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Dosage for cost-effective exercise-based falls prevention program for the older people: A systematic review of economic evaluations

Abstract

Background and objectives: Falls among older people is a global public health concern. Physical exercise is a useful and potentially cost-saving treatment option to prevent falls among older people. The study objectives are: 1) to summarize the research literature regarding the cost-effectiveness of exercise-based programs for falls prevention among the older people, and 2) discuss the implications of the review's findings for clinical practice and future research on the dosage for cost-effective exercise-based falls prevention program for the older people.

Methods: Multiple databases were searched from inception until February 2019. Studies were included if they: (1) were randomized controlled trials with an economic evaluation of exercise-based falls prevention programs for the older people aged 60 years and above, (2) assessed the incremental cost-effectiveness ratios, cost per quality-adjusted life year, the incremental cost per fall and benefit to cost ratio. Methodological quality was assessed using the Physiotherapy Evidence Database scale and the quality of economic evaluation using the Quality of Health Economic Studies.

Results: Twelve studies including 3668 older people were reviewed. Interventions for falls prevention were either exercise only or multifactorial programs. Five studies of high economic quality and two studies of high methodological quality provided evidence supporting exercise only programs as cost-effective for preventing falls.

Conclusion: There is evidence to support exercise-based intervention as a cost-effective treatment for preventing falls. Specifically, tailored exercise program including strengthening for lower extremities, balance training, cardiovascular exercise, stretching and functional training of moderate intensity done twice per week with each session lasting for 60 minutes for 6 months or over delivered in groups of 3 to 8 participants with home-based follow-up appears to be cost-effective in preventing falls among the older people. Further research is needed to fully establish the cost-effectiveness of such programs, especially in both developing and underdeveloped countries.

Keywords: Physical exercise, Dosage, Falls prevention, Older people, Cost-effectiveness.

Review registration: PROSPERO CRD42018102892

Introduction

Falls among older people is a global public health concern that reduces quality of life and increases the financial burden across the globe.[1] Twenty-eight to 35% of older people aged 64 years or older experience one or more falls per year.[2] Globally, falls are the second leading cause of deaths, due to unintentional injuries. The World Health Organization (WHO) reports 80% of fatalities relating to falls occur in low to middle-income countries while Western Pacific and South East Asian countries account for 60% of deaths due to falls.[3] In Hong Kong, 18% of the population is aged over 65 years in 2019, and it is estimated that the population of older people in Hong Kong will increase to 28% by 2036.[4] The prevalence of falls among the older people in Hong Kong is 19%, with an incidence rate of 270 falls per 1000 persons per year.[5]

Poor balance and gait, polypharmacy, and a previous history of falls are the most common risk factors predicting falls among the older people.[6] The risk of falls among the older people increases from 10% for those with no risk factor to 70% among those with more than four risk factors for falls.[5, 7] Outdoor falls is significantly more common than indoor falls.[8] Falls among older people can result in fractures, functional impairment, decreased quality of life and even death in some cases.[9] Recurrent falls occur in 12% of fallers, often resulting in the need for long-term nursing home care.[10] The cost of falls and falls related consequences are high among older people.[11] Injuries from falling are reported as the most expensive injuries sustained by older people, costing USD 75 to USD 100 billion annually across the globe.[12] In Hong Kong, in addition to the serious physical and psychological consequences of falls, the medical expenditure for fallers is HK$552 million higher than that of non-fallers.[13] Therefore, preventing falls among older people is of paramount importance.

Falls prevention programs can prevent functional disability caused by accidental falls.

Physical activity is a useful and potentially cost-saving treatment option for preventing falls among older people.[14, 15] Physical activity have the advantages of involving home-based practice and not requiring direct supervision from a therapist once the key components of treatment are learned.[16] Physical activity reduces the actual number of falls and injuries from falls thereby reducing the medical expenditure and impact of falls.[17] There is substantial evidence from Cochrane review to support physical activity for reducing the risk of falls among older people.[18] Perhaps due in part to the known benefits of regular physical activity for reducing falls risk, the American College of Sports Medicine (ACSM) recommends regular physical activity including a combination of aerobic activity and strengthening exercises for healthy ageing among older people.[19] In this paper, we report physical activity as physical exercise. Definitions of the key terminologies relevant to the understanding of this review are presented in Table1. A combination of aerobic activity, strengthening, flexibility and balance exercise reduces the risk of chronic medical conditions including falls and fall-related injuries by 35%-45% among the older people.[19, 20] Specific exercises for preventing falls include but are not limited to the Otago Exercise Program,[21] dual-task training,[22] Tai Chi[23] and brisk walking.[24] These exercises combine a spectrum of strengthening and balance training programs. Recommendations on physical exercises for preventing falls suggests involving in walking, strength and balance training for 3 hours a week. These exercises need to be ongoing for the sustained benefits of the falls prevention program.[25]

The cost benefits of exercise-based falls prevention programs are not yet completely understood, as cost-effectiveness analysis is not commonly conducted as a component of randomized controlled trials in this area. However, understanding the cost implications of falls prevention programs is important to better understand the value associated with the health benefits of falls prevention programs. For example, if these programs are found to essentially pay for themselves or even have a positive financial impact (i.e., to result in greater cost savings than they cost), this would help motivate policy-makers concerned about health care costs to develop policies that would result in more older individuals participating in such programs.

However, previous systematic reviews on the cost-effectiveness of falls prevention programs were either restricted to studies on home-based exercise interventions [26] or did not consider details about the falls programs reviewed, including their intensity, frequency, type and duration.[27] Over the past decade, the number of economic evaluation studies on falls prevention programs for older people has increased. Therefore, an update of the literature on this topic is warranted. Given these considerations, the current systematic review aims to (1) summarize the findings from the research literature on the cost-effectiveness of exercise-based programs for falls prevention among the older people and (2) discuss the implications of the review findings for clinical practice and for future research on the dosage for cost-effective exercise-based falls prevention programs for older people.

[Please insert table 1 about here]

Methods

This systematic review is presented in accordance with the PRISMA guidelines.[33] It was pre-registered on PROSPERO before the search was initiated. We searched relevant literature using the following databases from inception until February 2019: CINAHL, Scopus, Pubmed, NHS Economic Evaluation Database, ISI Web of Science Databases – Science Citation Index and PsycINFO. Search terms were constructed as three themes which included (1) older people (2) falls prevention and (3) economic evaluation. Related terms under each theme were combined using the Boolean operator OR and the three themes were combined using the Boolean operator

AND. Search terms used for Scopus are reported in Appendix 1.

