



The Effect of Fall Prevention Exercise Programmes on Fall Induced Injuries in Community-Dwelling Older Adults

Fabienne El-Khoury

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THÈSE DE DOCTORAT

SANTÉ PUBLIQUE - EPIDÉMIOLOGIE

par **Fabienne El-KHOURY**

The effect of fall prevention exercise
programmes on fall induced injuries in
community-dwelling older adults

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“There is an art to flying, or rather a knack. Its knack lies in learning to throw yourself at the ground and miss...”

‘The hitchhiker's guide to the Galaxy’ - Douglas ADAMS

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Résumé

Introduction

Épidémiologie

Les chutes et les blessures dues aux chutes représentent un véritable problème de santé publique; on estime que chaque année un tiers des personnes âgées de plus de 65 ans tombent avec une nette augmentation de l'incidence avec l'avancée en âge : 50% des plus de 80 ans vivant à domicile tombent au moins une fois dans l'année. De plus, la moitié de ces chuteurs font plus d'une chute par an (chutes répétées).

Les chutes peuvent entraîner des traumatismes physiques graves, laisser des séquelles psychologiques importantes, et engendrent des coûts économiques considérables. Environ 30% des chutes donnent lieu à une blessure, et autour de 10% des chutes résultent en une blessure grave telles qu'une fracture, une luxation des articulations, une lésion des tissus mous, ou une lésion cérébrale traumatique. Elles sont aussi une des principales causes d'hospitalisations et de mortalité chez les personnes âgées.

Les conséquences psychologiques incluent une perte de confiance avec limitation des activités quotidiennes et déclin des capacités fonctionnelles, et par la suite une augmentation du risque de la perte d'autonomie.

On estime que le coût financier des chutes est compris entre 0.85% et 1.5 % du coût total des dépenses de santé d'un pays.

La plupart des chutes sont dues à une interaction complexe de facteurs de risque qui, en se combinant, dépassent la capacité d'une personne âgée à maintenir ou à rétablir son équilibre à la suite d'une perte d'équilibre. On distingue des facteurs de risque biologiques ou intrinsèques (faiblesse musculaire, troubles de l'équilibre et de la démarche, déficiences visuelles ou cognitives, etc...), et des facteurs de risque environnementaux (aménagement du domicile et des lieux publics, chaussures et vêtements, éclairage, temps et climat).

L'exercice pour la prévention des chutes

De nombreux essais contrôlés randomisés et des revues systématiques des essais ont montré que des programmes d'exercices physiques simples, adaptés aux capacités des personnes et axés sur le travail de l'équilibre, permettaient de réduire de 30 à 40% le risque de chutes chez les personnes âgées vivant à leur domicile. L'inclusion dans le programme d'un entraînement spécifique de l'équilibre semble être un élément clé de l'efficacité du programme, et pourrait expliquer pourquoi des interventions de types et formats différents (Tai chi, exercice à domicile, exercice en groupe) ont une efficacité comparable et substantielle vis-à-vis des chutes. Une revue systématique des programmes d'exercice pour la prévention des chutes avait montré que les programmes d'exercice qui stimulent fortement l'équilibre (un entraînement spécifique de l'équilibre, et une plus forte 'dose' totale d'exercice) sont significativement plus efficaces vis-à-vis des chutes que ceux qui offrent une stimulation moins intense.

Cependant, l'efficacité des programmes d'exercice sur la prévention des traumatismes causés par les chutes n'a pas été clairement démontrée dans les essais. Quelques essais ont montré un parallèle entre la diminution des chutes dans leur ensemble et la diminution des chutes accompagnées de traumatismes, mais les traumatismes pris en compte varient selon les études, ce qui rend difficile la comparaison de leurs résultats. De plus, les essais n'ont généralement pas un effectif suffisant pour pouvoir montrer clairement un effet bénéfique de l'exercice sur la réduction des chutes traumatiques, en particulier les plus graves.

Par ailleurs, les mécanismes par lesquels l'exercice physique prévient les chutes et les traumatismes mériteraient d'être mieux compris de façon à pouvoir définir les programmes optima en termes d'efficacité. L'exercice physique a pour objectif d'améliorer les capacités physiques (équilibre, marche, coordination, etc.), mais il pourrait également agir en redonnant confiance en soi (diminution de la peur de tomber), en améliorant l'état de santé mentale et le fonctionnement cognitif, ou bien encore par le biais d'une augmentation du niveau général d'activité, mais ceci a rarement été étudié. L'impact des programmes d'exercice de prévention des chutes sur la qualité de vie des personnes a également rarement été évalué.

En plus, la participation des personnes âgées aux programmes de prévention des chutes est faible. Une meilleure connaissance du profil des personnes qui acceptent ou refusent de participer aux interventions proposées pourrait permettre de mieux cibler les interventions et apporter des

éléments utiles pour augmenter la participation des personnes âgées aux programmes d'exercice de prévention des chutes.

