NETSCC, HTA

5th October 2011

Prevention of Fall Injury Trial - HTA 08/14/41 Lamb et al

Summary of Amendments to LREC-Approved Protocol of 29th April 2010

Substantive amendments referred to in multiple sections:

- In our initial application we had proposed approaching all people aged over 70 years within each practice to participate in the trial. This could have been as many as several thousands of patients, and would have carried the risk of placing too large a burden on the services in each area. We have refined the sample size calculation, and will now approach a randomly selected cluster of 300 potentially eligible participants in each practice, assuming a 50% uptake rate to yield a cluster size of 150 participants per practice. The sample size has been checked very carefully to ensure it is valid, and that there are sufficient numbers of clusters of an appropriate size. Approach letters and information letters have been changed to reflect that we are now approaching a random selection of people over 70 years old as opposed to the entire practice population of over 70 year olds. We will only approach those individuals in the cluster to participate in the interventions.
- Peripheral fracture (primary outcome) will be collected at the individual level, rather than as a practice level aggregate for those individuals who are eligible and who have consented to provide access to their medical records. This means that the outcomes will be measured at the appropriate cluster level and is justified by the change in the sampling strategy. In addition, we may collect anonymised aggregated fracture rates for each practice during the pilot study to provide information on the variability between practices, and the representativeness of our sub-samples. We have altered the information and consent forms to ensure that patients are aware and consent to us accessing medical records to ascertain fracture outcomes at an individual level. We describe how the processes will be consistent with Good Clinical Practice and the Data Protection Act.
- We previously proposed to collect data from participants once during the follow-up period. However, this approach would not yield the type of data structure needed for the economic modelling. Hence we now propose to undertake repeated data collection on a subset of participants at 4, 8 and 12 months. We anticipate requiring outcome data on 2-3,000 participants at each follow-up. However, as we do not know what the response rate will be, we will collect data from all participants during the feasibility phase on the trial, which will be conducted in North Devon.
- We have included an additional measure in the baseline questionnaire, which we will pilot during the feasibility phase. This is a validated measure designed to assess markers of frailty, and will help characterise the population more fully (Strawbridge et al. 1998)
- We have submitted the protocol that has been approved by the MREC (approval number 10/H0401/36), using track changes to highlight where substantial changes have been made.

Additional changes:

1. Version Number and date added to footer
2. Section Numbers added

3. Changes to sections 3.10.1, 3.10.2 and 3.10.3. The changes here have been made for clarity and do not have an impact on the overall sample size required for the study with regards to the primary outcome. However, the changes in section 3.10.3 do have an impact on the number required for the secondary outcomes.
4. Reference added in as cited in section 3.10.2
5. Section 3.7. Removal of opportunistic screening during routine health checks.

1. Detailed Project Description

1.2 Title

Prevention of Fall Injury Trial (Pre-FIT). HTA 08/14/41

1.3 How the project has changed since the previous proposal was submitted (relevant to the funder)

a. The sample size calculation has been clarified and the basis for the design effect explained.
b. The costs have been reviewed with Trudi Simmons from the Department of Health.
c. Separate costs are provided for the feasibility and trial phases. (Research nurses non HEI, Cost has been included for the project welcome meetings. Details provided SEE LETTER

2. Planned investigation

2.1 Research objective

The aim of this project is to contribute a substantial body of evidence to inform UK healthcare practitioners, commissioners and other stakeholders on the relative effectiveness and cost-effectiveness of a range of primary care options for preventing falls and fractures.

We will conduct a pragmatic, cluster randomised controlled trial with a parallel economic study to answer the following questions

1. What is the uptake of interventions to prevent falls in primary care?
2. Does the type of intervention offered by a general practice affect the uptake?
3. What is the comparative effectiveness of advice, exercise and a multi-factorial fall prevention (MFFP) programme on
   - Proportion of people sustaining any peripheral fracture (primary outcome)
   - Peripheral fracture rates per person years of observation (primary outcome).
   - Fall rates per person years of observation (secondary outcome)
   - Generic health related quality of life
   - Physical and emotional function
   - Mortality
4. What is the relative effectiveness of these strategies in people of different ages (<=80 years or > =81 years); gender; cognitive capacity and fall history?
5. What are the relative costs of each strategy, and which is the most cost-effective strategy?

2.2 Existing research

Prompted by the ageing of the population, falls have become a focus of clinical and public health practice in the last 10-15 years. The rationale is to prevent fractures/injuries, disability and dependence. Despite this, no trial of fall prevention has been powered sufficiently to detect effects on peripheral fracture, and very few report quality of life outcomes. There has been no economic analysis within the UK, and very few outside the UK.

The first reports of risk factors for falling emerged in 1988, followed by explanatory trials of multiple risk factor reduction strategies (now called multi-factorial fall prevention (MFFP)) (Tinetti et al 1994; Close et al 1999). Risk factors include impairments of gait and balance, vision impairment, syncope and cardiac rhythm abnormalities, certain classes of medication, chronic and acute illnesses, environmental hazards, and footwear.

The early trials, although small, were promising. They provided the foundation for the National Service Framework for Older People to mandate the NHS to establish MFFP programmes for people with a history of a fall (i.e secondary prevention), and subsequently, for NICE to endorse this recommendation (NICE 2005). Little operational guidance was given, and falls services in the UK are of disparate and questionable quality (Lamb et al 2007; British Geriatrics Society (BGS) falls audit 2004, 2007).

However, there are now serious questions about whether or not MFFP is an effective or cost-effective method of fall prevention. There are over 100 trials investigating a wide variety of approaches to preventing falls. Many of the more recent trials are small and of low methodological quality. There have been a few well-conducted larger studies of MFFP, and these, somewhat surprisingly, reported no evidence of fall or fracture reduction (Lord et al 2005; Hendriks et al 2008). Hence two recent high quality systematic reviews concluded that MFFP might be substantially less effective than previously thought (relative risk reduction 9% for falls), with the possibility that they may not be effective at all (Gates et al 2008; Gillespie et al 2008 (update of Cochrane review)*)*. Our group has led/been involved in both these reviews.

The evidence around exercise is more encouraging. The recently updated Cochrane review of interventions to prevent falling in community dwelling people has suggested that exercise reduces fall rates by approximately RR 25% (dependent on mode of exercise) (Gillespie et al 2008). However, as with all other interventions, there are few robust data on fracture prevention, with only 3/29 trials reporting any information on injuries. Uptake, adherence to and attractiveness of exercise interventions remain a concern. Several well respect academic leaders in falls prevention have suggested that exercise maybe as effective as MFFP, but there has been no direct comparison (Campbell and Robertson 2007). A simple explanation as to why exercise could be as effective as MFFP is that gait/balance impairment is the most common fall risk factor, and therefore, exercise is a frequent component of MFFPs. If exercise is the effective component of the intervention then it is a cheaper, simpler method of delivering services, if acceptable to patients.