The criteria for selecting studies for this review was structured using the PICOS (Patient problem, Intervention, Comparison, Outcome measure and Study design) framework[34] and are reported in Appendix 2. Studies were included if they: (1) were randomized controlled trials (RCT), (2) evaluated the cost-effectiveness of exercise-based falls prevention programs and (3) were conducted among the older people aged 60 years and older. Manual searches of the reference list of the included studies were also conducted. Studies were excluded if they were: (1) study protocols, systematic reviews and conference abstracts; or (2) non-English publications. The outcome measures for this systematic review included the incremental cost-effectiveness ratio (ICER), the cost per quality-adjusted life year (QALY), the incremental cost per fall, and the benefit to cost ratio and cost-utility analysis.

All identified studies were subject to a four-step screening process. Duplicates were removed and titles were screened by one reviewer (CF). The abstract and full-text screening was then conducted by two reviewers (LH and LC). Discrepancies were resolved by discussion until consensus was reached. If consensus was not reached between the two reviewers (LH and LC), a third reviewer (SW) was consulted. The following data were extracted from all the included studies: author, publication year, country of origin, sample size, type of intervention including duration and frequency and follow-up period of treatment, economic analysis, perspective (societal, healthcare), cost data, economic outcome measure, currency, discounting, study perspective (healthcare or societal) and author’s conclusion. Since most of the studies on cost-effectiveness do not report detailed information on the study methodology and instead refer to a previous publication, we retrieved the information relevant to methodology from referred studies published elsewhere. Authors of the included studies were approached to obtain additional information not reported in the publication. Two reviewers (LF and PK) were involved in data extraction, discrepancies in the contents of data extraction were resolved by discussion and unresolved discrepancies were consulted with a third reviewer (SW).

The methodological quality of the included studies was assessed using the Physiotherapy Evidence Database (PEDro) scale.[35] The quality of economic evaluation was assessed using the Quality of Health Economic Studies(QHES) scale.[36] The PEDro includes 11 'yes' or 'no' questions with each 'yes' response scoring 1 point. Studies scoring ≥ 60% were classified as having good methodological quality, and studies scoring < 60% were classified as having poor methodological quality.[37] The QHES includes 16 questions relating to the evaluation of cost-effectiveness. Each question of the QHES is scored either 'yes' or 'no', with each 'yes' response counting for the total score. Studies scoring ≥ 75% were classified as being 'high quality' studies, and studies scoring < 75% was classified as being 'poor quality' studies.[26] Two reviewers (TL and LF) independently evaluated study quality using both quality rating scales, and any disagreements were resolved by discussion. A third reviewer (SW) was consulted if needed for unresolved discrepancies, and made a final determination. Studies were not excluded based on their quality score. However, the quality scores were considered when interpreting the findings. For consistency, all the study currencies were converted and reported as US dollars using a conventional currency converter (https://www.oanda.com/currency/converter/) [12.12.2018].

Results

The flow of data search is reported in Figure 1. As can be seen, the search yielded 5964 relevant citations, and 12 studies[38-49] met our inclusion criteria and were included for this systematic review. The flow of data search is reported in Figure 1. The included studies involved 3668 participants, with an average of 306 participants per study. The sample sizes of the included studies ranged from 68 [49] to 1090. [45] Table 2 summarizes the key data extracted from the included studies. The country of origin of the included studies was restricted to Canada, [38, 39, 43, 44] Australia, [45] the United States of America, [46] the United Kingdom, [41, 42] Netherland,[40] Finland, [49] and New Zealand.[47, 48] Except for three,[43, 44, 49] all remaining included studies followed-up with the study participants for 12 months or over.

[Please insert Table 2 and figure 1 about here]

Methodological quality:

The methodological quality according to the PEDro and quality of economic evaluation according to the QHES are reported in Tables 3 and 4 respectively. The methodological quality was good among five studies[40, 41, 43, 44, 47] and poor for seven studies[38, 39, 42, 45, 46, 48, 49]. Eight [38-43, 45, 48] of the 12 studies were rated having 'good' quality of economic evaluation. Owing to the study design, none of the studies blinded participants and therapists.

[Please insert Tables 3 and 4 about here]

Falls prevention programs:

We classified the interventions evaluated in the included studies as exercise-only programs and multifactorial intervention programs. The exercise only programs were those that included one or more physical exercises alone while the multifactorial intervention programs included exercises plus: (1) treatment or education by one or more health care provider specialized in for falls prevention; (2) other medical care for falls prevention such as the assessment and treatment of vision, hearing, balance, or cognitive dysfunction; and/or (3) medication adjustment. Among the exercise only programs, the participants were taught and asked to engage in exercises such as those that strengthen the lower limbs with or without exercises that strengthen the upper limbs, balance training, cardiovascular exercise, stretching or functional training. The multifactorial intervention included exercise plus risk management,[43] occupational therapy assessment,[40, 43] and environmental modification.[42, 44, 46] Seven studies[38, 39, 41, 45, 47-49] delivered exercise only interventions; the remaining five [40, 42-44, 46] delivered multifactorial interventions.

Dosage of the exercise-based falls prevention programs:

The duration of exercise intervention ranged from 15[46] to 90 minutes[49] per session and the frequency of intervention ranged between twice a day[46] to once per week.[38] Five of the studies[38, 39, 41, 45, 49] demonstrating that the treatment program was cost-effective instructed participants to exercise for 60 minutes per session, twice weekly for at least 6 months. Among the seven exercise programs that were found to be cost-effective,[38, 39, 43, 45-48] five [45-48] reported the exercise duration per session as 30 to 60 minutes, five programs[38, 39, 45, 46, 49] had exercise frequency of once or twice a week and three programs had three sessions or more per week.[41, 47, 48] The duration of the exercise program ranged from 15 weeks [45] to 12 months[38] inclusive of the follow-up period. Except for one study,[45] all the other studies reporting cost-effective exercise programs delivered treatment for 6 months or over.

With regards to the exercise type and format, ten studies[38, 39, 41, 42, 44-49] tested generic standard exercise protocols (i.e., all participants received the same intervention) for falls prevention while two [40, 43] tested the benefits of tailored exercises for falls prevention among the older people. Among the studies testing the benefits of standard exercise only protocols, all of them included lower limb strengthening exercise. Six studies [41, 42, 45-48] also included balance training, one study each included stretching exercise,[45] functional training[49] and cardiovascular exercise.[41] Except for two resistance training programs,[38, 39] the remaining included moderate intensity exercises. In terms of exercise format, six studies [38, 39, 41, 42, 45, 49] delivered the intervention as group-based treatment, while the remaining were provided using an individual-based, one-to-one format. No difference was found between the exercise format and cost-effectiveness of the program in that, three group-based exercises [38, 39, 45] and three individual-based exercise [43, 46, 47] were found to be cost-effective. Comparison between institution-based and home-based exercises found, three[38, 39, 45] of the five [38, 39, 41, 45, 49] programs that were delivered as institution-based format were cost-effective while two [43, 47] of the five[41, 43, 44, 47, 48] programs that were delivered as home-based format were cost-effective. One study that combined both institution-based and home-based exercises as a format of intervention delivery was found to be cost-effective.[46] The falls prevention exercises were delivered either by a certified physiotherapist (n=6),[42-46, 49] or a trained instructor (n=3)[38, 39] or an occupational therapist (n=1)[40] or a nurse trained by a physiotherapist (n=2).[47, 48]