Objectives du travail

Pour répondre à ces interrogations, mon travail de thèse a été divisé en 2 parties :

- une revue systématique de la littérature suivie d'une méta-analyse des résultats d'essais contrôlés randomisés de prévention des chutes chez les personnes âgées vivant à leur domicile afin d'évaluer dans quelle mesure les programmes d'exercice destinés à prévenir les chutes permettent aussi de prévenir les traumatismes causés par les chutes,
- l'analyse des données de l'essai contrôlé randomisé multicentrique 'Ossébo', dont l'objectif principal était d'évaluer l'efficacité d'un programme d'exercice physique de longue durée (2 ans) mettant l'accent sur l'équilibre et le renforcement musculaire, sur la prévention des chutes traumatiques chez des femmes de plus de 75 ans qui vivent à leur domicile et ont des capacités physiques locomotrices diminuées.

Méthodes

Revue systématique et méta-analyse

Des recherches bibliographiques ont été effectuées dans plusieurs bases de données (PubMed, Cochrane Library, Embase, CINAHL) pour repérer les essais randomisés contrôlés de prévention des chutes par l'exercice physique réalisés chez des personnes de plus de 65 ans vivant à leur domicile, et publiés jusqu'en juillet 2013. Les essais qui ciblent des participants ayant des problèmes neuro-dégénératives, les études qui comparent des interventions multifactorielles, ou qui ne présentent pas des données quantitatives sur les conséquences des chutes, étaient exclus.

Les recommandations de la 'Cochrane Collaboration' ont été appliquées pour évaluer le risque de biais de chacun des essais les domaines suivants : méthode de randomisation, dissimulation de l'allocation des groupes, évaluation à l'aveugle ou pas, méthode de confirmation de la blessure, et le traitement des données manquantes.

Une étape préliminaire essentielle a consisté à regrouper les définitions des chutes traumatiques trouvées dans les études sélectionnées en 4 catégories relativement homogènes :

1/ toutes les chutes ayant eu une conséquence, qu'il s'agisse d'un symptôme clinique spécifique (pouvant aller d'un simple hématome à un traumatisme plus grave) ou du recours à des soins médicaux.

2/ les chutes qui ont entraîné le recours à des soins médicaux.

3/ les chutes ayant entraîné un traumatisme grave tel qu'une fracture, un traumatisme crânien, une plaie profonde ayant nécessité des sutures ou tout autre blessure ayant conduit à une hospitalisation.

4/ les chutes ayant entraîné plus spécifiquement une fracture.

En fonction du type de données disponibles, une même étude a pu contribuer à l'analyse d'une ou plusieurs catégories de chutes traumatiques. On a réalisé une méta-analyse séparée pour chaque catégorie de chute traumatique, et un effet global (ou estimateur commun 'poolé' de l'exercice correspondant au ratio des taux d'incidence dans les 2 groupes (intervention vs. témoin) a été calculé par un modèle à effet aléatoire pour chacune de ces catégories. L'hétérogénéité statistique entre les études d'une méta-analyse était évaluée à l'aide du calcul d'I² et le Q-test. L'existence d'un biais de publication était examinée à l'aide graphique en entonnoir (funnel plot).

L'essai Ossébo

Recrutement et population

Les participantes à l'essai Ossébo sont des femmes âgées de 75 à 85 ans, vivant à leur domicile, et qui sont à risque de chute du fait des capacités physiques diminuées. Au total, 706 femmes ont été incluses dans 20 centres d'étude répartis à travers la France (Amiens, Annecy, Boulogne-Billancourt, Caen, Issy-les-Moulineaux, Lille, Lyon, Montpellier, Nantes, Nîmes, Paris {5e, 16e, 17e, 18e, 20e}, Reims, Rouen, St Etienne, Strasbourg, Villejuif).

Le recrutement a été fait à partir des listes électorales. Dans un premier temps, toutes les femmes âgées entre 75 et 85 ans domiciliées autour des centres d'examen ont été invitées à un bilan de l'équilibre et de la motricité qui comprenait notamment les tests de sélection dans l'essai. Les bilans ont été réalisés dans des consultations hospitalières de services gériatriques dans la plupart des cas, par des infirmières ou assistantes de recherche clinique spécialement formées pour l'étude.

Pour être éligibles à participer à l'essai, les femmes devaient avoir des capacités physiques locomotrices diminuées. La sélection des femmes était alors basée sur les résultats du test de marche sur 6 mètres et du test de marche funambule. Ces deux tests ont été choisis car ils sont

simples à mettre en œuvre, et parce qu'ils sont prédictifs du risque de chute et de fracture, dans l'étude prospective EPIDOS (Epidémiologie de l'Ostéoporose) qui portait sur une population comparable à celle de l'étude 'Ossébo'. Ainsi, les femmes qui ont présenté au moins un des deux facteurs de risque validés dans EPIDOS, c'est-à-dire une incapacité à faire quatre pas le long d'une ligne en position tandem (marche funambule) ou un temps moyen de marche sur 6 mètres supérieur à 7 secondes (valeur médiane dans la population EPIDOS) étaient potentiellement éligibles pour participer à l'essai Ossébo.