The NHS is committing substantial funding to MFFP. A conservative estimate of the annual cost is £34 million p.a (2006 costs, Lamb et al 2007). There has been no robust economic appraisal of alternative fall prevention strategies. In a recent scoping review undertaken on behalf of NICE, there was insufficient evidence to populate an economic model of any sensible policy options in falls prevention (Lamb et al 2007). The main driver of cost-effectiveness would be prevention of falls that result in serious injury and disability, but these outcomes have not been included within most trials owing to the large sample needed. Not all falls result in injury, and it is possible that minor falls can be prevented, but more serious falls cannot. Uptake will also be a key driver of cost effectiveness (Eldridge et al 2005), and we know that increasing the reach of the intervention into the population at risk will be essential. Reach of current services into the UK population is estimated to be 2% of those at risk (Lamb et al 2007). There is considerable uncertainty over the value of targeting interventions to higher risk groups. The most important information in this respect, which is lacking to date, are pre-specified sub-group analyses of simple screening criteria that would be able to distinguish responsiveness to treatment.

In summary, we will compare 3 strategies in primary care that are of direct relevance to UK policy makers. We will investigate an opportunistic and targeted screening linked to one of three interventions - advice, exercise or MFFP. The trial is designed to reflect the significant and contemporary dilemma in UK health policy, which is whether to introduce systematic screening and linked interventions from primary care (recently considered by the Quality Outcomes Framework Panel but rejected through lack of evidence (Oliver/Martin; personal communications)). We will investigate if (and how) more intensive treatments should be targeted to those most likely to benefit, and whether fall prevention should be expanded to include primary preventive strategies. The question is consistent with the most important research priorities identified by national and international guideline panels (NICE 2004; American Geriatrics Society /British Geriatrics Society (AGS/BGS 2008)).

2.2.1 How should we screen individuals and should we include advice as a comparator?

Several well-conducted trials have shown that advice based on traditional health education approaches do not reduce falls. However, these have been focused on providing older people with the tools to assess their risk of falling, and to undertake risk reduction strategies. Work by Yardley (co-applicant) has demonstrated that older people do not respond well to a risk-focused paradigm. Falls are associated with considerable stigma by older people, and for many, the suggestion they might be at risk or a “faller” is met with resistance and rejection. Further work demonstrated that advice strategies that associate older people with positive attributes (such as improving walking and vitality) are received much better, prompting the charity Help the Aged to launch a national campaign to educate those involved in the care of older people to focus on the positive.

For many of the same reasons we will not utilise a traditional screening method. The great majority of brief screening tools start with falls history and follow on with questions about negative health states (eg Do you have urinary incontinence?). We will use a screening method that is focused on motivating uptake into falls prevention services through a focus on maintenance of health and abilities. So instead of starting with falls history, we will start with "Is your balance and walking as good as it could be?" Supplementary questions will include the frequency of balance problems, fear of falling and fall history. The approach has been developed by Yardley et al (2006, 2008) and is ready for extended evaluation in primary care. The items in tool are able to predict falls on a par with other instruments (Lamb et al 2007, Lamb et al 2008). Within the context of this trial we will not utilise the summary score of the screening tool to determine access to services. Even those with apparently low risk of falling will be guided toward some type of preventive intervention. The self-assessment tool will be implemented by post. Previous studies have demonstrated postal self-assessment is effective in engaging older people in Comprehensive Geriatric Assessment (Rubenstein et al 2007).

We will include an optimised advice package as the "control" arm of the trial. Provision of advice is a requirement of the NICE fall guideline. Positive advice strategies have not been trialled previously, and would be considered the "best" advice strategy currently available. If they prove of similar effectiveness to either exercise or MFFP, we would anticipate these interventions to be the least costly. The positive approach will dovetail with our proposal for screening and engaging people in the services.

2.2.2 What type of exercise programme should we use?

There is reasonable evidence that the essential elements are that exercise should; [1] target gait, balance and lower limb muscular strength, [2] be prescribed by an appropriately trained health professional or fitness instructor (there are a range of national training accreditations available), [3] be progressed to ensure that a physiological challenge is maintained as people improve, and [4] be delivered in group or individual basis (Gillespie et al 2008). Issues of preference pervade, and the general consensus is that localities should provide group and home programmes, which should; [1] be a minimum of 12 weeks duration of supervised exercise, with a preference to longer term programmes, [2] aim for two sessions per week (Buchner et al 1997), and [3] utilise behavioural models to promote uptake and maintenance. We will incorporate all these elements of best practice into the trial, where local resources permit.

2.2.3 What format should the multi-factorial fall prevention programme take?

MFFP programmes use an observational assessment of fall risk factors. Interventions are then targeted to amelioration of the risks identified in the assessment. This means that not all participants will get exactly the same set of interventions. There is good consensus on what the assessment and linked treatments should be. We will select simple treatment protocols in accordance with the guidance issued jointly by the American Geriatrics Society, British Geriatrics Society and American Orthopaedic Society in 2008 (*in press*). The guideline is based on the MFFP developed by Tinetti in the early 1990's, which is proven in efficacy trials in the USA (Tinetti et al 1994). A subsequent non-randomised study has suggested that the Tinetti approach may reduce fall related injury (Tinetti et al 2008). Lamb has previously worked with Tinetti and is well versed with the intervention and training methods. Some updating will be required. For example the inclusion of vision interventions will be reviewed. Although a common component of MFFPs, recent trials have shown if vision is targeted in isolation, falls increase (Cummings et al 2001). One factor we believe essential is for services to assume responsibility for delivering as many of the components of the intervention as possible. Services that rely on poorly linked onward referral may not be effective (Gates et al 2008, Gillespie et al 2008), and will not be used in this trial. The MFFP assessment and interventions are in the most part simple, and well within the domain of practice of appropriately trained nurses and health professionals. MFFP teams will be supported by a geriatrician who will assume responsibility for the more complex interventions indicated in a minority of patients.

2.2.4 Should we include bone health interventions?

The NICE guidance stipulates that there should be close liaison between bone health and fall prevention services, although this does not occur in practice (Lamb et al 2007). This leads to the question of whether prescription of bone health agents should be utilised within the multi-factorial intervention (or indeed alongside any other intervention). For this trial we will not include Bone Health Interventions formally within the intervention protocols. The causal pathway we consider to underpin this trial is one in which a reduction in falls is causally linked to a

reduction in fractures. Bone health agents do not lie on this causal pathway and will complicate the interpretation of the trial. We are conducting other research to investigate bone health agents.

3. Research methods

3.1 Setting UK primary care.

3.2 Overview of the study (relevance to UK policy described above)
The design is a 3-arm, parallel group, cluster-randomised, controlled trial. The unit of randomisation will be the general practice. The trial will investigate a screening strategy that is linked to one of three interventions - advice, exercise and MFFP. We will also investigate if (and how) more intensive treatments should be targeted using pre-specified sub-group analyses. The primary outcome is peripheral fracture. Secondary outcomes are health related quality of life, function and falls, which are important intermediary end-points hypothesised to lie on the causal pathway and a significant focus of UK health policy. We aim to collect fracture reports from general practices, hospital episode statistics and self-report. Secondary outcomes will be collected from individuals by postal follow up questionnaire (with research nurses providing additional support if needs be). We have undertaken a substantial amount of preparatory work to support this trial application.

