

HEALTHLINES STUDY RANDOMISED CONTROLLED TRIAL PROTOCOL SUMMARY

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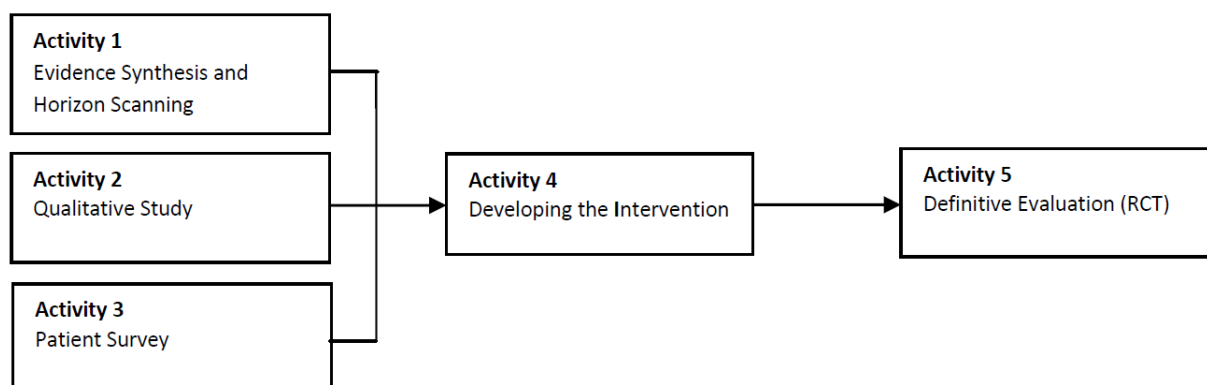


Effectiveness and cost-effectiveness of a NHS Direct-delivered telehealth intervention to support the management of long term conditions: a pragmatic randomised controlled trial.

1. Background

Over 15 million people in England have a long term condition (LTC) and the treatment of LTCs accounts for 70% of total healthcare expenditure. Improvements in LTC management could have major benefits in terms of patient health, quality of life and use of NHS resources.[1] There is strong interest in using new technologies (e.g. text messaging, phone support, internet, remote monitoring) to help patients manage LTCs.[2]

The Healthlines study aims to design and evaluate a telehealth intervention delivered by NHS Direct for patients with long-term conditions (LTCs). This is a 5 year project which commenced in November 2009 and is funded by the National Institute for Health Research (NIHR). The study is a collaboration between NHS Direct and the Universities of Bristol, Sheffield, Manchester and Southampton and the Royal College of Surgeons in Ireland. The project involved 5 linked research activities as presented below.



The results of activities 1-3, along with relevant NICE guidelines and existing theories about effective LTC management, have informed intervention development. The intervention will now be evaluated in a Randomised Controlled Trial (RCT).

2. Trial Design

2.1. Aim and Objectives

The aim is to determine the clinical and cost effectiveness of a NHS Direct-delivered telehealth intervention to support patients with two exemplar long term conditions; depression and raised cardiovascular disease (CVD) risk.

Specifically, the study will address the following research questions:

- Does the intervention in addition to usual primary care improve condition-specific clinical outcomes (10-year estimated CVD risk, PHQ-9) compared with usual care alone?
- Does the intervention have any effect on other patient outcomes including quality of life and satisfaction with care?
- What is the cost effectiveness of the intervention in each condition?

2.2. Trial Design

This is a multi-centre, parallel two-arm, individually randomised trial involving two different patient groups, those with raised CVD risk and those with depression. Study infrastructure (participating practices, research staff and intervention staff and underlying theoretical basis for the intervention) will be common across both patient groups, but the specific content of the intervention package, data analysis and reporting will be distinct, so the patient groups will effectively be treated as if they were in separate trials. In this document we will refer to these trials as the “CVD Risk Trial” and the “Depression Trial”.

The recruitment target is 600 patients in each of the two trials (1200 in total). An additional 80 patients (40 in each trial) will be recruited in a pilot study which will commence recruitment 3 months prior to the main trial.

2.3. Setting

34 general practices in the environs of Bristol, Sheffield and Southampton. 2 practices will participate in the run-in phase, the remaining 32 in the main trial.

