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Title page

Cost-effectiveness of a multifaceted podiatry intervention for the prevention of falls in older people: The REFORM trial findings

Short title: REFORM trial cost-effectiveness findings

Byline

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Abstract

Background: Falls are a major cause of morbidity among older people. Multifaceted interventions may be effective in preventing falls and related fractures.

Objective: To evaluate the cost-effectiveness alongside the REFORM (REducing Falls with Orthoses and a Multifaceted podiatry intervention) trial.

Methods: REFORM was a pragmatic multicentre cohort randomised controlled trial in England and Ireland; 1010 participants (>65 years) were randomised to receive either a podiatry intervention (n= 493), including foot and ankle strengthening exercises, foot orthoses, new footwear if required, and a falls prevention leaflet, or usual podiatry treatment plus a falls prevention leaflet (n=517). Primary outcome: incidence of falls per participant in the 12 months following randomisation. Secondary outcomes: proportion of fallers and quality of life (EQ-5D-3L) which was converted into quality-adjusted life years (QALYs) for each participant. Differences in mean costs and QALYs at 12 months were used to assess the cost-effectiveness of the intervention relative to usual care. Cost-effectiveness analyses were conducted in accordance with National Institute for Health and Clinical Excellence reference case standards, using a regression based approach with costs expressed in GBP (2015 price). The base case analysis used an intention to treat approach on the imputed data set using multiple imputation (MI).

Results: There was a small, non-statistically significant reduction in the incidence rate of falls in the intervention group (adjusted incidence rate ratio 0.88, 95% CI 0.73 to 1.05, p = 0.16). Participants allocated to the intervention group accumulated on average marginally higher QALYs than usual care participants (mean difference 0.0129, 95% CI -0.0050 to 0.0314). The intervention costs on average £252 more per participant compared to usual care (95% CI -£69 to £589). Incremental cost-effectiveness ratios ranged between £19,494 and £20,593 per QALY gained, below the conventional NHS cost-effectiveness thresholds of £20,000 to £30,000 per additional QALY. The probability that the podiatry intervention is cost-effective at a threshold of £30,000 per QALY gained is 0.65. The results were robust to sensitivity analyses.

Conclusion: The benefits of the intervention justified the moderate cost. The intervention could be a cost-effective option for falls prevention when compared with usual care in the UK.

Trial registration number: ISRCTN68240461

INTRODUCTION

Falls are common among older people with a high cost to health care systems and society [1-3]. The cost burden of falls to the UK National Health Service (NHS) is estimated of more than £2 billion per year [4]. Given that the number of people over the age of 65 is predicted to increase, we might expect the cost of falls to the NHS to rise further every year. It has been suggested that podiatry care play a role in falls prevention, as cohort studies have indicated a relationship between risk of falling and both foot and ankle problems [5, 6] and inappropriate footware [7]. There is evidence that a multifaceted podiatry intervention –which combines foot and ankle exercise, foot orthoses, foot advise and a falls prevention booklet combined with routine podiatry care - is effective at reducing the incidence of falls among older people in an Australian setting [8]. This trial did not include an economic evaluation.

The REFORM (REducing Falls with Orthoses and a Multifaceted podiatry intervention) trial evaluated the clinical and cost-effectiveness of a multifaceted podiatric intervention aimed at reducing the incidence of falls among people at high risk of falling within the UK setting [9]. There was a non-statistically significant reduction in the incidence rate of falls in the intervention group [adjusted incidence ratio 0.88; 95% confidence interval (CI) 0.73 to 1.05; p=0.16]. However, the proportion of participants experiencing a fall was reduced (50 vs 55%, adjusted odds ratio 0.78; 95% CI 0.60 to 1.00; p=0.05). Hence, there is a potential to improve health related quality of life (HRQOL) by preventing falls and to reduce health care costs. From an economic perspective, the recommendation is that estimation, and not hypothesis testing, be used to inform decision making for resource allocation in health care [10]. Therefore it remains important to assess whether the benefits of the intervention justify the extra costs of providing the multifaceted programme; addressing this will be important in order to deliver improved services to this population that offer good value for money to the NHS. This paper reports on the economic evaluation conducted alongside the REFORM trial.