3.3 Target population
People aged over 70 years living in the community. This includes people living in sheltered accommodation, but not residents of nursing or residential care.

3.4 Health technologies being assessed
We will be testing three interventions that are linked to a self-assessment (screening tool). Detailed justification of the various elements of the interventions has been provided in section 2. The interventions are (1) advice (provided to all arms of the trial) (2) exercise (3) MFFP. We do not anticipate rapid changes in the technologies during the lifetime of the project. As with most health care interventions, particularly those of a preventive nature, compliance will be an issue. However, this is a pragmatic trial. It is designed to test the implementation in primary care, including uptake.

An increasingly important component of the evaluation of complex interventions is to provide a theoretical justification for the interventions, and to ensure that the interventions are well documented and replicable. The theoretical basis for both exercise and MFFP is well established. Accepting that the interventions may require some modification to reflect more recent evidence, the manual for both exercise and MFFP is already prepared (and available on request). The main challenge with this trial is about implementation of the complex intervention – whilst we know what type of procedures need to be undertaken, what type of skill set and training is required, there are still tricky issues to decide with regard to implementation. For example, is it better to train general practices to deliver the MFFP or is it better to utilise a more traditional falls clinic model. Users will be key to helping us decide this and we will undertake a process evaluation to determine factors important to translation into practice.

3.5 Randomisation
The unit of randomisation is the general practice. Practices will be randomised once a record search has been undertaken at each practice and the initial cohort identified. An independent statistician will randomise the practices. We will use minimisation to ensure balance with respect to list size and socio-economic status of the practice locality.

3.5.1 Does the study need to be cluster randomised?
We have concluded that the unit of randomisation should be the general practice because
[1] We will be training general practice staff to screen and deliver some components of the interventions. For instance, they will be trained in encouraging people to attend and comply with exercise prescriptions. As the treatments cannot be blinded, there is a significant chance of contamination. Added to this, it is impractical to train primary care staff in three different complex interventions of this nature. It is too confusing.
[2] We want to avoid confounding estimates of uptake with the invitation to participate in a trial. The decision that the practice list will be exposed to the intervention will be taken by the practice, and the intervention will be presented as routine care.
[3] We will also seek permission from the practices and research ethics committees to have aggregated data at the practice level on peripheral fractures. This helps to minimise reporting bias. We will determine the primary data source at the end of a feasibility study when we have

an estimate of return rates and permission for access to identifiable information. We will approach PIAG if necessary
[4] In this situation, a cluster-randomised design will result in considerable logistical efficiency and will be the most cost effective design.

3.6 Eligibility criteria

Any practice will be eligible for inclusion provided that they lie within a region that has the infrastructure to provide the trial treatments, are willing to engage in training for screening and the various intervention pathways. We will target larger general practices (list size >6000) as it will increase efficiency of the trial.

Within each practice, all people aged over 70 years, who are not resident in nursing or residential homes (as identified from their address), will be eligible for the trial. Practices will be able to screen the list of potential participants to identify individuals who should not be approached for follow up or sent the postal screening intervention and advice (e.g. terminally ill).

We are excluding nursing and residential homes, as approaches to fall prevention in nursing homes are substantially different to those for community dwelling populations.

3.7 Practice and participant approach

We are proposing to retain 50 practices at the conclusion of follow up, in up to 5 regions across the UK, although the final spread will be determined at the end of the feasibility phase. This would yield a list size of in excess of 25,950 people aged over 70 years. We will need to approach about 60+ practices to account for the possibility of poor performance or withdrawal.

Practices will be asked to fulfil the following obligations [1] to approach a random sample of 300 community dwelling people aged over 70 years, after having screened the list for potential exclusions[2] To mail out a self-assessment screening tool to study participants that includes the triggers for the interventions to which the practice has been randomised [4] To mail out a request to participate in data collection and to collaborate with the research nurses in ensuring procedures to maximise response are implemented [4] To allow research nurses access to primary care record systems for individuals who have consented [5] To allow staff to attend training in the procedures, and [6] To comply with the clinical protocol devised for the interventions. For some practices the maximum period of follow up will be 36 months, for others it will be shorter.

3.8 Delivering the interventions

We will target localities that have an infrastructure of existing services. We know existing reach of services is very poor, and no service is currently being systematically accessed from general practice. We undertook an extensive service mapping project on behalf of SDO and NICE in 2006, and identified 46 out of 253 potential localities in the UK that have the necessary infrastructure to deliver the required service. The services in each region will have to be willing to adopt a standardised approach that will necessitate each having to make some small changes and to attend a training programme. The numbers of people entering services will undoubtedly increase and we have built this into estimates of NHS costs (see later). The feasibility study will take place in North Devon (Exeter), and further expansion is likely to focus on Worcester, Hereford, Birmingham, Oxfordshire, Berkshire and possibly London.

3.9 Measuring outcome.

We will measure the following outcomes **the number of people sustaining peripheral fracture and peripheral fracture rates** (primary);**fall rates per person years of observation**, **health related quality of life (including physical and emotional function)**, **resource use** and **mortality**.

Outcomes will be defined in accordance with the Prevention of Falls Network Europe (ProFANE) consensus on fall injury trials (Lamb et al 2005). This was a rigorous international consensus exercise that agreed a core set of outcomes for fall prevention trials.

Outcome measurement will need to be subject to a feasibility study as it is likely to be complicated. We have several sources from which to track data, and the pilot study will focus on refining which sources are most robust.

Table 1. Summary table of proposed outcome measures

	Measure		Source	Time points
Primary	Number sustaining one or more peripheral fractures Peripheral fracture rate per person years		Participant self-report/Primary care records/ hospital episode statistics	4 monthly for entire follow up period
Safety/ Secondary	Time to first fracture		Participant self-report/Primary care records/ Hospital episode statistics	4 monthly for entire follow up period
Secondary	Falls rate per person years (in sub-set) Health related quality of life (EQ-5D/SF12) (in sub-set) Emotional and physical function (SF12) (sub-set)		Participant self-report	4 monthly for entire follow up period
Secondary	Mortality		National Strategic Tracing Service/NHS registry	On-going
Economic	Resource use Out-of pocket expenses		Primary care records/ Individuals Hospital episode statistics	4 monthly for entire follow up period

3.9.1 Peripheral fracture (primary)

We will aim to collect peripheral fracture data from general practice records and/or locality based Hospital Episode statistics. At this stage of the trial we cannot be exact about which data source is the most accurate, and during the feasibility phase we will investigate fracture reporting from both these sources against self-report (Donaldson et al 2008). Fracture reporting needs to be as complete and timely as possible.

Peripheral fracture will be confirmed by radiograph (where films exist) and coded to ICD 10. Four monthly searches of primary care databases and HES will be undertaken to determine if a fracture has occurred among the study participants. This will trigger confirmation by location of a confirmatory radiograph. We will estimate the total number of person years of follow up contributed by each practice to ensure meaningful rates can be calculated.