Outcome measures and cost-effectiveness:

Cost-utility analysis (CUA) and cost-effectiveness analysis (CEA) were commonly used as the method for economic evaluation. Ten out of the twelve included studies used one of these statistical methods for economic evaluation. Two studies [39, 41] used CUA and five [42, 43, 46-48] used CEA, while three [38, 40, 45] studies used both. The remaining two studies [44, 49] did not perform an economic evaluation, but, reported the medical cost as cost-utility. Four studies [38, 39, 41, 45] adopting CUA chose quality-adjusted-life-year (QALY) as the primary outcome measure. Among studies using CEA, measurable and natural unit of gain were used, for instance, the number of prevented accidents were utilized. Among the eight studies adopting CEA, the number of falls during the follow-up period was used as the primary outcome. Other indicators, such as Frenchay Activity Index (FAI), nutritional status, changes in psychological status, gait and balance were less commonly used. Among the 12 included studies, seven [38, 39, 42, 45, 46, 48, 49] evaluated the cost-effectiveness of falls prevention program from a healthcare perspective while the remaining five [40, 41, 43, 44, 47] studied from a societal perspective.

Study perspective, source of cost data, mean costs, mean health effect, Incremental Cost-effectiveness Ratio (ICER) and author's conclusion are summarized in Table 5. Four studies[42, 45, 47, 48] reported ICER. Four studies [12, 38, 46, 47] reported the intervention as cost-effective, three studies[40, 43, 45] reported the intervention as potentially cost-effective and six studies[41, 42, 44, 48, 49] reported as not cost-effective. One of the cost-effective, trained nurse delivered home-based exercise program reported the incremental cost per fall prevented as NZ 1803 (1231.5 USD).[47] The cost of implementing cost-effective exercise only falls prevention program ranged between £ 52.37 (64.4 USD)[45] and 708 CAD (533.5 USD)[47] while implementing a cost-effective multifactorial falls prevention program costed USD 905[46] per person. One study implementing multifactorial falls prevention program reported the program as cost-effective when the willingness to pay (WTP) threshold was $ 25000 CAD (18600 USD) to prevent falls.[43] Two studies estimating the average incremental cost per falls prevented reported £652 (USD 840)[45] following exercise only program and USD 8824[46] following multifactorial falls prevention program.

[Please insert table 5 about here]

Among the four studies reporting the intervention as cost-effective, two studies[46, 47] that were of poor methodological quality compared the intervention with standard physiotherapy, while the remaining two studies [38, 39] both of poor methodological and high economic evaluation quality compared the experimental intervention against an active control intervention. Two studies included a follow-up assessment beyond 12 months of which, one study of high economic evaluation quality[45] applied 3% discounting and the other study of low economic evaluation quality[46] did not apply discounting. The remaining studies had a follow-up assessment for 12 months or less therefore, discounting was not applicable.

Discussion

This systematic review aimed at providing a comprehensive review of the current evidence for the dosage of cost-effective exercise-based falls prevention program for older people. Twelve studies were included in this review of which seven studies reported on cost-effective or potentially cost-effective exercise-based falls prevention programs for the older people. All the falls prevention programs included lower limb strengthening exercises. Exercise-only programs were more cost-effective in comparison to multifactorial falls prevention programs.

In order to be widely impactful, exercise-based falls prevention program would ideally be feasible, effective and cost-effective. From this review we found that among the cost-effective exercise only falls prevention programs (n=5), 60% were delivered in groups, 60% instructed home-based practice, 80% lasted for 60 minutes each session and 80% required 2 or more sessions of training per week. Among the cost-effective multifactorial falls prevention programs (n=3), all programs were tailored individually, 67% instructed home-based care, 67% lasted for 60 minutes each session and 67% required one session per month. All of the cost-effective exercise-based falls prevention programs offered strengthening exercises for the lower limbs and balance training. It is evident that increasing the frequency to twice a day and the duration of each session to 90 minutes may be clinically effective, but not necessarily cost-effective. Secondly, we did not find an inclination towards institution-based programs in terms of their cost-effectiveness.

Given these findings, we speculate that a moderate intensity of strengthening exercise for lower limbs (gluteal muscles, quadriceps, hamstring and ankle plantar and dorsiflexors), with or without exercise for upper limbs, and balance exercises for 60 minutes, done twice per week delivered as a group-based intervention with home-based follow-up may be a cost-effective exercise-based intervention for preventing falls. These parameters are in line with the recommended best practice for exercises for falls prevention among the older people.[50, 51] Since the effects of exercise on falls prevention are lost after cessation, ongoing exercises are needed for sustained benefits.[50] Except for one study,[41] the significance of moderate paced walking as a part of exercise package for falls prevention has not been tested. We recommend future studies to test the benefits of adding scheduled walking to the falls prevention exercise protocol.

No significant pattern was found when comparing the exercise format against their cost-effectiveness. Both group-based versus individual-based exercises and home-based versus institution-based exercise programs were found equally cost effectiveness. Considering the lack of inclination towards institution-based and individual-based exercise programs that could arguably have better outcomes due to direct supervision by a trained therapist, we speculate falls prevention programs for older people can be taught using group-based format and delivered as a home-based interventions. Such format (group-based learning and home-based practice) has the advantage of serving a larger group of older people at a lower cost in terms of expenditure and manpower. Research to evaluate the efficacy of such programs, in particular in comparison to other programs that may require more resources, are needed.

Cost is the major outcome measure for cost-effectiveness and the cost of the interventions may be influenced by inflation or deflation. Inflation or deflation should be taken into account if the follow-up period is longer than 12 months.[52] Among the included studies, two studies followed-up participants for more than 12 months. However, one of these studies did not discount the cost. As a result, the cost-effectiveness calculation used in this study may not be accurate. According to the World Health Organization, discounting is recommended, as the consumed cost may decrease over time.[53] As cost was measured when the intervention is implemented, while the health benefit was measured at a period of time after the intervention, the cost measured may potentially be inaccurate to weigh the health benefit compromising the accuracy of findings. Therefore, discounting should be implemented for future studies which investigate cost-effectiveness that have follow-up periods longer than 12 months.