METHODS

Overview

We conducted a pragmatic open two-arm, cohort randomised controlled trial [11] with an economic evaluation. The REFORM protocol has been published elsewhere [12]. In summary, participants were recruited to an observational cohort study from podiatric clinic lists in the UK and the Republic of Ireland and followed up for falls data. Participants, who fulfilled the REFORM trial eligibility criteria, were then randomised into the trial, when podiatrists had capacity to deliver the trial intervention. All participants received routine podiatry care which typically aimed to reduce painful conditions such as corns, callouses and pathological nails, which have been found to be associated with an increased risk of falls. In addition to this, all participants received a falls prevention leaflet produced by Age UK (Staying Steady June 2010) along with a group specific trial newsletter informing them about the progress of the trial. Participants allocated to the intervention group additionally received footwear advice, provision of new footwear if current footwear was judged to be inappropriate (supplied by Hotter Footwear® and DB Shoes Ltd); foot orthoses (x-line®, Healthystep, Mossley, UK); and a 30 minutes a day, three times a week home-based foot and ankle exercise programme supplemented with a DVD and explanatory booklet [8]. Intervention participants were invited to attend two podiatry appointments, with further appointments offered if required.

A cost-utility analysis with health outcomes expressed in terms of quality-adjusted life years (QALYs) in accordance with the NICE (National Institute for Health and Clinical Excellence) reference case [13] was undertaken. Cost-effectiveness in terms of cost per fall everted was assessed for comparison. The evaluation took the perspective of the NHS and personal social services for a time horizon of 12 months; with costs presented in UK pounds sterling at 2015 prices. A regression approach on an intention-to-treat basis was used. The base-case analysis was conducted on the dataset generated by multiple imputation (MI) methods [14]. Sensitivity analysis included complete-case (CC) analysis to test the impact of excluding participants with missing data on the final results. All analyses and modelling were conducted in Stata 13.1 (StataCorp 2011, TX, USA).

Health outcomes

The primary outcome measure was QALYs. Therefore, in addition to the participant-reported outcomes described in the clinical paper [9], participants also completed the EQ-5D-3L (EuroQoL Group Rotterdam, The Netherlands) at baseline, six and 12 months post-randomisation. The EQ-5D-3L is comprised of five dimensions of health status (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with three severity levels (no, some, extreme problems/unable to) for each dimension. The EQ-5D has been recommended by The Prevention of Falls Network Europe Consensus as a measure of health related quality of life (HRQoL) in trials [15] and has been used before in UK settings assessing HRQoL implications of falls in older people [2]. The EQ-5D-3L health states were converted into utilities using a UK-based social tariff [16]. A utility of one indicates perfect health, a utility of zero indicates "as bad as death", and negative utilities identify states considered worse than death. These utilities were used to weight duration of survival and estimate QALYs, that were calculated using the area under the curve method [17] and were adjusted for baseline utility [18].

Resource use and costs

Resource use associated with falls was collected prospectively using participant-reported questionnaires at baseline, six and 12 months. We collected information on resource use that we considered could potentially relate to the intervention, to allow us to assess the possibility that the provision of the multifaceted intervention prevents costs that would otherwise be incurred. Hence we asked participants to report visits to primary care professionals (General Practitioner (GP) and GP nurse), community care (occupational therapist), hospitalisations (inpatient, day-case, outpatient and A&E) and visits to podiatry clinics. The cost of the podiatry intervention was assessed based on the data collected as part of a baseline appointment questionnaire and the podiatrist database, which included information directly related to the podiatrist assessments and the intervention package received by the participant (e.g. orthosis prescription, exercise programme and exercise equipment). Participants allocated to the intervention would receive at least one baseline visit to the podiatrist plus at least one follow-up appointment. The first appointment was assumed to last for 1 hour; the second appointment for 30 minutes and all the rest were assumed to be the same duration as a GP clinic consultation (11.7 minutes). The cost for the visits was estimated according to NHS pay scales on the Agenda for Change for NHS podiatrist staff in England, Wales, Scotland and Northern Ireland (https://healthcareers.nhs.uk/ glossary#Agenda_for_Change). Podiatrists delivering the intervention ranged from band 6 to band 8. The base-case analysis includes only costs falling within the NHS and, hence, the cost of the provision of new footwear was not considered in the analysis. The total cost per each participant was estimated by multiplying each resource use item by their associated unit costs (**Table 1**).

