Home-based Extended Rehabilitation for Older people (HERO)

Individually randomised controlled multi-centre trial to determine the clinical and cost effectiveness of a home-based exercise intervention for older people with frailty as extended rehabilitation following acute illness or injury, including internal pilot and embedded process evaluation.

Health Economics Analysis Plan (Version 1.9)

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Abbreviations

AUECR	Academic Unit of Elderly Care and Rehabilitation (AUECR)
AUHE	Academic Unit of Health Economics
AUC	Area under the curve
BNF	British National Formulary
CE	Cost Effectiveness
CEA	Cost Effectiveness Analysis
CRF	Case Report Form
CTRU	Clinical Trials Research Unit
EQ-5D-5L	EuroQoL 5 Dimensions Health Questionnaire 5-Level
HEAP	Health Economics Analysis Plan
HERO	Home-Based Rehabilitation for Older people
HES	Hospital Episode Statistics
HRQoL	Health Related Quality of Life
ITT	Intention-to-Treat
NHS	National Health Service
NICE	National Institute of Clinical Excellence
PSS	Public Social Service
PSSRU	*Personal Social Services Research Unit*
QALY	*Quality Adjusted Life Year*
RCT	Randomised Controlled Trial
SAP	Statistical Analysis Plan

Amendments

Revision History

Protocol version no.	Updated HEAP version no.	Section revised	Description of and reason for change	Date changed
2.0	1.0	Original version	N/A	7th March 2018
3.0	1.1	Throughout.	General tidying up no material changes made to analysis Included: General typos. 'HERO programme' changed to 'HOPE programme' Effectiveness metrics SF-36 section added: These will be converted into the SF6D utility scores using the University of Sheffield MS Excel Bayesian programme (Kharroubi et al, 2007).	31st May 2018
5.0	1.2	Front page Cost data p9	Charlotte Kelly removed as health economist replaced by Silviya Nikolova Addition of intervention delivery	11th February 2022
5.0	1.3	Effectiveness metrics p8 Cost data p10	Updated method of EQ5D-5L valuation to mapping to EQ5D-3L and updating respective worst and best values. Table 1 update: Delivery of intervention to include travel time and administration time. Inclusion of detail about intervention equipment, residential care and removal of GP database as a resource use source. Expansion of detail about how the HES data will be costed.	11th September 2023

		Heterogeneity p11 Longer term model p12 Data access and storage p13	Heterogeneity section added Update of model structure and example states. Updated that utility weights are those from EQ5D-3L. Update of which statistical software will be used for analysis (R and SAS)	
5.0	1.4	Long term decision model	Figure of example sketch inserted	16th October 2023
5.0	1.5	References	Updated references throughout. No content change	11th December 2023
5.0	1.6	Front page Throughout: Trial background p6 Method p7 Long-term model p12	Silviya Nikolova removed as Health Economist and replaced by Chris Bojke and Rebecca Bestwick Re-structuring to align with the Bristol Synopsis, including: Addition of detail of trial structure, intervention, and comparator. Updating this section to include discounting of the longer-term model (was previously stated but in a later section) Addition of model development section	13th March 2024
5.0	1.7	References p14	Updated references throughout.	18th March 2024
5.0	1.8	Data access and storage	Updated that data was stored on secure folder in CTRU and accessed in that secure environment. (This replaced previous detail about SEED environment)	21st March 2024
5.0	1.9	Utility	Removal of use of SF-36 sensitivity analysis	25th March 2024

			Update to method for addressing parameter uncertainty	

Introduction

This document describes the planned approach for the health economics analysis for the HERO trial.

Trial Background

Frailty is a condition that is common in older age. It develops because as we get older our bodies change and can lose their inbuilt reserves. These changes mean that older people with frailty can experience sudden, dramatic changes in their health when they have an illness or injury. For example, an apparently minor illness such as an infection, or an injury such as a fracture, can cause an older person with frailty to become less mobile and unable to carry out day-to-day tasks [1]. This can often result in admission to hospital, and a further period of immobility. This is a major problem because in frailty even short periods of immobility can cause muscles that are already weak to become even weaker, preventing movements such as getting out of a chair, getting out of bed, getting on and off the toilet and climbing stairs.