The country of origin of the included studies was restricted to Canada, Australia, the United States of America, the United Kingdom, Netherlands, Finland and New Zealand. Barriers including lack of resources, lack of experts and low preference of economic studies among researchers have been identified as the reasons for the lack of cost-effectiveness studies among the Asian, African and South American countries.[54, 55] Since culture, policies and resources vary across countries, the available findings on cost-effective falls prevention programs may have limited generalizability to Asian, African and South American regions for a number of reasons. First, countries have different cultures. Among the East Asian countries, for example, exercises based on Chinese martial arts, such as Tai Chi, are popular.[37] Older people in East Asia, perhaps not surprisingly, prefer Tai Chi over the routine strengthening and balance exercises. Second, among most of the developing and under developed countries, the healthcare provider to population ratio does not reach the desired levels. Statistics from the Hospitals Authority (HA) of Hong Kong reports that the physiotherapists to population ratio is 1:2397, while the nurses to population rate is 1:137.[56] Considering the deficiency in the number of physiotherapists in countries like Hong Kong, more research on testing the benefits and cost saving by utilizing the registered nurses to teach simple exercises during falls prevention programs for the older people are warranted. The use of nurses to deliver exercises following adequate training and supervision by a certified physiotherapist is supported in one of the included studies justifying its credibility.[47] Lastly, individualized training program needs to be planned according to the health status of the older people. Some countries have higher life expectancies and physical activity levels than others. Therefore, the intensity, frequency, and duration of exercise treatment may need to be adjusted according to the level of physical fitness of the patients.

Strengths and limitations

This systematic review has several strengths. First, a comprehensive search strategy was used to identify studies on cost-effectiveness of exercise-based falls prevention programs for the older people. Seocnd, we used a rigorous and systematic methodology to identify and evaluate the studies included. Third, we used reliable, valid and appropriate quality appraisal tools, the PEDro scale and the QHES.

However, this review also has a number of limitations that should be included when interpreting the findings. First, studies were restricted to the English language. We may therefore have missed studies evaluating the cost-effectiveness of falls prevention programs published in other languages. Second, the quality of studies was not considered as one of the criteria for inclusion. This may have influenced the outcomes of our systematic review.[57] Finally, the studies included for this systematic review are diverse in terms of the interventions tested, intervention parameters, outcome measures used and country of origin. As a result of this high level of heterogeneity, we were unable to conduct a meta-analysis.

Conclusion

This systematic review found evidence for exercise-based interventions as being cost-effective for preventing falls among older people. Although exercise only format were found to be more cost-effective than multifactorial intervention, there were not enough studies of each to draw firm conclusions regarding the relatively efficacy of these formats. Future research is needed to systematically compare different formats. Exercise programs of moderate intensity done twice per week for 60 minutes each session for 6 months or over, delivered to groups of 3 to 8 participants with home-based follow-up is likely to be cost-effective in preventing falls among the older people. However, due to the heterogeneity of the tested interventions, a strong recommendation on the treatment dosage of cost-effective exercise-based falls prevention program cannot be made. All existing research on cost-effectiveness is restricted to Europe, North America and Oceania. There is a need for conducting cost-effectiveness studies in developing and underdeveloped countries since the available evidence has limited generalizability to such countries.

Clinical implications

- Exercise-only program of moderate intensity of strengthening exercise done twice per week lasting for 60 minutes each session for 6 months or over is likely to be cost-effective in preventing falls among the older people.
- Strengthening exercise for the lower limb (gluteal muscles, quadriceps, hamstring and, calf and ankle plantar and dorsiflexors) and balance training need to be included in the falls prevention exercise program. Scheduled walking, upper limb exercises and functional exercises may provide additional benefits.
- Training by a physiotherapist or a nurse trained and supervised by a physiotherapist, for groups of 3 to 8 participants with home-based follow-up of exercises may be considered for designing future fall prevention programs for the older people.