3.9.2 Falls

Capturing data on falls is problematic in the context of a large trial (Lamb et al 2005; Hauer et al 2006). We need to collect data on falls because if in the eventuality that there is no fracture reduction, it will be very difficult to guide practice without this information. We will use the internationally agreed definition of a fall "an unexpected event in which the participant comes to rest on the ground, floor or other lower level" (Lamb et al 2005). The gold standard method of data capture for falls is monthly self-report diaries/calendars, with a confirmation telephone call to ensure the reported incident meets the case definition of a fall. The reason for such an intense method is to minimise recall and reporting bias. Nevitt et al 1989 reported substantial recall bias in reporting of falls with between 13 and 32% of individuals failing to recall events if the recall period ran beyond 3 to 4 months. A recent UK study has suggested that recall bias may not be as substantial as previously estimated and is most problematic with repeat falls (Fleming et al 2008). Within Pre-FIT it is infeasible to measure falls at monthly intervals. Falls are not recorded well in primary care records, and we have excluded this as a possible method.

3.9.3 Health related quality of life/Physical and emotional function/Health Utility.

In line with the ProFANE consensus we will use the SF12 and EQ5D as measures of health related quality of life. Both measures provide health utility data for economic analysis. The SF12 also provides a measure of physical function, engagement in usual activities and mental functioning. These outcomes will be measured by postal questionnaire using the sampling method described above. Nurses will be available to assist with follow up if needs be.

3.9.4 Resource

Health resource use will be ascertained from hospital and primary care records, and from participant self-report (as described above). Apart from expenditure on major elements including nursing, residential home and private health care we do not plan to collect information on personal expenditure.

Table 2: Cost information to be collected.

Primary/community costs	**Local authority/benefits**	**Secondary care**
1. GP contacts 2. Primary care health team contacts 3. GP home visit 4. Primary care health team home visit 5. GP emergency call out 6. Transport costs 7. Community rehab & health care 8. Prescription costs 9. Emergency department contacts	1. Residential home admission 2. Nursing home admission 3. Home help 4. OT/social work 5. Transport 6. Benefits paid out	1. Surgical procedures (by HRG) 2. Hospital admissions (by HRG and procedures) 3. Major investigative procedures 4. Out-patient services 5. Transport costs

3.9.5 Baseline information

We will gain aggregate data on the characteristics of the practice populations to include age profile, gender and previous fractures. Allpeople approved by the practice for approach will be asked to provide self-report demographic information at baseline, access to medical records over time and to participate in follow up by postal questionnaire and/or telephone interview. Information requested at baseline will be SF12, EQ-5D, frailty measure, and number of falls and fractures in the last year.

3.9.6 Blinding

Researchers responsible for data entry will be blind to the allocation of participants, as will statisticians. It is not possible to blind participants to the treatments they are receiving, or the health care professionals delivering them.

3.10 Sample size estimation

There are a three comparisons [1] Advice versus exercise [2] Advice versus MFFP [3] MFFP versus exercise. The last comparison is the important driver of the sample size. The costs of delivering MFFP are of a scale of approximately 3 times greater than exercise, MFFP will have to prove substantially more effective than exercise to be cost-effective (ie superior).

3.10.1 Primary outcome

We have used a variety of studies to inform our estimates of fracture rate. The most robust and recent estimate of fracture incidence in the general population (age and sex stratified) is from Donaldson et al 2008, with supplementary information from van Staa et al (2001).

In the UK, the annual incidence of reporting one or more fractures is 2.6 per 100 for ages 55-74, and 7.6 per 100 for women of the same age band. Adjusting for differences in gender in the general population (Population summary ONS 2006 Serive VS no 33 PPL no 29) yields a fracture rate of 6 per 100 people (6%) over the age of 70 years but does not account for repeat fractures within a person and hence is a conservative estimate of the fracture rate.

Table 3: Sample sizes for fracture end-points

Fracture incidence Control	Fracture incidence interventions	Relative Risk	Sample size **per arm** 80% power p<0.05
6%	4%	0.67	1872
6%	4.2%	0.70	2356
6%	4.5%	0.75	3489

We have powered the trial to detect a moderate difference in peripheral fracture rate. To detect a 2% reduction in fracture rates, i.e. from 6% to 4% (relative risk reduction, 0.67), using 80% power and significance level of 0.05, 1872 participants per arm or 5616 overall would be required.

3.10.2 Further clarification on sample size

The trial is cluster randomised and hence requires inflation to account for design effects. The unit of randomisation is the general practice. Qualifying eligibility for the unit of randomisation is being a member of the general practice and being aged over 70 years

A typical general practice will have 500-700 patients who meet these criteria; we will seek to recruit just 150 of these. There is little statistical advantage from recruiting a larger number per cluster. We have estimated the total number of patients required and the number of GP practices needed assuming for varying degrees of design effect (i.e. for different ICC values ranging from 0.001 to 0.003) and allowed for 10% of patients who may either die or are lost-to-follow up. Previous studies conducted with this age group, and using similar record and self reported outcomes have yielded high levels of follow up (Grant et al 2006; Fletcher et al 2004) (Table 4). We aim to go mid-range and therefore will be recruiting approximately 60 GP practices with 9000 patients.

Sample size estimates for varying ICCs and fixed recruitment of 150 participants per practice

ICC	Practice recruitment target	Number of practices required	Number of patients required
0.0010	150	50	7464
0.0015	150	54	8076
0.0020	150	58	8688
0.00226	**150**	**60**	**9006**
0.0025	150	62	9300
0.0030	150	66	9911
0.0040	150	74	11135

We have planned for a mean cluster size of 150. We have estimated the design effect from a variety of sources. (Eldridge et al 2006) in planning for a study of fracture prevention interventions reported small intra-cluster correlation co-efficient of 0.000224 for primary care groups serving populations of approximately 100,000. Although we recognise that the unit of randomisation we are dealing with is significantly smaller, given our current knowledge of other primary care clustering effects, we have opted for a lower rather than higher ICC. The options we have chosen are well within the range of expected values for similar variables in primary care (Adams et al 2004). The ICC will need to be monitored very closely during the trial. We realise that the sample size is sensitive to a whole range of assumptions (not just design effect). However, we anticipate being able to cope with relatively large variations within the sample size with the funding applied for. The main driver of costs will be number of practices needed. The costs of following up individuals are relatively smaller. The relationship between cluster size, ICC and, co-efficient of variation will be re-modelled at the end of the feasibility phase. Using fracture as the primary end-point necessitates a substantial sample size we will therefore have ample power for all of our secondary outcomes.

3.11 Analysis of data

Analysis will be by intention to treat. Initial data presentation will focus on simple graphical and tabular summaries, and will follow CONSORT reporting standards. For data aggregated at the practice level we will use cluster level analysis weighting by cluster size. Otherwise we will use individual level marginal modelling (population averaged model) using generalized estimating equations. Link functions will vary depending on the type and distribution of data. For fracture and falls data these will be either poisson or quasi-likelihood (falls data often has problems related to over-dispersion). All estimates will be reported with a 95% confidence interval. Initial comparisons will be drawn between advice and the two other arms, and between exercise and MFFP. A relative hazard for time to first fracture will be calculated. All modelling will account appropriately for multiple fractures within one individual (Schaubel 2005). Data analysis will be carried out using SAS.