Older people with frailty are therefore likely to need a period of rehabilitation to improve overall muscle strength and ability to carry out day-to-day tasks before returning home from hospital. In the NHS, around a third of older people with frailty receive rehabilitation after a hospital stay [2]. This rehabilitation may be in the form of 'intermediate care', which is a range of community rehabilitation services provided either in a setting such as a community hospital or at home. However, current guidelines recommend that intermediate care should be for a relatively short period of between 2 to 6 weeks [3]. A large national audit shows that people discharged from intermediate care often do not feel ready to leave the service and research suggests that the initial improvement from this short period of rehabilitation may not be sustained in the longer-term [3].

HERO is a multi-centre randomised control trial [4]. The population is community-based older people with frailty who have had a recent hospital admission, and the intervention is ‘HOPE’ (Home-based Older People’s Exercise programme) plus usual care [4]. HOPE is a 24-week home-based manualised, graded, progressive exercise intervention aimed at improving

strength, endurance, and balance, delivered by community therapy staff. The comparator is usual care alone.

Aims and objectives

The aim of the economic analysis is to establish whether the HOPE programme (+ usual care) is a cost-effective extended rehabilitation programme for older people with frailty discharged home from hospital or from intermediate care services after acute illness or injury, when compared with usual care alone. Cost-effectiveness will be evaluated by an improvement in health-related quality of life (HRQoL) and reduction in healthcare resource use.

The analysis will involve a within trial cost-effectiveness analyses (CEA), across the 12-month trial period, and a long-term decision analytical model.

Method

Perspective, time horizon and discounting

The perspective adopted with be that of the National Health Service (NHS) and Public Social Services (PSS). The analysis will be undertaken on the intention to treat (ITT) population, which includes all randomised participants in their allocated treatment group, regardless of level of treatment adherence. The primary within-trial analysis will compare direct costs and 12-month outcomes of patients randomised to the HOPE programme (+ usual care) versus control (usual care alone). No discounting of costs and outcomes will be required for the within-trial (one year) analysis. The longer-term model will be over a lifetime horizon, and costs and effects will be discounted at 3.5% per annum.

Identification and measurement of outcome

The main outcome measure is the Quality-adjusted life year (QALY). QALYs are a generic measure of health state that take into account both the quality and length of life such that one QALY is equal to one year in full health.

The study will use the EQ-5D-5L, which is a commonly used generic measure of HRQoL and are one of NICE's preferred outcomes measure for CEA [5,6]. It is comprised of five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/ depression. Each domain consists of five levels: no problems, slight problems, moderate problems, severe

problems and unable to. This is completed alongside the EQ-5D Visual analogue scale (VAS), which is a 0 – 100 scale where individuals are asked to indicate their overall health today.

Responses to the EQ-5D-5L will be completed by the participants at baseline and at 6 and 12 month follow up using postal questionnaires. These responses will be converted to HRQoL index scores by mapping to EQ-5D-3L and taking the corresponding 3L utility value [6,7]. Based on the English value set, the EQ-5D-3L index ranges from -0.594 (the worst possible health state) to 1.000 (perfect health) with 0 representing the health state of being dead [7].

Converting from the HRQoL scores to the QALY will be undertaken using the area under the curve (AUC) approach to estimate the mean QALYs in the HOPE programme + usual care and usual care groups. The AUC will be obtained as the product of the average of two consecutive HRQoL scores by the time interval between score measurements (i.e. assuming a linear transition between each follow-up time point). Should an individual die during the trial we will assume that his/ her HRQoL is 0 from the date of death until the end of the trial and we will assume a linear transition to this zero value from the last non zero score.

Costs data

The cost data can be classified into two main categories:

- The cost of delivering the HOPE programme
- The consequences of the HOPE programme on the NHS and PSS budgets through health care resource use.