Figure 1: Flow of studies screening

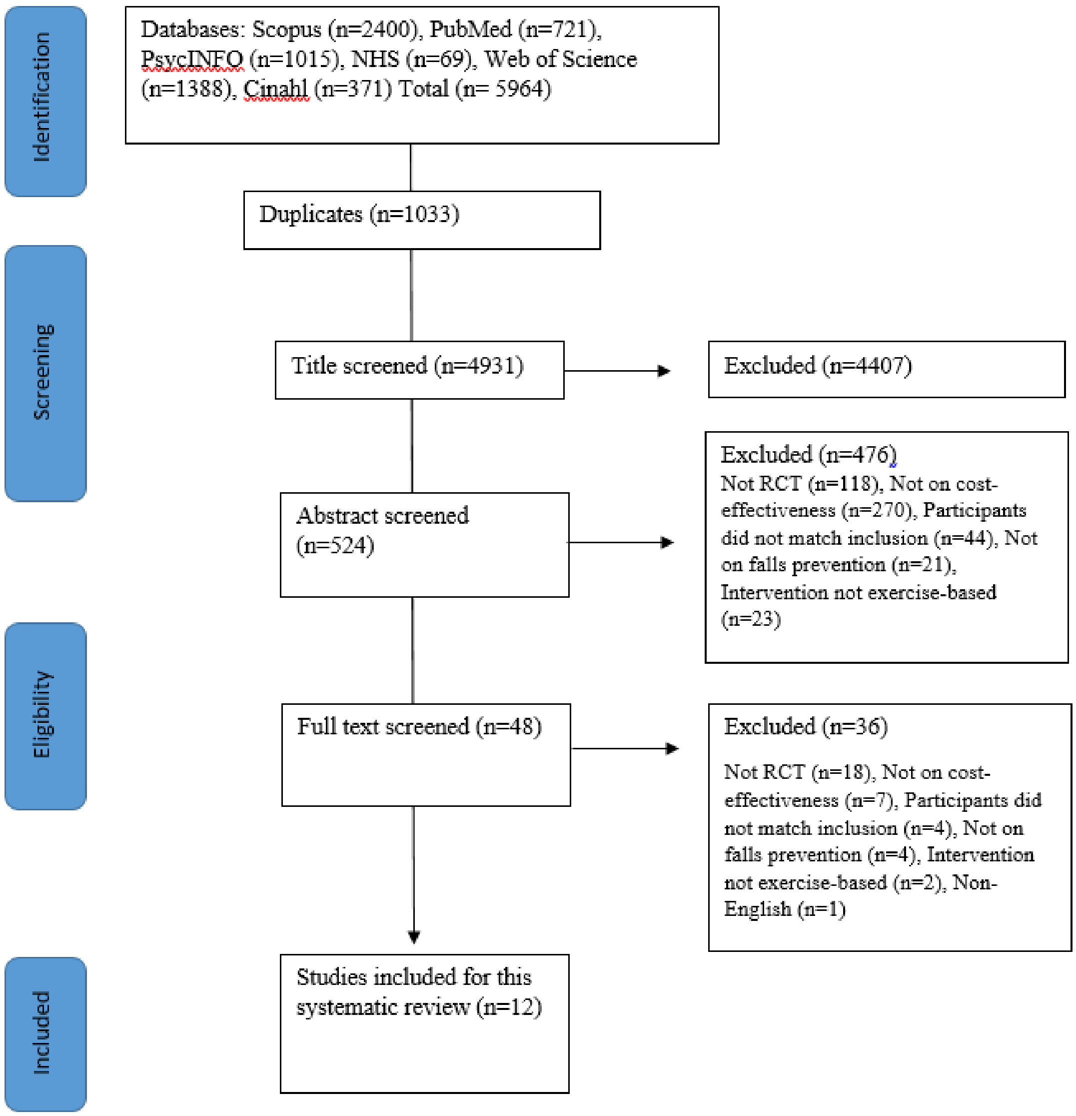

Table 1: Definitions for the key terminologies

Terminology	Description
Exercise intensity	Refers to the extent of energy expended during the exercise. The American College of Sports Medicine (ACSM) describes the exercise intensity based on metabolic equivalents (METs), with low being those requiring <3METs, moderate being 3-6 METs and vigorous exercises as those requiring >6 METs.[28] Moderate intensity refers to an activity that results in a slight but noticeable increase in the heart and respiratory rate, while vigorous intensity is hard enough to make the person run out of breath. During vigorous intensity exercise the person is unable to perform the activity and talk simultaneously.[29]
Exercise frequency	Refers to the number of sessions of exercise per week or day
Exercise duration	Refers to both the length of time of each bout of exercise per session and the number of days the program needs to be continued.
Exercise type	Is described as the mode of exercise performed. The ACSM classifies exercise types into the following categories: cardiovascular training, strength and endurance training for muscles, flexibility exercises and neuromuscular fitness exercise for the older adults.[19]
Mode of delivery	In this review, mode of delivery implies to the exercise format (group-based versus individual-based) and the venue of delivery (institution-based versus home-based)
Exercise only intervention	Those programs that included physical exercises alone
Multifactorial intervention	Interventions that address multiple risks for falls involving a spectrum of healthcare professionals including but not limited to a physician, physiotherapist, occupational therapist, pharmacist, nurse and social worker.[30]
Cost-effective program	The degree to which the program is effective in relation to its cost. In this review we report the program as cost-effective based on the conclusion of the included studies.
Quality-adjusted-life-year (QALY)	Is defined as the overall score of an individual's health related quality of life score. The QALY is measured on a 0-1 scale where 1 indicates perfect health and o indicates death due to the disease.[31]
Cost per QALY	Is the cost of the intervention required to provide a year of the best quality of life.[32]
Cost-effectiveness ratio	Also called the incremental cost-effectiveness ration (ICER) is the ratio between the difference in cost (ΔC) of the tested interventions divided by difference their effect (ΔE)

Table 2: Summary of the included studies

Reference Country of origin	Study Participants	Intervention	Cost-effectiveness Outcome Measures, Follow up period, Economic evaluation method
Davis et al. 2011 (a)[38] Canada	N=155 (women) Age 65-75 Community-dwelling	Classification: Exercise only Group 1: Once weekly resistance training Group 2. Twice-weekly resistance training Group 3. Control group, twice-weekly balance and tone classes ***Dosage*** Intensity: Progressive and high intensity Frequency: Once or twice weekly depending on the group allocation. Duration: 60 minutes each session for 12 months Type: Resistance, strengthening, balance, relaxation and tone exercises Mode of delivery: Institution-based intervention delivered to groups of three participants	ICER Health outcome: Number of falls per participant group, QALYs Follow up period:12 months Cost-utility analysis and Cost-effectiveness analysis
Davis et al. 2011 (b)[39] Canada	N= 98/123 (women) Age 65-75	Classification: Exercise only Group 1: Once weekly resistance training Group 2. Twice-weekly resistance training Group 3. Control group, twice-weekly balance and tone classes ***Dosage*** Intensity: Progressive and high intensity. Two sets of six to eight repetitions of strengthening exercise.	Incremental cost per QALY Health outcome: EQ-5D to QALYs Follow up period:12 months Cost-utility analysis

		Frequency: Once or twice weekly depending on the group allocation. Duration: 60 minutes with 10 minutes warm-up and cool-down plus 40 minutes of core training each session for 12 months Type: Resistance, strengthening, balance, relaxation and tone exercises Mode of delivery: Institution-based intervention delivered to groups of three participants	
Hendriks et al. 2008[40] Netherland	N=333, Intervention group(n=166) Control group(n=167)	Classification: Multifactorial intervention Intervention group: Medical screening and occupational-therapy assessment. Usual care: Protocol for falls prevention in the Netherlands was adopted. ***Dosage*** Intensity: Not applicable. Frequency: Not reported Duration: 3.5 months Type: behavioural change, functional needs and home safety Mode of delivery: Institution-based assessment by the multidisciplinary team followed by home visits by the occupational therapist.	Using cost-effectiveness planes (CE-planes) to visualize the results of a bootstrap analysis, every dot representing an ICER computed for one bootstrap sample. Primary outcome: no. of fall Secondary outcome: FAI and QALY Follow up period:12 months Cost-effectiveness analysis and cost-utility analysis
Iliffe et al. 2014 [41] UK	N=572 FaME group n=184	Classification: Exercise only Intervention group 1: Otago Exercise Program (OEP). Intervention group 2: Community centre-based group exercise program (FaME).	Mean difference in QALY scores per cost Health Outcome Measure:

	OEP group n=178 Usual care n=210	Usual care group: Free to participate in any non-trial related exercise. ***Dosage*** Intensity: Moderate. Frequency: Exercise thrice a week and walking twice a week Duration: 30- 60 minutes each session lasting for 24 weeks Type: OEP: 30 minutes of lower limb strengthening and balance retraining exercises done three times a week and walking twice a week. Ankle cuff used to provide resisted exercises for the lower limb. FaME: 1-hour group exercise involving 15 participants. In addition 30 minutes home exercise similar to the OEP protocol. Exercises included floor and cardiovascular exercises, lower limb strengthening, balance training, flexibility training, arm and truck strengthening. Ankle cuff, TheraBands^{TM} were used for resisted exercises. Mode of delivery: Institution-based individual training followed by home-based exercises.	1. the number and nature of falls, and fear of falling 2. Health-related quality of life and QALYs Follow up period:12 months Cost-utility analysis
Irvine et al. 2010 [42] UK	N=352 n=172 in control and intervention group	Classification: Multifactorial intervention Intervention group: Falls prevention leaflet plus standard falls prevention program offered in England and Wales. Control group: Falls prevention leaflet alone. ***Dosage*** Intensity: Not reported.	ICER Health outcome: no. of fall Follow up period:12 months Cost-effectiveness analysis

