. They also provide some interpretation of the data based on pre-determined parameters.
- Automated feedback and reminders. The systems used in this trial are able to provide timely reminders and automated feedback for patients, which will not have been previously available to them
- The way in which the data is shared and used. The data record will be almost instantly available to both patients and healthcare professionals.

It is hypothesised that tele-monitoring will impact at three levels:

1. Patients may improve their knowledge and understanding of their condition as they monitor and receive timely and relevant feedback on their situation.
2. Professionals may feel more confident to offer self-management within the structure and on-going supervision of tele-monitoring
3. Appropriate access to services may be facilitated by the tele-monitoring as patients become more confident when they need help and advice and with the easy sharing of monitoring data.

The theoretical model developed by Glasziou ***et al***. describes the complementary and evolving roles of periodic professional reviews and on-going patient self-monitoring.[1] A newly diagnosed condition is assessed and brought under control with professional support, before the patient assumes responsibility for self-management as the stable maintenance phase is established.

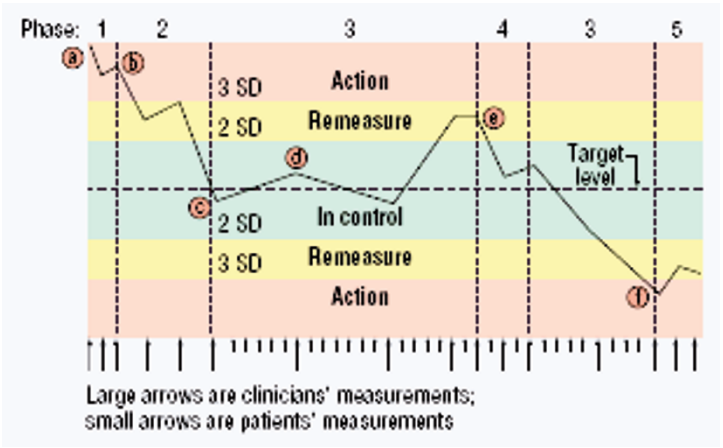


Figure 1. The five phases of treatment monitoring. After Glaziou ***et al.***[1]

The context for the tele-monitoring trials is the maintenance phase where patients are monitoring a relatively stable situation, and expected to act (either by initiating treatment, or seeking appropriate professional advice) if measurements fall outside pre-defined limits. The impact of this will vary according to the condition being monitored. For people with an asymptomatic condition such as hypertension this may the first time they have been aware of their control of a daily basis. Patients with COPD often have difficulty distinguishing the onset of an exacerbation from a 'bad day',[2][3] and one possible mode of action is that tele-monitoring will define exacerbations more clearly and increase patient's confidence to commence treatment promptly.

Kennedy argues for a whole systems approach to the provision of effective support for self-care.[4]

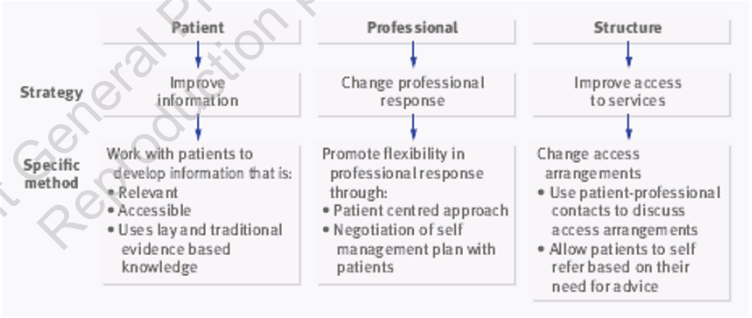


Figure 2. Example of an intervention based on a whole systems perspective. After Kennedy ***et al.***[4]

The anticipated outcomes are dependent on changes to behaviour: i.e. whether patients and/or professionals successfully use the equipment and change the way they manage the long term conditions being monitored. However, the way people act when they come into contact with an innovation does not always appear logical. There is a large literature on both the diffusion of innovations literature and health behaviour change, both underpinned by social learning theory which suggests people's perceptions of a situation determine how they behave.[5] Factors likely to influence this include

- ∞ self-efficacy, or belief in one's ability to perform a behaviour.[6]
- ∞ Perceived benefits weighed against perceived barriers to the action.[7][8]
- ∞ Perceptions of the attitudes of important others to the behaviour.[6][9]
- ∞ Reinvention and identity.[6][10]

The 'diffusion of innovations' model is the most comprehensive description of how new technologies (including behaviours) are adopted.[6] It includes a pattern of how an innovation spreads through a social group, a comparison of characteristics of those who adopt the innovation at different stages of its spread, and a staged model of the innovation-decision process (knowledge, persuasion, decision, implementation, confirmation), which an individual goes through when deciding to adopt or reject an innovation. Factors which may influence this process include the mode of communication (e.g. the presence of a change agent), prior conditions (including previous practice, felt needs and problems, innovativeness and norms of the social system), perceived characteristics of the innovation, disruptive or competing technologies or path dependence which may lock other technologies in place. A (self) criticism of this model is that it does not explain why individuals adopt or reject particular innovations at an early stage, sometimes seemingly irrationally.[6]

A related, but more explanatory model, the 'technology transfer communication and feedback' model[7] suggests that much of the unpredictability in the adoption of new technologies arises because individuals do not share a common perception of it or their need for it.[7] It introduces the concepts of technology push (the perceived merits of the new technology), and market pull (the perceived need for the new technology), both being required for the successful transfer of the new technology into practice.

Because of the complexity of the intervention, the explanatory aspect of this programme will be qualitative and involve interviews, focus groups and observation with patients, professionals, carers, and service planners. It will explore prior perceptions and conditions, the experience of using the system, and changes to perceptions and behaviour. The initial topic guides and data coding frame will based on the factors identified by the diffusion of innovations, social learning theory and our pilot work, but will be developed iteratively and be open to new approaches. The exceptions to the qualitative approach will be that patients will be asked to complete a quantitative measure of self-efficacy in chronic disease,[11] and (in the case of COPD) an assessment of knowledge about the respiratory condition.[12] The 'Self-Efficacy for Managing Chronic Disease' scale is widely used and will give some comparability with other research.

A specific aim of the qualitative work will be to explore the apparent paradox or tension in this service model where the aim is to increase self-care, but the model also increases professional surveillance of the patient. Our qualitative pilot work with hypertensive patients showed that even patients who were very committed to self-management welcomed this, but was not detailed enough to explain why. Work in the fields such as asthma monitoring and obesity management have also highlighted this paradox – that interventions which apparently take some control away from patients can result in their feeling of overall control increasing.[13][14] These are important issues in a policy context which advocates increasing self-care.

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