Intervention delivery

Details of intervention delivery will be taken from the trial case report forms (CRFs). Staff costs of providing the intervention (including costs incurred from travel, delivery, and administrative tasks) will be calculated using salary rates for their corresponding grade.

Identification and measurement of resource use:

Patient's resource utilisation will be captured using Hospital Episode Statistics (HES) data and a self-completed patient questionnaire. The patient questionnaire is completed at baseline and 6 and 12 months and asks the participants to recall resource use over the prior 3 months. When collected at 6 or 12 months, the resource use will be extrapolated to reflect the prior six-month period.

For primary care, the questionnaire asks patients to recall the number and mode of contacts with different staff (such as GPs, nurses). This information will be costed using the unit costs from PSSRU [8]. Secondary care resource use will be identified through HES data. The HES data will include that from admitted patient care (APC) and accident and emergency (A&E). The hospital resource use will be costed by running the data through the NHS Grouper Software [9] and applying the relevant unit cost from the National Cost Collection [10].

The patient questionnaire is the predominant identification source for community social care service use (such as meals on wheels, respite, or residential care), which will be costed using unit costs from PSSRU [8]. Permanent moves to residential care will also be identified from change in patient address on CRFs.

The methods for identifying, measuring, and valuing resource use are outline in table 1.

Table 1: Cost Categories and data sources

Resource Category	Resource Use Measurement	Unit cost Source
Delivering the intervention		
Training the physiotherapists and therapy assistants	CRF – The following information is being recorded: Attendance, duration and training providers	PSSRU [8]
Delivering the intervention • Time taken in home visit for describing the HOPE exercises. • 5 face to face meetings • 7 telephone sessions • A further 12 weeks of telephone-based support	CRF – The following is recorded: The number of contacts and sessions, date and duration of sessions, mode of delivery, location and type of session. Therapist travel and admin time	PSSRU [8]
Intervention equipment • Exercise programme manuals • Exercise diary	CRF – the following is recorded: Issuing of manual and diary	Similar interventions equipment costs, such as Bruce et al [11]
Consequences of intervention on NHS and PSS		
Hospital, primary care, and Community Care Use	HES and Self-Reported Health Resource Use questionnaire	PSSRU [8], NHS Cost Collection [10]
Residential/permanent residential care	Self-Reported Health Resource Use Questionnaire	PSSRU [8]
Support from PSS (e.g. meals on wheels, home care)	Self-Reported - Health Resource Use questionnaire	PSSRU [8]
New equipment used	Self-Reported - Health Resource Use questionnaire	PSSRU [8]
Secondary Analysis		
Productivity costs	Self-Reported - Employment questions	National Living Wage [12]
Out of pocket costs	Self-Reported Travel questions	

Secondary analyses will adopt a societal perspective taking account of productivity costs and out-of-pocket expenditures incurred by participants. These data will also be captured using the self-reported patient questionnaires.

Cost Effectiveness Analysis (CEA)

The costs of healthcare resources used during the 12-month trial period and the HRQoL data collected at baseline, six and twelve months will be used to estimate the incremental cost effectiveness ratios (ICERs) comparing the intervention and control groups. Parameter uncertainty will be assessed using Probability Sensitivity Analysis using draws from the regression output (vector of parameter estimates and variance-covariance matrix with correlations between estimates preserved). Outputs will be presented as ICERs, cost effectiveness acceptability curves and expected net benefit. As well as identifying the most cost-effective means of achieving a QALY, the NICE threshold of £20,000 per QALY will be applied [5].

Statistical decision rules

We will present the associated 95% Confidence Intervals for the mean differences in costs and QALYs between the treatment groups.

Addressing missing data

The impact of missing data will be examined. Missing data might not be missing at random (MAR), hence we will explore and summarize the missing data patterns and reasons for data being missing as far as is possible using the data we have. If this confirms that it is reasonable to assume data are MAR the analysis will use multiple imputation to deal with the missing data.