Handling missing data

Complete case (CC) assessment excludes all participants with any missing or incomplete data. To avoid biases associated with CC analysis [19] incomplete data on cost and QALYs were handled using multiple imputation analysis assuming the data were missing at random (MAR), via chained equations and predictive mean matching [20, 21]. The same set of covariates as in the clinical effectiveness analysis was selected for the analysis (age, sex, history of falls, centre, costs and utilities). Rubin´s rules were used to combine point and variance estimates across imputed datasets, allowing the estimation of the difference in costs and QALYs between both groups. Five imputed data sets were generated as this has been deemed sufficient to obtain valid responses [22, 23]. Despite MI being the most robust method to handle missing data in economic evaluation, we analysed the pattern of missing data following economic guidelines [24] to ensure that the pattern of REFORM data reflects the assumption made for the base-case analysis (e.g. data are MAR). The association between missingness and baseline variables was explored by means of logistic regression.

Base case analysis

The base-case analysis was conducted on the imputed dataset on an intention to treat (ITT) basis, and included only fall-related health care visits. Since the NHS will not cover the cost of the provision of new footwear this was not considered for the base-case analysis.

The cost-effectiveness of the intervention was calculated by comparing the mean differences in expected costs and QALYs between the two groups [25]. If the intervention (or usual care) is less costly and more effective, it would 'dominate' the alternative and hence be considered cost-effective. If not, the incremental cost-effectiveness ratio (ICER) would be estimated as the difference in mean total costs at one year divided by the difference in mean total QALYs for the intervention compared to usual care. The mean estimates and their 95% confidence intervals (CI) were generated by means of seemingly unrelated regression (SUR) using bias corrected and accelerated (BCA) bootstrap methods. According to NICE, the cost-effectiveness threshold (e.g. quantity that the NHS is willing to pay (WTP) per person for an additional QALY ranges from £20,000 to £30,000 per QALY gained. The ICER was also arranged in terms of net monetary benefit (NMB), which translate the health benefits into monetary value using the cost-effectiveness thresholds (e.g. incremental QALYs multiplied by the WTP threshold) [26]. The intervention would be considered cost-effective if the NMB were positive. Non-parametric bootstrapping was used to determine the level of sample uncertainty associated with the mean ICER by generating 5,000 estimates of incremental costs and benefits, represented graphically in a cost-effectiveness plane and a cost-effectiveness acceptability curve that shows the probability that the intervention is more cost-effective than usual care for a range of cost-effectiveness thresholds.

Cost per fall averted

Cost-effectiveness was also estimated in terms of falls prevented following guidelines for economic evaluation of fall prevention strategies [27]. This other form of analysis has the potential to strengthen the case for the multifaceted intervention by exploring the cost per fall averted and how this links to health care saving. The number of falls averted was estimated as the difference in mean reduction in the fall rate between the two groups in the trial estimated as per the adjusted negative binomial model.

Sensitivity analysis

Several sensitivity analysis were undertaken to assess the impact of uncertainty on the economic evaluation. These were conducted to test the robustness of the results using four scenarios: (i) restricting the analysis to CC, assuming the data were missing completely at random (MCAR); (ii) MI by imputing HRQoL at an aggregated level (e.g., at QALYs level); (iii) MI recalculating the average costs including both fall and non-fall resource use; and (iv) MI from a wider societal perspective that included costs incurred by the patients (e.g., cost of the shoes as a personal expense for the patient).