2.4. Inclusion Criteria

Both trials

- Access to a telephone (landline or mobile), the Internet and an e-mail address for personal use. In addition:

CVD risk trial

- Aged between 40 – 74 years
- 10-year risk of cardiovascular event of $\geq 20\%$ calculated using the QRISK2 score.[3]
- Present one of the following modifiable risk factors: previous GP recorded diagnosis of hypertension, current systolic blood pressure, ≥ 140 , BMI ≥ 30 or currently smoking.

Depression trial

- Age ≥ 18 years
- Confirmed diagnosis of depression using the Clinical Interview Schedule – Revised (CIS-R) [4] and PHQ-9 ≥ 10 [5]

2.5 Exclusion criteria

Participants must not:

CVD risk trial

- have a history of established diagnosis of cardiovascular disease
- be currently pregnant or planning to become pregnant within the next 12 months
- Patients eligible for the NHS Health Checks Programme during the period of the trial (only where this is requested by the local Primary Care Trust)

Depression trial

- be receiving case management from a specialist mental health worker
- be receiving face-to-face, telephone or computerised CBT or similar psychotherapy
- have given birth in the previous 12 months

Both trials

- Severe mental health or cognitive difficulties, substance misuse, suicidal risk or receiving palliative care.
- Inability to communicate in English

For more detail on the specific health conditions excluded please refer to the full protocol.

2.6. Recruitment Procedures

Potentially eligible patients will be identified using MIQUEST search of general practice computerised records. CVD Risk patients will be selected using Framingham risk scores, and a random sample of identified patients will be checked by a GP for suitability to participate. Depression patients will be identified by searching for a depression related read code on the computer records, which again will be checked for suitability; or by direct referral during their consultation with a healthcare professional in a participating GP Practice.

Patients identified as suitable will be sent a recruitment pack and will be asked to return a freepost acceptance or decline form to the research team. On receipt of an acceptance form all participants will be telephoned to assess eligibility. In addition CVD risk participants will be asked to attend their GP practice for an assessment of their CVD risk factors. This risk factor information will be communicated with the research team who will calculate an up-to-date QRisk2 score to determine eligibility. Depression participants will be asked to complete the CIS-R and PHQ-9 to assess eligibility (the CIS-R will be done over the telephone by the research team and the PHQ-9 is included in the baseline questionnaire).

Eligible patients will then be sent a consent form and asked to complete a baseline questionnaire online or by post. Once the consent form has been received by the research team the patient will be randomly allocated using an automated web randomisation service. The outcome of which will be communicated with the patient and their GP

Patients allocated to the intervention group will be provided with more information about the NHS Direct Healthlines Service via email. The research team will also pass on their details to NHS Direct who will initiate contact, complete an initial assessment and also request that CVD risk participants with high blood pressure collect a blood pressure monitor from their GP practice to use during the study.

2.7 Randomisation

Eligible participants will be allocated in a 1:1 ratio to receive either:

- Usual care plus NHS Direct Healthlines Service (intervention group)
- Usual care alone (control group)

2.8. Trial Run-in Phase

A run-in phase will commence before the start of the main study and will involve two GP practices each recruiting 40 patients (20 depression, 20 CVD risk). The purpose of the run-in phase will be to test study recruitment and follow-up procedures, and allow adjustments ahead of the main trial. It will also allow intervention staff to develop their skills in using the intervention software and treatment protocols. In the run-in phase, a 3:1 randomisation ratio in favour in the intervention will be used.

3. NHS Direct Healthlines Service

3.1. Intervention Staff

The intervention will be delivered by a team of NHS Direct health information advisors with experience in providing telephone-based support.

3.2. Hours and Mode of Operation

The hours of operation will be 10am – 8pm Monday to Friday and 10am – 2pm Saturday. The service model will predominately involve intervention staff contacting patients at pre-arranged appointment times. Patients will also be able to request a call back via the intervention website or answer phone service.

3.3 Initial Assessment

An initial telephone assessment will be conducted by NHS Direct intervention staff to provide additional information about the research and intervention, obtain medical history and current health needs, and agree a treatment plan.

3.4. Available treatment components

A variety of telephone and internet-based treatment options will be available to patients. The menu has been developed by reviewing UK treatment guidelines for depression and CVD risk factors and relevant research literature including Cochrane Reviews. For example depressed patients will be offered access to either an online or workbook-based CBT package alongside regular telephone support and outcome monitoring. Patients with high blood pressure will be supplied with a home blood pressure monitor. Advice and support for smoking cessation, diet and exercise changes will also be on offer to patients in the CVD risk trial. For a more comprehensive list of the available interventions components please refer to the full protocol.