All individuals will be included in the analysis regardless of whether they have changed address or moved into a nursing or residential home, provided that they remain registered with the GP practice.
The frequency of analysis will be determined in conjunction with the DMEC at the outset of the trial.

3.12 Planned sub-group analyses

We have selected sub-group criteria using simple data available in primary care –
[1] Age. We will examine whether interventions are best targeted to the oldest old ((<=80 years or > =81 years).

[2] Gender – there is considerable excess risk of falling and fracture in women.
[3] Cognitive impairment – although we are unlikely to encounter large numbers of people living with severe cognitive impairment, the ability to engage in falls prevention strategies may be affected by mild to moderate levels of cognitive impairment. The most likely indicators we will use for cognition are prescription records for drugs relating to dementia and cognitive impairment, along with consultations for the same.
[4] Previous history of falls in the last 12 months. This is not well recorded in primary care, and hence will be depend on individual returns.

Sub-group effects will be tested through formal interaction tests (Brookes et al 2001). Power for sub-group effects is adequate to detect larger interactions provided variance in the sub-groups is reasonably similar (Brookes et al 2001).

We will seek ethical approval to allow us to have access to information on the age and gender of non-responders (anonymised) so that we can consider and estimate this bias.

3.13 Economic analysis

The most significant costs associated with falls are long term care costs (Chrischilles et al 1997), although these are likely to be relatively infrequent in the community dwelling population. Hospitalisation costs are likely to predominate, along with rehabilitation costs associated with post-fall management (Rizzo et al 1998). The economic analysis will therefore focus on the following major components of costs: NHS primary and secondary care, local authority care, the costs of other agencies or organisations, costs associated with institutional care and home care support (summarised in Table 2). Intervention costs will reflect the costs necessary to implement the fall prevention strategy in clinical practice, including development and training, the fall screening technology, overheads, equipment, and staff-related expenses.

Two economic evaluations will be undertaken – *a within trial evaluation* will compare the outcomes and cost during follow up and, secondly, *a decision analytic cost effectiveness model* will be used to estimate the expected incremental cost per life year gained for each of the interventions in comparison to advice only, and if appropriate, in comparison to one another. For both analyses, the perspective will be that of the UK NHS and social services.

The within trial analysis will compare the costs and outcomes between the study arms at the end of follow up. The primary outcome measure will be the QALY. We will also calculate the cost per fracture prevented. Utility weight will be taken from the UK General Population tariff for the EQ-5D (Dolan et al Medical Care 1997, Kind BMJ 1999). Unit costs will be taken from national databases including the NHS reference costs and the PSSRU costs of health and social care. Where national unit cost estimates are not available unit costs will be agreed in consultation with Trusts recruiting to the study. In line with current recommendations for best practice in economic analyses, costs and outcomes will be discounted at 3.5% per annum. Probabilistic sensitivity analysis will be undertaken using the non-parametric bootstrap.

The decision analytic cost effectiveness analysis model will use a lifetime time horizon to capture the full impact of any mortality differences on the long term cost effectiveness. It is likely that the model will have a semi-markov structure to capture the time trend in the underlying risk of mortality, health related quality of life, and costs of care. The methods for estimating health related quality of life and utility, unit costs and discounting will be the same as for the within trial analysis. Probabilitstic sensitivity analyses will be undertaken using monte carol simulation techniques. The outputs reported from the analysis will be the same as for the within trial analysis.

4. Ethical and governance arrangements

This study is a cluster randomised trial of a complex intervention and therefore raises a number of ethical issues including consent to cluster randomisation, individual consent to the intervention, participation in research assessments and access to records. We have substantial experience of successfully conducting trials of this type and will take appropriate steps to address these issues.

- Involvement of relevant user groups to inform the design and implementation of the trial.
- The practices will consent to randomisation, to providing the interventions, and to approaching potential participants to take part in the outcome assessments.

- Individual consent will not be obtained for the intervention as part of a research study. However consent to the active interventions of exercise or multi-factorial falls prevention programme will be obtained from all individuals as part of clinical care, following best practice guidance on consent to treatment.
- Individual consent will be sought for access to medical records and to postal or telephone follow up.

We do not anticipate particular difficulties with this approach, and our study team includes an ethicist who will support us in developing an appropriate ethical framework.

4.1 Risks and anticipated benefits for trial participants and society.

The risk are small. There is a small risk of increased falls in response to exercise interventions (all three arms of the trial will encourage more physical activity). Of 29 studies on exercise for falls prevention only one reported an increased fall rate (in unsupervised walking). Overall the consensus is that the health benefits of exercise outweigh the risks substantially. The main serious risk is of fractures and cardiovascular events occurring during exercise sessions, but these are extremely rare events and we anticipate an overall reduction in these over the lifetime of the study. We are not utilising aerobic exercise, so stress on the cardiovascular system will be minimal. We will monitor the incidence of such serious events during supervised exercise sessions. We will monitor time to first fracture as our main safety outcome measurement. We anticipate that a successful trial will yield substantial societal benefits. Either we will demonstrate that one or both of our trial interventions has a significant overall health benefit which if implemented nationally will produce substantial health gain for the older population, or we will demonstrate that these approaches are ineffective or not cost-effective allowing NHS resources to be re-directed to other, more effective interventions.

4.1.1 Informing potential trial participants of possible benefits and known risks.

As described above all participants who are offered the active interventions will be provided with information about the benefits and possible known risks of the intervention as part of the consent process according to best practice in clinical care.

4.2 Obtaining informed consent from participants.

We will obtain informed consent to follow-up from participants. The approach will be by mail, with a return slip indicating either

- They agree to participate in the study,
- they decline to participate, or

We will seek ethics approval for anonymous data on the age and gender of those patients approached so that we can consider the effect of recruitment bias.

4.3 Proposed time period for retention of relevant trial documentation.

5 years.

4.4 Trial sponsorship and independent oversight

The trial will be sponsored by Warwick University. The trial will be overseen by an independent data monitoring committee (3 independent members + trial statistician), and a trial steering committee that will comprise a minimum of three independent members, the senior investigators, the trial statistician and co-ordinator. Users will input into the trial as described in a following section.

4.5 Proposed action to comply with 'The Medicines for Human Use (Clinical Trials) Regulations 2004'.

This is not a medicinal trial. We will be compliant MRC GCP guidance. The trial will be run in accordance with the standard operating procedures of the Warwick Clinical Trials Unit, which has been given full UK-CRN accreditation.