		Frequency: Not reported Duration: 12 months Type: Gait re-education, muscle strengthening, provision of walking aid and functional training Mode of delivery: Individual and institution-based intervention	
Isaranuwatchai et al. 2017 [43] Canada	N=92 Intervention group n=43Control group n=49	Classification: Multifactorial intervention Intervention group: Home care service arranged by the Community Care Access Centre plus monthly in-home visits by an inter-professional team with specialized training in the area of falls prevention. Control group: Home care service arranged by the Community Care Access Centre. ***Dosage*** Intensity: Not reported. Frequency: Not reported Duration: 12 months Type: Manage modifiable risk factors for falls, provide support, education on falls prevention Mode of delivery: Individual-based home care.	Net benefit regression (NBR) framework Health outcome: no. of fall Follow up period:6 months Cost-effectiveness analysis
Markle-Reid et al. 2010 [44] Canada	N=109, Intervention group(n=54) Control group(n=55)	Classification: Multifactorial intervention Intervention group: Usual care for falls prevention plus monthly home visits by the Community Care Access Centre team professionals × 6 months. Control group: Standard home care arranged by the Community Care Access Centre × 6 months.	Primary outcome: no. of fall Secondary outcome: self-reported slip or trip, functional health status and quality of life, nutritional status, gait and balance, depressive symptoms, cognitive function,

		Dosage Intensity: Not reported. Frequency: Once per month Duration: 6 months Type: Intervention included home visits by a multi-disciplinary team including a physiotherapist. The type of exercise delivered is not reported. Mode of delivery: Standard care plus individual home visits by the multi-disciplinary team.	confidence in performing ADLs without falling Follow up period:6 months No Economic evaluation method
McLean et al. 2015 [45] Australia	Community-dwelling older people aged > 70 years. Sample size: 1090	Classification: Exercise only Intervention group (n=541): Standard care plus exercise training Control group (n=549): Standard care ***Dosage*** Intensity: Not reported. Frequency: Once weekly Duration: 60 minutes each session lasting for 15 weeks Type: Strength and balance exercises to improve flexibility, lower limb strength and balance. Mode of delivery: Once weekly group-based exercise supplemented by daily home exercises.	ICER Health outcome: 1.No. of falls in 18 months, 2.health-related quality of life measured by quality-adjusted life years (QALYs) Follow up period:18 months Primary analysis: cost-utility analysis Secondary analysis: cost-effectiveness analyses
Rizzo et al. 1996 [46] US	Ambulant older people aged >69 years. Sample size: 301	Classification: Multifactorial intervention Intervention group (n=153): Behavioral change, medication adjustment, environmental modification and exercise. Control group (n=148): Social worker conducted interviews on structured life reviews as home visits, the number of visits matched the visits made for the intervention group.	Comparing total cost of TI and UC group Health outcome: no. of fall Follow up period: 2 years Cost-effectiveness analysis

	Mean age: 77.9 (5.3) years	***Dosage*** Intensity: Not reported. Frequency: Twice daily Duration: 15-20 minutes each session lasting for 3 months. Type: Exercise included progressive balance and strengthening exercises using an elastic band. Mode of delivery: Individually prescribed institution-based training.	
Robertson et al. 2001 (a)[47] New Zealand	Men and women aged >75 years Sample size = 240 Mean age: 81.1 (4.5) years	Classification: Exercise only Intervention group (n=121): Usual care plus progressive exercises. Control group (n=119): Usual care. ***Dosage*** Intensity: Not reported. Frequency: Thrice a week Duration: 30 minutes each session lasting for 12 months. Type: District nurse delivered exercise program. Five home visits delivered over 6 months period. Exercises included progressive ankle strengthening, balance retraining and walking plan. Mode of delivery: Individually prescribed home-based training.	Comparing total cost of control and exercise group Health outcome: No. of falls and any injuries or resources use as a result of the falls Follow up period:12 months Cost-effectiveness analysis

Robertson et al. 2001 (b)[48] New Zealand	Community-dwelling older people aged >80 years. Sample size = 233 Mean age: 84.1 (3.3)	Classification: Exercise only Intervention group (n=116): Usual care plus progressive muscle strengthening and balance exercises and walking for Control group (n=117): Usual care for falls prevention ***Dosage*** Intensity: Not reported. Frequency: Sessions of walking and exercises each thrice weekly Duration: 30 minutes of exercise and 30 minutes of walking sessions lasting for 12 months. Type: Individually prescribed exercises including muscle strengthening, balance retraining and suggestions for walking. Mode of delivery: Individually prescribed home-based training.	Comparing total cost of control and exercise Health outcome: No. of falls resulting moderate and serious injuries Follow up period:2 years Cost-effectiveness analysis
Timonen et al. 2008 [49] Finland	Included female patients aged >75 years admitted for acute illness to a primary-care health-centre. Sample size = 68 Mean age: 83.5 (4.1)	Classification: Exercise only Intervention group (n=34): Progressive resistance training for the lower limb Control group (n=34): Received one home visit by a physiotherapist who taught home-based exercises and was advised to continue for 10 weeks. ***Dosage*** Intensity: Not reported. Frequency: Twice a week Duration: 90 minutes session lasting for 10 weeks (20 sessions in total). Type: Progressive resistance training for the lower limbs, functional exercises such as rising form chair, toe raise and	Total cost of group training program Health outcome: No. of falls Follow up period:10 week No Economic evaluation method

	hip flexion and extension. Mode of delivery: Institution-based exercises prescribed for groups of three to eight participants	

ICER- Incremental cost-effectiveness ratio, QALY- Quality-adjusted-life-year, EQ-D- Euro-Qol 5 dimension, CE plane- cost-effectiveness plane, FAI- Frenchay Activity Index, OEP- Otago Exercise Program, FaME- Community centre-based group exercise program, NBR- Net Benefit Regression, ADL- Activities of daily living.

Table 3: Summary of methodological quality of the included studies according to the PEDro scale

PEDro Scale	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total Score/10
Davis et al.2011(a)[38]	Y	Y	N	N	N	N	Y	Y	N	Y	Y	5
Davis et al.2011(b)[39]	Y	Y	N	N	N	N	Y	Y	N	N	Y	4
Hendriks et al, 2008[40]	Y	Y	Y	N	N	N	Y	N	Y	Y	Y	6
Iliffe et al.,2014[41]	Y	Y	Y	Y	N	N	N	N	Y	Y	Y	6
Irvine et al., 2010[42]	Y	Y	Y	N	N	N	N	Y	N	Y	Y	5
Isaranuwatchai et al., 2017[43]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Markle-Reid et al, 2010[44]	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	6
McLean et al, 2015[45]	Y	Y	N	N	N	N	N	N	Y	N	N	2
Rizzo et al. 1996[46]	Y	Y	N	N	N	N	N	Y	N	N	N	2
Robertson et al., 2001(a) [47]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Robertson et al., 2001 (b) [48]	Y	Y	N	N	N	N	N	Y	Y	Y	Y	5
Timonen et al., 2008 [49]	Y	Y	N	Y	N	N	Y	N	N	Y	Y	4

Item 1- Eligible criteria (item does not contribute to total score), Item 2- Random allocation, Item 3- Concealed allocation, Item 4- Baseline similar, Item 5- Subject blinding, Item 6- Therapist blinding, Item 7- Assessor blinding, Item 8- Adequate follow-up, Item 9- Intention-to-treat analysis, Item 10- Between group comparison, Item 11- Points estimate.