3.5. Ongoing management and support

Patients will be followed-up regularly by telephone and it is estimated that the average patient will receive approximately 5 hours contact time during the 12 month period. The NHS Direct Healthlines team will also maintain good communication with the patient's GP during the intervention period.

3.6. Intervention Completion

Patients can remain in receipt of the treatment for 12 months. The final patient contact will involve a review of progress and sources of further support, a final summary will be sent to the GP and the care of the patient will be returned solely to the GP.

4. Outcome measures

4.1. Primary Outcomes

CVD risk trial: Maintenance or reduction of 10-year cardiovascular risk estimated using QRISK2 [3] after 12 months.

Depression trial: PHQ-9 <10 and an absolute reduction in PHQ-9 of ≥ 5 after 4 months. [5;6]

4.2 Secondary Outcomes

Secondary outcomes include behavioural and cognitive outcomes, quality of life, patient satisfaction, perceived access to care and use of telehealth. A full list of secondary outcomes, related to both CVD and depression can be found in the full protocol.

4.3 Data Collection and follow up

The baseline questionnaire will include socio-demographic characteristics, co-morbidities, current treatments, employment status, , and all secondary outcome measures.

Follow-up questionnaires will include all secondary outcome measures and use of healthcare resources. The timings of which is specific to each condition:

CVD risk trial: Self-report questionnaires will be completed at baseline, 6 and 12 months after randomisation. At each of these time points, participants will also be asked to attend a nurse appointment at their GP practice where CVD risk factor information will be collected.

Depression trial: Self-report questionnaires, including the PHQ-9, will be completed at baseline, 4, 8 and 12 months after randomisation

Information about the type, number and length of contacts with intervention staff will be collected from NHS Direct Healthlines team records, and information from medical records about medication prescriptions and primary care contacts will be collected for all participants 12 months after randomisation.

5. Statistical considerations

5.1. Sample Size

It will be necessary to recruit 300 patients in each of the intervention and control groups for each trial, or 1200 patients in total. This equating to 18.75 patients per trial in each of the 32 participating practices.

5.2 Descriptive Analysis

The analysis and presentation of each trial will be in accordance with CONSORT guidelines. Furthermore appropriate descriptive statistics will be used to compare characteristics of invited patients who did or did not agree to take part and eligible patients who were randomised or not randomised. We will also examine the patient characteristics across the trial arms.

5.3. Primary Analysis

Intention-to-treat analyses will compare groups using appropriate regression models adjusted for baseline value of the outcome and stratification/ minimisation variables, paying attention to 95% confidence intervals as well as p-values.

5.4. Secondary and Sub-group Analyses

Pre-planned analysis of secondary variables and subgroup analyses for the primary outcome will be conducted. The subgroups of interest are age, sex and baseline CVD risk or PHQ9 score. Subgroups relating to the type of modifiable risk factor at baseline (i.e. high blood pressure, obesity, smoker) will be analysed in the CVD risk trial only.

5.5. *Protection against bias*

Allocation will be concealed by use of a remote automated system. Blinding of participants or health professionals is not possible. Patients in the control group may be able to access similar information from other websites which may impact outcomes therefore we will collect data about use of all relevant web based resources by all participants.

6. Economic Evaluation

The aim of the economic evaluation will be to estimate the cost and benefits of the NHS Direct Healthlines intervention in the two conditions. There will be two stages to this evaluation: (i) patient-level evaluations covering the period of the trial and (ii) modelling of future costs and benefits to cover the lifetime of the trial population.

The patient-level evaluations will be carried out from the perspectives of the health care provider (NHS) & personal social services (PSS), and patients. The intervention will be costed using data collected during the trial supplemented by information supplied by NHS Direct. Costs will be compared with benefits as measured using the primary outcomes of QRISK2, PHQ-9, and quality adjusted life years (QALYs).

The second stage of the economic evaluation will use data from the trial along with other from the literature to develop simulation models, these will estimate cost per QALY over the lifetime of the trial population and indicate parameters of importance in the implementation of the programme at a national level.

Threshold analysis will be performed to identify required uptake, effectiveness and costs of the package for the intervention to be cost-effective for given levels of prevalence. In addition, sensitivity analysis will explore uncertainty around parameter and structural assumptions used in the models.