5. Timetable, including feasibility study

This will be a complex trial to undertake but based on our prior experience of working in primary care, and the support we have from the falls prevention community it is achievable. At several points in the application we have discussed a feasibility stage. We have identified that the main risk to the success of one or more of the interventions is uptake. The main risk in terms of design is the estimate of fracture incidence in the control arm, and whether we are able to set up sufficient localities. We are proposing a feasibility phase that will report by 24 months. The aims will be

[1] Finalise the methods of delivering the interventions, focusing on refining and implementation methods and maximising the potential for uptake. This will involve agreeing the final elements of the intervention packages and setting the benchmarks for training and competency. It is essential to gain stakeholder buy-in this process from various professional bodies.
[2] To engage user perspective and involvement (see next section).
[3] To develop and test the mechanisms for data capture as described previously. We will compare the accuracy of primary care records and HES alongside self-report.
[4] To deliver the intervention packages and training in one locality and evaluate the effectiveness of the training. To train and launch about 12 practices in the research processes.
[5] To assess the level of uptake of the intervention for the exercise and MFFP arm in one locality.
[6] Develop a futility analysis for the trial. We will need to extend and refine the framework developed by Eldridge et al 2004, to include a linked monitoring plan.
[7] Undertake a detailed scoping exercise on a variety of localities and agree NHS costs and approvals for each locality.

A project timetable is provided overleaf (Table 6). The feasibility phase in shown in grey shaded area. We will launch one region during the feasibility phase, and recruit sufficient practices to maintain a minimum recruitment base of 10 practices. The feasibility site will continue to recruit whilst we undertake the first stage of our futility analysis, working on the premise that it is unwise to halt recruitment once a locality has been launched.

We will develop a framework for a futility analysis (FA) during the feasibility stage. This would be a significant methodological extension to current data monitoring techniques for academic and complex intervention trials. The FA will incorporate various elements of conditional probability modelling to determine whether the interventions proposed have a chance of being either effective or cost-effective. We anticipate that the futility analysis will be inform as to whether uptake is sufficient to ensure the intervention has a reasonable chance of being effective. We would expect the TSC, DMEC and funder to review the viability of the trial at 24 months.

As part of the feasibility study we will be approaching primary care trusts, practices and the UK Primary Care Research Network to and these regions will have to be selected to ensure that they have an existing infrastructure that allows for the delivery of community based exercise classes and a MFFP clinic that comprises a multi-disciplinary team. We know from a national survey that we have conducted that there are 50 PCTs in the area that meet these criteria. However, we will have further requirements. The clinics and services need to be willing to deliver a standardised intervention package and to change some aspects of their practice. We do not anticipate that this will be a difficultly, as there is broad support from the practice community for this trial. The final negotiations will be to identify the amount of additional NHS cost needed in each area.

Assuming that the trial is feasible, we will continue to launch localities and practices from 20 months onward (when we will have the preliminary results of our feasibility). We will aim for each practice to return a minimum of 150 people to the analysis, based on up to 60 practices participating. We may modulate this to a larger number of people, and fewer practices, but we need to build in the possibility that some practices will drop out. The total possible number of person years of follow up is 163500, but this assumes no mortality or drop out. Table 7 gives the recruitment targets in terms of the number of practices to be launched each month, as well as the number of participants to be accumulated. All practices will be followed up for a minimum of 12 months. Those practices recruited earlier will contribute >12 months of follow up.

Table 6 Proposed project timetable (figure is months in which task is running)

Month of completion	**-6**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	**33**	**36**	**38**	**42**	**45**	**48**	**51**	**54**	**57**	**60**
MREC and feasibility site agreements	*																				
Refine approach materials		*	*				*	*													
User consultations			*	*				*	*											*	*
Ethics appraisal	*							*	*				*	*	*	*	*	*	*	*	*
Finalising interventions/		*	*	*																	

Training																					
Site evaluations			*	*	*	*															
Site agreements				*	*	*	*														
Feasibility study Recruitment					*	*	*	*	*	*	*										
Develop framework for futility analysis		*	*	*	*																
Feasibility/futility appraisal									*	*	*										
Main trial recruitment								*	*	*	*	*	*								
Last follow up completed																	*				
Record searches							*	*	*	*	*	*	*	*	*	*	*	*	*		
Data entry and cleaning						*	*	*	*	*	*	*	*	*	*	*	*	*	*		
Data base closed																			*		
Health economics		*	*	*	*				*	*								*	*	*	*
Statistical services		*	*	*	*				*	*		*		*		*		*	*	*	*
Implementation Appraisal	*	*	*	*	*							*	*	*	*	*	*	*	*	*	*
Preparation of final reports and disseminations																					*

Table 7 Proposed recruitment targets

Month	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26-34**
Stage	**F**	**F**	**F**	**F**	**F**	**M**	**M**	**M**	**M**	**M**	**M**	**M**	**M**	**M**	**follow up**
New practices per month	2	2	2	2	2	4	4	6	6	10	10	6	4	4	0
Cumulative practices	2	4	6	8	10	14	18	24	30	40	50	56	60	64	0
Number of participants per month	300	300	300	300	300	600	600	900	900	1500	1500	900	600	600	0
Number of participants (cum)	300	600	900	1200	1500	2100	2700	3600	4500	6000	7500	8400	9000	9600	9600
Number of months of follow up	25	24	23	22	21	20	19	18	17	16	15	14	13	12	
Maximum person yrs follow up	7500	7200	6900	6600	6300	12000	11400	16200	15300	24000	22500	12600	7800	7200	
Number of individuals per practice		150													
Maximum possible person yrs follow up	163500														

F = Feasibility M= Main

5.1 Further clarification of futility analysis

At this stage we are not able to specify these parameters because of the amount of work that is involved in developing the model. In pharmaceutical trials, futility analyses are relatively simple and based on a one-sided stopping rule on the primary outcome measure. For a health technology assessment trial, there are many more parameters to consider. The first (and by no means least) is how we define what is effective. Members of our team have undertaken modelling to determine futility and we will utilise this as an initial template but it requires careful (and time consuming) thought.

One approach is to define effectiveness using a net benefit measure where the trial will go ahead after modelling the pilot data if there are potential net benefits to implementation

$R\Delta E - \Delta C > 0$

Where
R - the amount the government is willing to spend to achieve a given improvement in health.
E -Effects of the intervention
C - Costs of the intervention

The drivers for effectiveness of the intervention (E) are likely to be as follows:
1. The number of older people who respond to the invitation to undertake a self assessment and participate in an intervention.
2. The number of people who will have at least one risk factor for falls.
3. The number of people who have one risk factor for falls and are referred to the appropriate intervention
4. How many of those referred, or assessed and not referred will get preventive treatment/
5. The effect of the intervention on those individuals who receive it.

We will need to think about this very carefully. It is possible that a multi-factorial fall prevention intervention will reduce falls, improve quality of life, but have no impact on fractures. It seems sensible to model E based on HQoL. The estimation of R is traditionally difficult and not explicit and we need to think about what we do with this.

We anticipate that we would use this trial as a vehicle for developing methods of futility analysis, and construct a model which tells us the probability of the intervention providing net benefit at the end of the pilot. The process will require us to build a model, populate the parameters with either data gained during the pilot or by a systematic literature search. We are not in a position to do either of these (or construct the models) at this stage.