HRQoL beyond the trial

HRQoL was extrapolated to 5 years to explore how the differences in HRQoL evolve beyond the duration of the trial. We used a decision-model approach –using evidence from REFORM trial - assuming (i) two health states (alive and dead); and (ii) the initial podiatry intervention, when displacing usual care, is expected to continue to bring gains of 0.0129 QALYs per patient per year and incur costs of £251 more per year when alive (e.g. incremental cost estimates in the trial are considered fixed over the five years).

RESULTS

Patient population and missing data

The analysis was based on the 1010 trial participants (493 intervention vs 517 usual care). Twenty four participants died during the trial [9 (1.8%) intervention vs 15 (2.9%) usual care]. The proportion of participants with complete data decreased with follow-up: from 72.0% (baseline) to 54.4% (12 months) for the intervention group; and from 71.8% (baseline) to 61.3% (12 months) for the usual care group. The missing data followed non monotonic pattern (i.e. there were participants with missing six month data but complete data at 12 months); showing that complete case assessment would be, as a minimum, inefficient as it would discard observed data from individuals with some missing outcomes. The results of a logistic analysis regression showed that participants that were older (OR 1.04; 95% CI 1.02 to 1.06), with lower EQ-5D at baseline (OR 0.68; 95% CI 0.35 to 1.32), and those with a history of falling (OR 1.26; 95% CI 0.89 to 1.77) were more likely to have missing QALY data. This suggests that data are unlikely to be MCAR.

Resource use and costs

In total, 413 out of 493 (83.8%) participants allocated to the intervention had at least one visit to the podiatry clinic and 183 (37.1%) had at least two. A total of 260 participants received a new pair of shoes. Moreover a total of 241 participants also received a pair of insoles: X-Line red (n = 23), X-Line blue (n = 209) or Formthotics insoles (n = 9). They also received resistive therapy bands and therapy balls for the exercises. The intervention cost on average £115.50 (SD £33.06), and £155.79 (SD £55.02) when the price of the shoes (societal perspective) was included (Table 2). On average intervention participants had more hospital admissions, outpatient visits and A&E attendances related to falls than usual care participants over the trial duration, but had on average fewer falls-related visits to the GP (Table 3). In total, 413/493 (83.8%) participants allocated to the intervention group had at least one visit to the podiatry clinic, and 183/493 (37.1%) had at least two. Costs associated with falls-related hospital inpatient stay and the intervention itself were the major cost drivers for the analysis.

Effectiveness

At baseline, participants reported problems in mobility (59.7% intervention vs 56.9% usual care) and pain (78.4% intervention vs 56.6% usual care) more than in other dimensions. The intervention showed a reduction in the number of participants reporting problems from baseline to 12 months both for mobility (11% intervention vs 1% usual care) and pain (15% intervention vs 10% usual care). The likelihood of remaining in perfect health decreased over time; however the reduction in the number of participants in perfect health in the intervention group (7.4%) was lower than for the usual care group (17.7%). The data also showed that improvement in anxiety/depression was proportionally greater than the other dimensions, especially in the intervention group: 19% reduction in number of participants reporting anxiety problems compared to 1.5% reduction in the usual care group. Participants in the intervention group started from a lower baseline utility on average (0.67 intervention vs 0.70 usual care); differences in HRQoL were very small across the 12 month follow-up and the 95% CIs overlap at each time point (Figure 1). At the end of the trial, the difference in QALYs (intervention – usual care) when controlling for baseline utility (for available cases: n=377 intervention vs n=415 usual care) showed a marginally higher QALY gain for the intervention group (0.008 QALY gain; 95% CI -0.009 to 0.026).