Table 4: Summary of the quality of the economic evaluation of the included studies according to the QHES

QHES	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item12	Item13	Item 14	Item 15	Item16	Total Score (%)
Davis et al.2011(a) [38]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	99
Davis et al.2011 (b)[39]	Y	N	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y	87
Hendriks et al, 2008 [40]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	93
Iliffe et al.,2014 [41]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Irvine et al., 2010 [42]	Y	Y	Y	N	Y	Y	N	Y	N	Y	N	Y	Y	Y	Y	Y	79
Isaranuwatchai et al., 2017 [43]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	91
Markle-Reid et al, 2010 [44]	Y	Y	Y	Y	N	N	N	Y	N	N	N	Y	Y	Y	Y	Y	57
McLean et al, 2015 [45]	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	94
Rizzo et al. 1996 [46]	Y	Y	Y	Y	Y	Y	N	Y	Y	N	N	N	N	N	Y	Y	61
Robertson et al., 2001 (a)[47]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	N	Y	Y	66
Robertson et al., 2001 (b)[48]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	93
Timonen et al., 2008 [49]	Y	N	Y	Y	N	N	Y	Y	N	N	N	N	N	N	Y	Y	39

Item 1- study objective, Item 2- perspective, Item 3- Study design, Item 4, Subgroup analysis, Item 5- Sensitivity analysis, Item 6- ICER between alternatives, Item 7- Data abstraction, Item 8- Discounting, Item 9- Cost measurement, Item 10- Economic outcome, Item 11- Health outcomes reliability, Item 12- Calculation procedure, Item 13- Limitations, Item 14- Potential bias, Item 15- Conclusion, Item 16- Funding

Table 5: Summary of cost and cost-effectiveness of all included studies

Study	Study Perspective, type, source(s) of cost data	Mean Costs Mean (SD) Health Effects	Difference in Incremental Cost-effectiveness Ratio (ICER)	Author's conclusion, Methodological quality(PEDro)/Economic Evaluation Quality(QHES)
Davis et al. 2011[38]	Perspective: Healthcare Cost: Program cost, Visits to healthcare professionals (including general practitioners, specialists, physiotherapists etc); all visits, admissions, or procedures carried out in a hospital, and laboratory and diagnostic tests Discounting: N/A	Control group: Twice-weekly balance and tone Mean incremental cost: $1880 (CAD 2008) No. falls: 24 QALY by EQ-5D: 0.816 Intervention group: Once-weekly resistance Mean incremental cost: $1522 (CAD 2008) No. falls: 18 QALY by EQ-5D: 0.814 Twice-weekly resistance Mean incremental cost: $1665 (CAD 2008) No. falls: 20 QALY by EQ-5D: 0.855	ICER per QALY: Twice-weekly balance and tone (control) Once-weekly resistance -358/-0.002 =179,000 Twice-weekly resistance -215/0.039 =-5,513 (Calculated by reviewers)	Once/ twice resistance training more cost-effective than balance and tone class. PEDro: Poor QHES: Good

Davis et al. 2011[39]	Perspective: Healthcare Cost: Program cost, visits to healthcare professionals, admissions to or procedures performed in a hospital, and laboratory and diagnostic tests Discounting: N/A (Inflated to CAD 2009 by consumer price index reported by Statistics Canada)	Control group: Balance and tone Cost: $2580 QALY based on EQ-5D: 5.45 Intervention group: Once-weekly resistance Cost: $1126 QALY based on EQ-5D: 5.40 Twice-weekly resistance Cost: $1591 QALY based on EQ-5D: 5.49	ICER per QALY: Balance and tone: As reference Once-weekly resistance: -1857/-0.051 = 36411 Twice-weekly resistance: -1077/-0.081 =13296 (Calculated by reviewers)	Cost-benefit of 12 months, sustained in once/twice weekly resistance group. PEDro: Poor QHES: Good
Hendriks et al. 2008[40]	Perspective: Societal Cost: Program costs+ other healthcare costs+ patient and family costs Discounting: N/A	Intervention group Cost: €4,857 No. of people sustaining a fall during 1 year of follow-up: 55 FAI: 25.6 QALY: 0.70 Control group Cost: €4,991 No. of people sustaining a fall during 1 year of follow-up: 61 FAI: 24.5 QALY: 0.72	ICER per QALY: €9,293 ICER per fall averted: €−5,871	Not cost effective PEDro: Good QHES: Good

Iliffe et al. 2014 [41]	Perspective: Societal Cost: Programme cost, out-of-pocket expenditure, healthcare service Discounting: N/A	Intervention group(OEP) Cost: £496 No. of fall: 42 Intervention group(FaME) Cost: £653 No. of fall: 59 Control group Cost: £367 No. of fall: 53	ICER per fall averted (FaME):£-47.7 ICER per fall averted (OEP):£11.7 (Calculated by the reviewer)	No significant difference in the effect between FaME and OEP. FaME program is more expensive that FaME. PEDro: Good QHES: Poor
Irvine et al. 2010 [42]	Perspective: Healthcare Cost: According to NICE guidance, cost on healthcare service Discounting: N/A	Intervention group Cost: £2238 Fall per person-year: 2.07 Control group Cost: £1659 Fall per person-year: 2.85	ICER per no. of fall averted(base-case): £3320 ICER per no. of fall averted(including outlier): £738	Not cost effective PEDro: Poor QHES: Good

Isaranuwatchai et al. 2017 [43]	Perspective: Societal Cost: HSSUI (cost of primary care, emergency department and specialists, hospital days, other health and social care professionals, prescription medications and lab services) Discounting: N/A	Intervention group Change in Cost: −$15,028 Change in no. of fall: 0.3 Control group Cost: −$21,350 Change in no. of fall: 0.3 2006 Canadian dollars	ICER per no. of fall: [−$15,028-(−$21,350)]/0.3-0.3=N/A] (Calculated by reviewers)	Potentially Cost effective PEDro: Good QHES: Good
Markle-Reid et al. 2010 [44]	Perspective: Societal Cost: Health and Social Services Utilization Inventory (HSSUI) Discounting: N/A	Intervention group Cost: $18,869 Mean no. of fall: 1.45 Control group Cost: $16,430 Mean no. of fall: 1.33	ICER per fall averted: $20,325 (calculated by reviewers)	Intervention is effective and no more expensive than the usual care. PEDro: Good QHES: Poor