5.2 Trial management

The trial will be managed using the principles of modern project management, including target setting and regular review and action to ensure both a high quality result, and adherence to the proposed timetable. Trial progress will be monitored on a weekly basis by the Chief Investigator, Senior Project Manager (SPM) and Trial Co-ordinator, and by the trial team on a monthly basis. The SPM is responsible for staff recruitment, and ensuring that trial staff are appropriately supported. Warwick University has a well-established framework for the management and supervision of academic performance and staff, including a minimum of annual appraisal for contract staff. Investment and availability of training is excellent.

6. Completed preparatory work

We have completed substantial amounts of preparatory work in support of this trial application. These include testing the acceptability of various advice and self-assessment strategies (Yardley et al 2006a), and appraisal of psychological factors associated with uptake of exercise (Yardley et al 2007a). In 2005 we undertook a series of systematic reviews and consensus building exercise to determine the most appropriate methods of measuring outcome (Lamb et al 2007). Eldridge and Underwood have developed a precursor for modelling futility (Eldridge et 2004). Lamb and McCabe have led a scoping review to determine the feasibility of economic modelling, undertaking as part of that process an extensive review of the literature, and national service mapping exercise (Gates et al 2008; Lamb et al 2007) enabling us to determine potential sites. We have also engaged sites in preliminary feasibility discussions for a main trial.

7. User involvement

We are able to benefit from the NHS Centre for User Involvement that is based at the University of Warwick, which is working with us to improve the methods we utilised to engage user involvement. User involvement (patients, carers and the public) will act in two capacities within the trial: 1. as co-investigators ('partners' in the research process – used here to refer to user involvement) and 2. as data providers (User Perspectives - feasibility study). User involvement will not be a 'stand-alone' activity but rather an integral part of the trial. A representative from Help the Aged has been involved in some of preparatory work and will be nominated as a member of the Trial Steering Committee.

Involvement will happen through a combination of consultation, collaboration and user-led activity (using guidance provided by INVOLVE, 2007). A minimum of two users will be invited to be part of the project tream. An invitation to be involved will be through established mechanisms (e.g. People Bank Partnership and UNTRAP, University of Warwick) and by contacting target groups e.g. Help the Aged. A virtual user advisory group (maximum 10 people – facilitated by email) will also be developed to provide further user support to the project as appropriate. All leadership and support for user involvement will be provided by Dr Herron-Marx (National Centre for Involvement). User involvement will contribute to:

[1] The trial steering committees and project management decisions on all stages of the project
[2] The project approval through NRES
[3] The refinement of the self-assessment tools
[4] The refinement of the Optimised Advice Package (OAP), exercise intervention and MFFP.
[5] The training events for the health professionals
[6] The interpretation of the findings – through the development of recommendations for practice and any relevant tools for instance, older people information leaflets
[7] The evaluation of user involvement in the trial.
[8] Dissemination through user networks

The trial will involve parallel data collection to gather user perspective on the ethical framework of the trial. Users will be involved closely in this process, and will participate in data capture, analysis and interpretation. We will explore the utility of a conversation café approach (CCA, conversationcafe.org) in comparison to others methods of accessing user views on ethics.

7.1 Evaluating involvement

The proposed trial provides an opportunity to develop user research capacity for future trials and the opportunity for user voices to develop recommendations and tools to support clinical practice. It is imperative to evaluate involvement in this trial from a multi-stakeholder (members of the project team and the user advisory group) perspective. This will inform the design of future studies with significant user involvement. A focus group consisting of all the stakeholders will be conducted at the end of the project. An independent user researcher will facilitate this, as well as undertaking the analysis. Lessons learned and futures recommendations will be disseminated widely.

8. Implementation appraisal

Each of the interventions that will be tested will be documented in a standardised manual format, in accordance with MRC guidance on the evaluation of trials of complex interventions (MRC 1999). We will investigate issues relating to implementation throughout the trial through careful evaluation of the processes we implement, and feedback from trial participants and clinicians on various aspects of the interventions. We will utilise parallel qualitative interviews to gain greater insight into the experience of the interventions. Our implementation appraisal will also consider the possibility that disinvestment in services is one of the potential conclusions of the trial.

9. Justification of costs

This is an ambitious trial, and will necessitate an experienced team to bring it to a successful completion. The trial involves limited face-to-face contact with participants. The majority of individual follow up will be ascertained by postal follow up although there is likely to be a small number of people who require either telephone or proxy follow up. We will utilise staff who are experienced with communicating with members of the general public, they will be either healthcare professionals, or trained non-professionals. The trial will require careful negotiation to pull together sufficient numbers of practices, exercise and MFFP services, and significant expertise in health informatics. We have requested a principal research fellow to lead and undertake this work, and they will take responsibility for the day-to-day management of the academic and logistical aspects of the project. They will be supported by a senior project manager (fractional appointment) and a trial co-ordinator. We have electronic data capture methods available, and we will endeavour to build these into the project wherever possible, minimising the amount of data entry clerks needed, and the carbon foot print of the trial. We have included senior investigator costs (some of which we anticipate being offset against our recent HTA pump priming funding).The trial also includes cost contributions towards a research fellow who will work with the team to develop and deliver the training, to contribute to process evaluation work, appraisal of user involvement methods, and qualitative research. We include costs for Herron Marx from the NHS Centre for Involvement, to cover the costs of her contribution to the trial, which are not covered from any existing funding mechanism. We have specified travel costs recognising that the trial will require a substantial amount of travel to establish, maintain and support sites. We have requested a full time research nurse for each of the sites, and hope to secure additional research nurse support from the research networks. We

have included a payment to each practice (that will be staged according to achievement of targets) of £4000 to cover the costs of list searches for participant approach, time to attend research training, quarterly searching of practice based records for fracture and other events, and supporting research nurses in accessing clinical records for data capture.

Our estimates of NHS costs are based on the feasibility site of Coventry and are for the Coventry site only at this stage. Each area will have a unique configuration of services, and services in each area will need to accommodate approximately 400 additional contacts (roughly split between MFFP and exercise) during the trial. Treatment costs will need to be injected because of this increased demand, although at this stage we confirm exactly where. Therefore we have estimated excess treatment resource to be a minimum of 70 consultant contacts and 300 outpatient contacts (or equivalent if provided in primary care) and a technical exercise instructor for two years.