Cost-effectiveness and uncertainty

The incremental analysis (Table 3) shows that on average, the intervention cost £252.17 more per participant when compared to usual care (95% CI £-69.48 to £589.38); but yields slightly greater benefits, namely 0.012 of a QALY (95% CI -0.00 to 0.03) when adjusted for all covariates (including baseline utility). Therefore, the ICER for the base case analysis was estimated at £19,494 per additional QALY. In order to take uncertainty into account, the paired bootstrapped costs and QALYs were plotted on the cost-effectiveness plane and the corresponding probability that the intervention is more cost-effective than usual care in a cost-effectiveness acceptability curve was presented graphically (Figure 1). The probability of the intervention being cost-effective is 65% at the £30,000 NICE WTP threshold. Several sensitivity analyses were undertaken to test the impact of different assumptions about costs and imputation (Table 4). None of these analyses markedly changed the ICER or the probability of cost-effectiveness, except the complete-case which indicated that the Intervention was dominated by usual care.

Cost per fall averted

The intervention was both more costly and more effective (mean incremental effect 0.19 falls averted per person year; 95% CI -0.05 to 0.44) than usual care, with an incremental cost per fall averted of £1,253.82 (ICER).

HRQoL beyond the trial

At year five the difference in HRQoL between the intervention and usual-care groups observed in the trial was predicted to remain higher for patients allocated to the intervention group (0.0117 QALYs) than the usual care group. The expected incremental cost-effectiveness of the podiatry intervention was £21,460 per QALY gained.

DISCUSSION

REFORM is the largest study to evaluate the cost-effectiveness of a multifaceted podiatric programme to reduce the risk of falling. Over the 12 month follow up, the podiatric programme cost £252.17 more per participant than usual care, but led to an average improvement of 0.012 QALYs. These findings suggest that the podiatric programme costs £19,494 for every additional QALY gained. Therefore, given the NICE WTP threshold, our base-case results suggest that, on average, the podiatric programme could represent a cost-effective use of NHS resources. However, the uncertainty around the trial estimates means that the probability of the intervention being cost-effective is 65% for a threshold of £30,000 per QALY gained.

REFORM was a pragmatic trial conducted across ten sites that adhered closely to its novel design (a cohort randomised trial), which aimed to reduce the incidence of attrition, and provided a robust design to evaluate this podiatric intervention. The engagement of participants with the intervention was high, with 84% of intervention participants attending at least one trial podiatry appointment. Intervention participants were asked at 3, 6 and 12 months post-randomisation how many times a week they typically undertook the prescribed foot and ankle exercises. At 12 months, compliance with the exercise component was reasonable (29% reported performing the exercises at least three times a week, and 75% at least once a week). An instrumental variable CACE analysis approach was used for the primary trial analysis to account for non-compliance with the intervention (defined as not attending a trial podiatry appointment). In this analysis, the intervention was seen to have a marginally greater effect than in the ITT analysis (incidence rate ratio 0.86, 95% CI 0.69 to 1.06; p=0.16).

There are a number of potential limitations with our analysis to note. The first caveat relates to the problem of missing data. This is a common problem in trial-based economic evaluations that is amplified where there are frequent assessments, as here. The difficulties in dealing with missing data are driven by the fact that the true mechanism is usually unknown given the observed data. The pattern of missing data was analysed according to economic guidelines to ensure that REFORM data support the main assumption that drives the MI mechanism assumed for our base case analysis. This analysis shows that data is unlikely to be MCAR, which in turn suggest that CC analysis might lead to biased estimates. The analysis also showed that missing data followed a non-monotonic pattern, indicating that even if complete case analysis was unbiased, it would be inefficient as it discards observed data from patients with some missing outcomes. Finally the fact that outcome can be predicted by baseline variables suggest that MI is the best approach for the analysis, as it can handle non-monotonic missing data while incorporating the uncertainty around the unobserved data and maintaining the correlation structure. It is therefore very unlikely that assumptions regarding missing data will change the conclusions of the base case analysis.