McLean et al. 2015 [45]	Perspective: Healthcare Cost: Program cost + cost of falls Discounting: 3%, converted from 2010 Australian Dollars to British Pound Sterling (GBP)	Intervention group Cost: £84.98 Fall rate: 0.309 QALY: 0.495 Control group Cost: £38.94 Fall rate: 0.390 QALY: 0.494	ICER per QALY: £51483 ICER per fall averted: £652	Not cost effective for mixed gender, cost-effective for women only PEDro: Poor QHES: Good
Rizzo et al. 1996 [46]	Perspective: Healthcare Cost: Cost of the Intervention, hospitalization and emergency department (ED), outpatient, home care, and skilled nursing facility. Discounting: N/A	Cost of the Intervention: $138393 The average cost per medical fall prevented: $8,824 No of fall in intervention group: 86 No of fall in control group: 152	ICER not mentioned 8824/(50) =176.48 (calculated by the reviewer)	Cost-effective PEDro: Poor QHES: Poor

Robertson et al. 2001a [47]	Perspective: Societal Cost: Exercise nurse (i.e. time. travel, accommodation), PT, materials, Transport, Recruitment, programme prescription, and follow up Discounting: N/A	Intervention group Cost: NZ$52299 Cost per participant: NZ$432 No. of fall: 80 Control group Cost: N/A No. of fall: 109	ICER: Incremental cost per fall prevented was $NZ1803 The exercise programme was considerably more cost-effective for those aged 80 years and older than for the total sample (cost saving of $NZ576 per fall prevented and $NZ1553 per injurious fall event prevented).	Considerably cost effective PEDro: Good QHES: Poor
Robertson 2001b [48]	Perspective: Healthcare Cost: Recruiting cost Prescribing the programme (i.e. exercise instructor time, exercise instructor transport) Materials for the programme (i.e. ankle cuff weight, instruction booklet) Participant follow up cost Discounting: N/A	Intervention group Cost: NZ$20122 in 1st year Cost per participant in 1st year: NZ$173 Cost per participant in 2nd year: NZ$22 No. of falls: 88 in 1st year, 50 in 2nd year Control group Cost: N/A No. of falls: 152 in 1st year, 68 in 2nd year	ICER: Cost per fall prevented after 1 year is NZ$314 after 2 years is NZ$265. Cost per injurious fall (moderate or serious injury) per year is NZ$457 after 1 year, NZ$426 after 2 years.	Not cost effective PEDro: Poor QHES: Poor

Timonen et al. 2008 [49]	Perspective: Healthcare Cost: Group training program (i.e. 2 physiotherapists' working time, transportation, meals) Discounting: N/A	Intervention group Cost:€19310 Cost per participant: €37.3 Control group Cost: €1527 Cost per participant: €44.9 No. of falls For intervention group, 10 of them did not fall, 11 of them fall once, 13 of them fall twice or more For control group, 13 of them, did not fall, 9 of them fall once, 12 of them fall twice of more	ICER not reported	Not cost effective PEDro: Poor QHES: Poor

ICER- Incremental cost-effectiveness ratio, QALY- Quality-adjusted-life-year, EQ-D- Euro-Qol 5 dimension, CE plane- cost-effectiveness plane, , OEP- Otago Exercise Program, FaME- Community centre-based group exercise program, CAD- Canadian Dollars, NZ$- New Zealand Dollars.

Appendix 1

Database: Scopus

1. 'Fall prevention'
2. 'Trip prevention'
3. 'Prevent fall'
4. 'Control fall'
5. 'Control balance'
6. 'Elderly'
7. 'Senior'
8. 'Old people'
9. 'Older adult'
10. 'Community dwelling older adults'
11. 'Aged'
12. 'Old aged'
13. 'Old adults'
14. 'Cost effectiveness'
15. 'Value'
16. 'Money'
17. 'Effectiveness'
18. 'Economic analysis'
19. 'Economic evaluation'

20. 'Cost efficiency'

21. 'Economical'

22. "Fall prevention " OR "Trip prevention " OR "Prevent fall " OR "Control fall " OR "Control balance "

23. "Older people" OR "Senior " OR "Old people " OR "Older adult " OR "Community dwelling older adults " OR "Aged " OR "Old aged " OR "Old adults "

24. "Cost effectiveness " OR "Value " OR "Money " OR "Effectiveness " OR "Economic analysis " OR "Economic evaluation " OR "Cost efficiency " OR "Economical"

25. 22 AND 23 AND 24

Search strategy used for Scopus: FALLS ("Fall prevention " OR "Trip prevention " OR "Prevent fall " OR "Control fall " OR "Control balance") AND ELDERLY ("Older people" OR "Senior " OR "Old people " OR "Older adult " OR "Community dwelling older adults " OR "Aged " OR "Old aged " OR "Old adults ") AND COST-EFFECTIVENESS ("Cost effectiveness " OR "Value " OR "Money " OR "Effectiveness " OR "Economic analysis " OR "Economic evaluation " OR "Cost efficiency " OR "Economical")

Appendix 2: Criteria for inclusion according to the PICOS framework:

Inclusion	Criteria	Exclusion
Older adults aged 60 years and above	Patient	Older adults with Parkinson's disease, Stroke, Dementia or other chronic health conditions associated with old age.
Exercise-based falls prevention program	Intervention	Fall prevention programs without physical exercise component
Study must have exercise-based falls prevention delivered to the experimental group. Control groups included no treatment control, usual care and active control.	Comparison	NA
Incremental cost-effectiveness ratios (ICER), cost per quality-adjusted life year (QALY), incremental cost per fall, benefit to cost ratio and cost-utility analysis.	Outcome measures	NA
Randomized controlled trials with economic evaluation	Study type	Study protocols, systematic reviews, conference abstracts and non-English publications

Appendix 3: PRISMA checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Yes
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 9 and appendix 2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 8, 9 and Appendix 1

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 9 and Appendix 2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Tables 2 and 5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Tables 3 and 4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Results, page 12-16
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not applicable

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Authors contribution:

Stanley Winser and Priya Kannan: Conceptualization; Data curation; Analysis; Interpretation of results; manuscript drafting and proof reading.

Chan Hei Tung Fion, ***Lam Ho, Lau Sze Chung, Lau Tsz Ching, Tom Kin Lok Felix***: Review registration; Conceptualization; Data screening, Data extraction; manuscript drafting and proof reading.

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