Sampling uncertainty and sensitivity analysis

Sensitivity analyses will consider key cost drivers and factors that might affect the outcomes measured to explore uncertainty in the conclusions drawn.

Heterogeneity

It is expected there will be heterogeneity amongst the trial participants in attributes such as age, Clinical Frailty Score (CFS), recent healthcare use and baseline home care input. Patient heterogeneity will be explored through regression modelling and sub-group analysis will explore any variation in cost-effectiveness.

Long-term Decision analytical model

The long-term cost effectiveness model will compare the effectiveness of the HOPE programme (+ usual care) versus usual care only. The decision analytic CEA model will use a lifetime time horizon to capture the full impact of any mortality differences on the long-

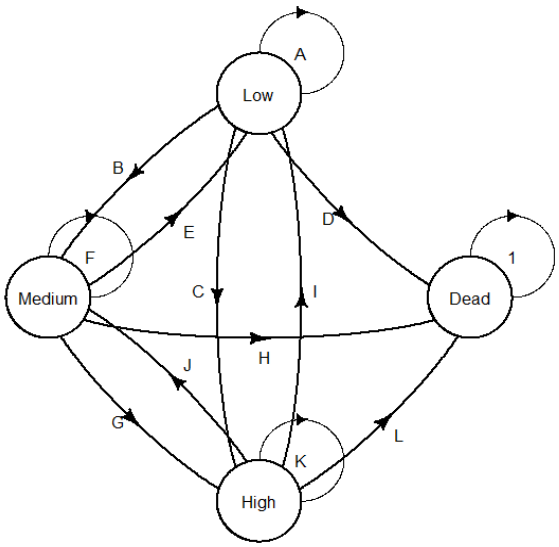
term CEA. The primary outcome measure will be the QALY. Utility weights will be taken from the UK General Population tariff for the EQ-5D-3L, and unit costs will be taken from national databases including NHS Cost Collection and the PSSRU costs of health and social care, as for the within trial analysis [7,8,10]. A discount rate of 3.5% per year will be used for costs/benefits occurring after year 1, as in accordance with NICE recommendations [5].

Model type and structure

It is likely that the model will be a Markov model and include states that reflect the varying resource use needs of patients and thereby healthcare cost. There will also be the fully absorbing dead state, to which patients can transition from any of the other states.

Figure 1 is an example sketch of the model and shows three alive states (Low, Medium, High) representing different magnitudes of resource use.

Figure 1: Example model



Model development

There are limited examples in the literature of longer-term models for interventions within this important population (older adults with frailty) and a recent literature review identified only one such example [13]. In response to recognising the challenges of modelling in frailty, Afzali et al developed an aid to conceptualise such models and proposed an example structure [14]. However, although there are limited frailty-specific models, there are other useful models within similar relevant settings, such as those focusing on the community

aged care sector [15] or interventions for older populations [16]. Notably however, the longest time horizon of these models was 5 years.

Our model represents a stochastic non-homogeneous process and includes three states that represent different degrees of resource-use. Levels of resource-use were chosen as an appropriate way to synthesize the various sources of healthcare costs that this people in this cohort can incur (for example from home care, hospitalisation, or respite). Similar categories have previously been used in models of health promotion interventions in older populations [16], and link to the recognised relationship between frailty and dependency.

Methods for identifying and estimating the parameters

The specific state definitions, including categorisation cut-offs will be developed from the trial data. As far as possible the parameters for the model will also be estimated through regression-models on the trial data.

Model uncertainty

Probabilistic sensitivity analyses will be undertaken using random draws from distributions of regression coefficients and regression-covariance matrix. The outputs reported from the analysis will be the same as for the within study analysis and presented with associated 95% Confidence Intervals.

Data Access and storage

A download of the data will be transferred to a secure folder within CTRU for access by the Health Economics team. The data will be accessed through this secure server with the CTRU environment.

The data will be analysed using SAS and R. The data will be available for final analysis after the final participant has completed their 12 month follow up.

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