Amendments to costs

1. ***The feasibility study will run in years 1 and 2 (£906,588; £936,450 including NHS costs) and the main trial in years 3 to 5 (£1,603,260; £1,724,710 including NHS costs). Total cost of the trial £2,509,848 (£2,661,160 including NHS costs).***
2. ***Based on the HTA's comments have:***
    a. Re-assigned the research nurse costs as non-HEI.
    b. Inserted costs for welcome visits.
    c. Have left the dissemination costs as they stand. They cover the costs not only of dissemination, but also training for a very large team of people who will be involved in this study, and all of the costs related to feeding back results to practices that participate, all the services that participate, and the patients who participate. We are mindful of value for money and will limit the number of overseas trips to 2.
    d. Removed £9,000 of recruitment costs – these relate to recruitment of staff. As not all posts fall to HEI we have left £5,000 to cover the costs of nurse recruitment.
3. ***Adjusted NHS costs following a teleconference with Trudi Simmons***
    a. Checked that the £200,000 for practice research costs have been appropriately apportioned and costed. Trudi confirms that they are, and hence they have been retained in the same section.
    b. NHS excess treatment costs were provided for Coventry only. Trudi has advised that in the absence of better information, these costs should be used as the indicative costs across the other PCTs. Hence the excess treatment costs have been inflated by a factor of 5.
    c. Trudi advised that the NHS excess treatment costs of £659 should have been assigned as research costs. As they are a cost for each cluster, and we had only provided costs for the Coventry cluster, they have been inflated by a factor of 5 and re-submitted as a research cost.
    d. We discussed the role of the NHS networks which is unclear at the moment. We will modify the split between research and NHS costs at a later date if needed.

10. Role and expertise of the team

The responsibilities of each member of the trial are detailed in section 2.1. The trial team comprises senior and experienced investigators. Lamb is Director of the Warwick Clinical Trials Unit, and has experience of leading trials of complex interventions in both primary and secondary care. She is a recognised expert in fall prevention and injury management and rehabilitation. She is an NiHR Senior Investigator. Lamb is a co-author of the Cochrane review group for interventions to prevent falling in community dwelling older people. We have recently updated the 2003 version of the Cochrane review (update as yet unpublished), have published several high quality systematic reviews of interventions and screening methods (Gates et al 2007), and completed a scoping exercise for an economic evaluation of fallers clinics commissioned by NCCSDO/NICE (Lamb et al 2007). Underwood is an academic general practitioner and trialist and has a wealth of experience in recruitment and data capture in primary care. Friede and Eldridge provide statistical expertise on data monitoring, sample size re-estimation for count data and cluster randomised trials. McCabe is a health economist with expertise in decision analytic modelling. Martin and Oliver are geriatricians who are

academically active at an international level in falls prevention. Duggan is an experienced senior project manager, having managed trials in both industry and academia. Yardley is a health psychologist with academic and practical expertise in self-assessment and motivational strategies with older people. Slowther is a general practitioner and ethicist, with a particular interest in the issues and acceptability of cluster randomised trials in a variety of settings. Herron-Marx is a Principal Research fellow at the NHS Centre for Involvement and has extensive experience of research involving patient and public involvement in the NHS. The trial will be run and managed in the fully accredited Warwick Clinical Trials Unit by experienced and well-supported staff.

11. Other trials in progress

We have searched research registers to identify trials in progress. There are no large scale trials that use fracture as an end-point. An RCT of 312 high-risk people in New Zealand has examined MFFP versus usual care. A small UK study (MFFP versus usual care in a Day Hospital setting) was due to report in mid 2007, no results are available as yet (N = 400) (Masud et al 2006). A small study is underway in the Netherlands (N= 200), again comparing MFFP versus usual care (Geeske MEE et al 2007). None of these studies have made comparisons to treatments other than usual care, used fracture as an end-point, conducted a comprehensive economic analysis, and two fail to comply with recognised methods of measuring and analysing fall data (Lamb et al 2005

12. Dissemination strategy

Dissemination will be through a mixture of traditional academic routes (peer reviewed journal papers, conference presentations etc), and user dissemination. This trial application does not include costs for dissemination into the practice community in the form of training, although we will publish the clinical protocols and manuals on a web-forum and in paper based format.

13. References:

Adams G, et al (2004). J Clin Epidemiol 57:785-94.AGS/ BGS/ AAOP (2001). J Am Geriatr Soc 49(5): 664-672./Boutron, I., et al. (2008). Ann Intern Med 148(4): 295-309./Brookes, S. T., et al. (2001). Health Technology Assessment 5(33)./Campbell, A. J. et al. (2007). Age & Ageing 36(6): 656-62./Close, J., et al. (1999). Lancet 353(9147): 93-7./Cumming, R. G., et al. (1990). Ann Epidemiol 1(1): 49-56./Cummings, S. R., et al. (1998). J Am Geriatr Soc 36(7): 613-6./Donaldson, L. J., et al. (2008). J Epidemiology & Community Health 62(2): 174-80./Eldridge, S., et al. (2005). J Health Services & Research Policy 10(3): 133-42./Eldridge, S. M., et al. (2006). Int. J. Epidemiol. 35(5): 1292-1300./Elley, C. R., et al. (2007). BMC Public Health 7: 185./NICE. (2004). Clinical guideline 21. /Fleming, J., et al. (2008). BMC Geriatrics 8: 6./Fletcher, A. E., et al. (2004). Lancet 364(9446): 1667-77./Gates, S., et al. (2008). BMJ 336(7636): 130-3./Gillespie, L. D., et al. (2003; 2008 in press). Cochrane Database of Systematic Reviews(4): CD000340./Grant, A. M., et al. (2005). Lancet 365(9471): 1621-8./Hendricks et al 2008 Int J HTA 24:2 193-202./ NSF for older people. DoH. 2001 London./Lamb, S. E., et al. (2007). (NCCSDO published report)./Lamb, S. E., et al. (2005). J Ameri Geriatr Soc 53(9): 1618-22./Lamb, S. E., et al. (2008 in press). J Gerontol./Lord SR, et al. (2005). J Am Geriatr Soc/Masud, T., et al. (2006). Trials 7./Nair, V., et al. (2008). Am J Public Health 98(8): 1354-1359./Nevitt, M. C., et al. (1992). Am. J. Epidemiol. 135(5): 490-499./Peeters, G. M. E. E., et al. (2007). BMC Geriatrics 7: 15./Physicians, R. C. o. (2007). National Clinical Audit of Falls and Bone Health in Older People. T. H. Commission. London./Rubenstein LZ et al J Am Geriatr Soc 2007 55 (2): 166-74./Schaubel et al Biometrica 2005 6 (3) 404-19./Tinetti, M. E., et al. (2008). N Engl J Med 359(3): 252-261./Tinetti, M. E., et al. (1994). N Engl J Med 331(13): 821-827./Tinetti, M. E., et al. (2008). Update of AGS/BGS/AAOS guideline on prevention of falls in older people. New York./Tinetti, M. E., et al. (1988). N Engl J Med 319(26): 1701-07./van Staa, T. P., et al. (2001). Bone 29(6): 517-22./Yardley, L., et al. (2007). Quality & Safety in Health Care 16(3): 230-4./Yardley, L., et al. (2006). Health Education Research 21(4): 508-17./Yardley, L., et al. (2007). J Gerontol Series B- 62(2): P119-25. Strawbridge, W., S. Shema, J. Balfour, H. Higby & G. Kaplan (1998) Antecedents of frailty over three decades in an older cohort. *J Gerontol B Psychol Sci Soc Sci,* 53**,** S9-16.

Flow diagram

PRIMARY CARE PRACTICES IN 5 LOCALITIES IN THE UK