The second limitation relates to the duration of the study, as one year might be considered too short to account for any differences in costs and HRQoL that might be expected with such an intervention. The analysis shows that the podiatry intervention has a positive impact on HRQoL as measured by the EQ-5D, providing improved levels of mobility and anxiety and depression in the intervention group. Furthermore the improvement in anxiety and depression was proportionally greater than the other dimensions. This might be a chance finding but it is possible that the added reassurance of contact with a health professional, or a decreased likelihood of experiencing at least one fall, together with the improved levels of mobility, may have led to a decrease in anxiety in the intervention group. Although cost-effectiveness was demonstrated based on QALYs gained and not necessarily on reducing falls, falls could potentially have a negative effect on patients' HRQoL, and any intervention to improve this is worthy of consideration. In order to account for the limitation related to the duration of the trial we explored how the differences in HRQoL observed in REFORM may evolve beyond the trial. The extrapolation of the within trial HRQoL estimates indicates that the podiatry intervention remains cost-effective at five years. Nonetheless, the value for money of the intervention decreases with time, as this was only a conservative projection that excludes potential costs savings associated with the intervention. It is notable, however, that a large proportion of the intervention costs are incurred during the first year. Furthermore, the mean incremental effect of the intervention (e.g 0.19 falls averted per person year) observed in the study, which might be interpreted as only slight clinical significance, was obtained with an incremental cost per fall averted of £1,253.82. In terms of value for money, this spending on the care of falls may account for approximately 26 visits to a podiatrist based on current NHS reference costs**.** This also shows that there are other potential cost savings that can emerge from the trial that make it more likely that the intervention would yield long-term cost savings for the NHS.

REFORM findings to some extent support those of Spink and colleagues [5], however this study did not include an economic evaluation. To the best of our knowledge there is no evidence that specifically focusses on the cost-effectiveness of podiatry-related programmes in relation to falls prevention. Previously reported economic evaluations have mostly looked at exercise programs founded on the home-based "Otago Exercise Programme" [28-32] which has been proven to be cost-effective in people aged over 80 years. Similarly there is a form basis to consider exercise programmes as a cost-effective intervention in reducing fall-related injuries among community-dwelling older women [33]. These evaluations have reported cost-effectiveness in terms of cost per fall averted. However there are concerns about the lack of ability of cost-effectiveness analysis to inform decision makers on whether the strategy for fall prevention represents good value for money compared to other health care programmes. Cost-utility analysis, based on QALYs – which capture the value of improvements in morbidity and mobility - can facilitate the comparison of different health care interventions and therefore are the preferred method to guide resource allocation within the health care systems. The results of previous cost-utility analyses have found group-based exercise programmes to be cost-effective for fall prevention for patients at high risk of falling (e.g. previously fallen) [34] and for older women [35]. It is difficult to assess how these economic analyses compare with our analysis as there are essential differences in the methods, interventions and comparators, and populations across studies. However, a Cochrane review looking at falls prevention strategies (none of which were similar to the multifaceted podiatry intervention investigated in REFORM) concluded that, similar to REFORM, there was some evidence that these were cost-saving during the trial period and could be cost-effective over the participants' remaining lifetime [36].

There is a need to identify cost-effective means for preventing falls to guide appropriate use of limited NHS resources. From this analysis, we conclude that the podiatry programme could represent a cost-effective option within the NHS to reduce the risk of falling among older people. In terms of clinical practice, there is also potential for the cost of the intervention to be further reduced if podiatry assistants rather than the podiatrist undertook the assessment of participant's footwear, and measuring, ordering and fitting of new footwear. However, the differences in benefits between the podiatry intervention and usual care are small and although the intervention is more cost-effective than usual care, decision makers should be aware of the uncertainty associated with our results. Despite the promising results, future research on long term impact of the intervention on HRQoL and costs would strength the results of the current economic evaluation.

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Contributors

BC was the trial economist and was responsible for conducting the economic evaluation and produced the first draft of the paper. SC was a co-investigator (co-I) and trial manager. AS contributed to the process evaluation. CF was the trial statistician. CEH was a co-I and lead statistician. KH was a trial coordinator. AMK was a co-I and provided podiatric expertise. SEL was a co-I and falls expert; CM was a co-I and led the Irish centre; HBM was a co-I and Chief investigator from previous trial; ACR was a co-I and podiatry expert; SR was a trial co-ordinator; JW was co-I; DJT was chief investigator and oversaw the conduct of the economic analysis. All authors contributed to the writing of the paper and read and approved the final manuscript.

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