7. Process Evaluation

7.1. *Aim and Design*

The process evaluation will consider the acceptability of the intervention, and facilitators and barriers to the delivery of, use of, and compliance with the intervention. This will be achieved by conducting a qualitative interview study with staff involved in delivering care to patients and patients in the intervention group of the trial.

7.2 *Methods and setting*

The process evaluation will take place in six of the 34 general practices. Face-to-face semi-structured interviews with patients and a mix of face-to-face and telephone interviews with professionals involved in delivering care will be conducted.

7.3. *Sampling*

Six practices will be selected, one in Bristol, one in Southampton and four in Sheffield, which represent different levels of deprivation.

Staff interviews (n= 15-25) will adopt a purposeful sampling strategy to reflect the range of relevant professionals within the trial including NHS Direct staff, GPs and practice nurses.

Patients interviews (n= 20-30), will adopt a purposeful sampling strategy to ensure the interviews belonged to the intervention arm of the trial and that half of interviewees have depression and half have risk factors for CVD. Then maximum variation sampling will be used so that patients of different socio-economic background, gender and age are interviewed

7.5. Recruitment

Staff will be contacted via letter to a GP and a practice nurse in the six practices asking for consent to participate in an interview. We will include an information sheet and consent form. Patients will be asked if they are willing to be approached by a member of the research team for process evaluation when taking consent for the main trial. If they agree, we will write to them with an information sheet and consent form if they are sampled for interview.

7.6. Analysis

Interviews will be recorded and transcribed verbatim. Framework analysis will be used; the thematic framework will be informed partly by issues arising in earlier phases of the programme and partly by themes emerging from the interviews.

8. Research Governance

8.1 The trial will be conducted to protect the human rights and dignity of the participant as reflected in the 1996 version of the Helsinki Declaration.

8.2. Monitoring and Adverse Events

This study will monitor details of any Serious Adverse Events (SAEs) occurring to study participants during the study. Further details of the procedures associated with the monitoring SAEs are outlined in the full protocol.

8.3. Patient and Public Involvement

Patient and public representatives will be involved in the design and management of the study, as well as the design and testing the usability of the interventions. Two patient representatives are members of the Healthlines Programme Management Group and the Healthlines Trial Steering Committee who will contribute to management decisions relating to the study.

9. Study management

9.1 Research Sponsor

The University of Bristol will act as sponsor for the research and will also provide relevant public liability cover. The Healthlines trial is funded by the NIHR Programme Grant for Applied Research (ref: RP-PG-0108-10011).

9.2 Study Oversight

Study management will be overseen by a Trial Steering Committee and an independent Data Monitoring Committee will be convened to report to the TSC during the Trial. A Programme Management group will also meet to discuss issues pertaining to the overall management of the research programme. Membership of these groups can be found in the full protocol. The Principle Investigator for the research is Alan Montgomery, University of Bristol. All aspects of trial design, conduct, analysis and reporting will be in accordance standard operating procedures from Bristol Randomised Trials Collaboration (BRTC), a UKCRC-registered clinical trials unit.

9.3 Study Timeline

The NHS Direct Healthlines intervention will be delivered to “run in” and main study participants between July 2012 and March 2014. Final follow-up, 12 months after randomisation will be complete for all patients by March 2014.

9.4 Dissemination

The attention of clinicians and the public to our findings will be achieved through publishing the results of the study in peer reviewed journals, submitting abstracts to relevant conferences, and disseminating the results within NHS Direct. A short summary of the results will be distributed to all trial participants, participating GP practices, as well as patient and other interest groups. Finally, we will aim to ensure coverage of our findings in the wider media by issuing a press release.

10. References

- (1) DH/Long Term Conditions. Raising the Profile of Long Term Conditions Care. A Compendium of information. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_082069
- (2) Murray E. Providing information for patients. *BMJ* 2008; 337:a280.
- (3) Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, Minhas R, Sheikh A et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. *BMJ* 2008; 336(7659):1475-1482.
- (4) Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for lay interviewers. *Psychological Medicine* 1992; 22:465-486
- (5) Kroenke K, Spitzer R, Williams JW. The PHQ-9 Validity of a Brief Depression Severity Measure. *Journal of General Internal Medicine* 2001; 16:606-613.
- (6) McMillan D, Gilbody S and Richards D. Defining successful treatment outcome in depression using the PHQ-9:A comparison of methods. *Journal of Affective Disorders* 2010; 127: 122-129