5 STUDY DESIGN AND METHODS OF DATA COLLECTION AND DATA ANALYSIS

Participants will be recruited across 4 sites: Royal Sussex County Hospital in Brighton, Ashford and St Peter's Hospital in Ashford, Medway Hospital in Kent, and Royal Devon Hospital in Exeter. The proposed study is a Randomised Control Trial (RCT), as patients will be randomised into either the NHS DMS alone (control arm/standard care), or RPT-stratification plus MMP linked to the NHS DMS (intervention arm).

Sample size/power details

In determining the sample size, let the proportion of subjects developing MRH when given the standard care be p_1, while the proportion of subjects developing MRH among those put through intervention arm be p_2. Common measures for comparing whether the two proportions are statistically significantly different are:

1. Difference, $\delta = p_1 - p_2$
2. Odds-ratio, $\Psi = \frac{p_1/(1-p_1)}{p_2/(1-p_2)}$

Then the two equivalent hypotheses for evaluating whether the two proportions are different are H_0:δ=0 and H_0:Ψ=1. The values of Ψ close to 1, indicate no difference and those further from 1 are the ones that specify differences that may be clinically important. The sample size formula can be expressed so that the only parameters needed are the prevalence of MRH in the population receiving standard care and odds-ratios and there is no need to directly incorporate δ in calculations. In this case Ψ is the fixed parameter and sample size can be calculated for various values of prevalence. The advantage of using the odds-ratios as fixed is that it is straightforward to define clinically important differences from a range of admissible values. Once desired value of odds-ration is selected, the corresponding values of δ (defining clinically important difference), can be computed for the observed prevalence value.

The choice of the value of odds-ratio to use is based on the range of values of odds-ratios that normally show up as significant in statistical analyses. As it is not expected that the two arms of the study would be dramatically different, we recommend the choice of medium values of odds-ratios.

A systematic review of MRH in older adults found that between 17% and 51% of patients experience MRH within 30 days of hospital discharge. In the UK, approximately 28% of older adults (≥65 years) use health services due to MRH within the 8 weeks following hospital discharge (6). Therefore, our choice of the prevalence to use in the sample size calculation is limited to MRH rates between 20% - 40%. In particular, we take the prevalence of MRH among the group under standard treatment to be 35% and an odds-ratio of 1.6 is considered large enough to result in a clinically important difference in MRH rates between arm 1 and arm 2. These choices of p_1 and odds-ratio corresponds to δ=0.098.

To determine the required sample size to estimate a difference δ that is clinically relevant, the method of Fleiss, Tytun, and Ury (53) was used. This method has been implemented in the function "bsamsize" given in R package "Hmisc" (54). To calculate sample size using this method, one needs to provide the following parameters: the prevalence of MRH among people given standard treatment (p_1) and among people given the new care/intervention ($p2$), odds-ratio (Ψ), the statistical power we wish to achieve, and the margin of error.

We found that a sample size of n=682 (341 subjects on each arm) will be required to detect δ=0.098 (i.e., odds-ratio=1.6), with 80% statistical power, and a 5% margin of error, if we assume that the prevalence of MRH among those on standard treatment is 35%.

5.1 CLINICAL EFFECTIVENESS

Baseline Data Collection

The baseline data collected and methodology will correspond to that of the original PRIME Study (36). Consenting participants (and participants consenting through their consultee) will have baseline data collected by a trained research nurse.

Demographic (age, gender, ethnicity), clinical (discharge diagnosis, co-morbidities, renal function, electrolytes, hepatic function), and social indicator data (living arrangements and care package on discharge) will be collected. Admission and discharge medication data (drug name, frequency, dosage) and use of compliance aids will be collected and coded using the WHO-ATC code (37). The above are routine clinical data, and so can be collected directly from the hospital notes.

Validated tools will be used to collect data on comorbidities, nutritional status, physical function and cognitive function. The Charlson Comorbidity Index (CCI) which predicts 10-year survival in patients based on age and co-morbid status will be collected by the research nurse (38). The Malnutrition Universal Screening Tool (MUST) score is a nutritional screening tool routinely used on elderly care wards to stratify and manage overall risk of malnutrition (39). The Barthel ADL Index is a validated scale used to measure performance in activities in daily living (ADL) (40). Barthel's Index, MUST and Abbreviated Mental Test Score (AMTS) will be collected from patients' notes only.

Data collection will take place using a form designed to be scanned into an electronic database. At the point of data collection, each participant will be allocated a unique participant identification number (UPIN). Data will be anonymised prior to upload to the electronic database. The anonymised data base will be stored on NHS and University Computers. Hard copy non-anonymised data will be stored in locked cabinets in each respective study site with access provided to the CI and each respective PI only. Hard copy data will be destroyed in compliance with local protocol at 3 years.

Follow up Data Collection

The research pharmacist will conduct a telephone interview and GP records review after eight weeks post-discharge for every participant. The phone interview with study participants will take form 5 minutes to 30 minutes depending on the amount of information study participants have to share with the pharmacist around your medications. A standardised questionnaire will determine whether the patient has experienced MRH. Suspected ADRs, medication adherence, and primary/secondary care usage will be explored. MRH severity will be assessed using the Morimoto scale (45). If an ADR is suspected, causality will be assessed using the Naranjo algorithm (46). Medication adherence will be assessed using the Morisky scale (47).