Toutefois, les femmes les plus fragiles, c'est-à-dire celles qui ont fait le test de marche en 12,5 secondes ou plus (95e percentile dans la cohorte EPIDOS), ou qui ne pouvaient pas tenir en équilibre pieds joints, étaient exclues de l'essai car elles avaient un risque élevé de chute et nécessitaient des exercices physiques personnalisés.

Les autres critères d'exclusion étaient : avoir des problèmes de santé contre-indiquant la pratique d'exercices physiques, assister à des cours de gymnastique ou des ateliers de prévention des chutes, difficulté pour suivre les ateliers (troubles cognitifs évidents, surdité, absences répétées ou prolongées du domicile, etc).

Les femmes éligibles pour rentrer dans l'essai et qui ont accepté d'y participer ont ensuite été randomisées en deux groupes : un groupe qui a reçu l'intervention (programme d'exercice physique) et un groupe témoin, sans intervention.

Intervention

L'intervention a été conçue et mise en œuvre en partenariat avec l'association S.I.E.L Bleu (Sport Initiative et Loisir) qui regroupe des professionnels de l'activité physique adaptée aux personnes âgées. Elle comprend des ateliers d'exercice en petits groupes (10-15 personnes), une fois par semaine pendant 2 ans, complétés par des exercices simples à faire au domicile, basés sur ceux réalisés lors des ateliers et adaptés par l'animateur aux capacités physiques des femmes. Les séances en groupe ont eu lieu dans des milieux communautaires servant généralement pour des activités similaires. Le plus souvent, les ateliers ont eu lieu dans des lieux associatifs tels que des clubs pour personnes âgées. Alternativement, dans d'autres cas l'intervention a eu lieu dans un auditorium ou une salle de mairie, ou dans un hôpital.

Le programme d'exercice avait pour but : l'amélioration des facteurs physiques pouvant influencer sur l'équilibre, la prévention de la chute et la réduction des conséquences de la chute, l'éveil à la prévention des risques de chute, et l'éducation à long terme de l'entretien de l'équilibre. Les

animateurs des ateliers ont reçu la même formation afin d'assurer la standardisation du déroulement et de la progression des exercices dans tous les centres, cette standardisation était guidée par un manuel d'instructions détaillées.

Suivi et critères de jugement

La survenue de chutes a été enregistrée tous les mois grâce au renvoi par les femmes de cartes-calendriers sur lesquelles elles devaient noter les jours où elles avaient éventuellement fait une chute (méthode de référence). Un entretien téléphonique était réalisé en cas de signalement d'une chute afin de connaître les circonstances et les conséquences de la chute. Les dossiers médicaux ont été demandés en cas d'hospitalisation, et le compte rendu radio a été demandé en cas de fracture. L'enregistrement et le classement des chutes en fonction de leurs conséquences ont été réalisés à l'aveugle ; un gériatre a classé 'à l'aveugle' les chutes en 3 classes (pas de conséquence, traumatisme modéré, traumatisme grave) sur la base des dommages physiques et des soins médicaux reçus.

Les participantes ont été invitées à revenir à 1 an et 2 ans après inclusion pour passer un nouveau bilan, selon le même protocole que pour le bilan initial. Celui-ci comprenait notamment des tests fonctionnels simples : le test de 'Timed get up and go' (temps mis pour se lever d'une chaise, marcher sur trois mètres, faire demi-tour et revenir s'asseoir) , le test de 'levers d'une chaise' (temps mis pour se lever d'une chaise cinq fois), le temps en équilibre monopodal (temps pendant lequel la participante peut rester en équilibre sur un pied), le temps moyen de marche sur 6 mètres, et le test de marche funambule (capacité à faire quatre pas le long d'une ligne en plaçant le talon avant contre le gros orteil du pied arrière (oui/non)).

On a aussi mesuré la peur de tomber à l'aide d'une échelle validée, la 'Fall Efficacy Scale' (FES-I), ainsi que le niveau général d'activité physique à l'aide d'un questionnaire adapté aux personnes âgées qui porte sur différents types d'activité : les sorties pour les courses, la marche promenade, les autres activités physiques sportives ou de loisirs (jardinage, natation, danse, vélo, exercices à la maison, etc). La qualité de vie liée à la santé (SF36 short form) était aussi examinée.

Le critère principal de jugement de l'efficacité de l'intervention est le taux d'incidence des 'chutes traumatiques' (modérée et graves).

Les autres critères sont le taux d'incidence de l'ensemble des chutes, le taux d'incidence des chutes traumatiques les plus graves, les capacités physiques (appréciés par les tests fonctionnels),

ainsi que les autres facteurs mesurés dans les bilans et susceptibles d'influencer le risque de chute (peur de tomber, qualité de vie perçue...).

Analyse statistique

Les chutes étant des événements récurrents, des modèles à fragilité (modèles de survie avec un effet aléatoire pour prendre en compte la corrélation intra-individuelle des événements) ont été utilisés pour modéliser les taux de chutes traumatiques dans les 2 groupes (les 'hazard ratios' (HR) des taux de chutes, et leur intervalle de confiance à 95% sont rapportés). La moyenne du nombre cumulatif des événements (chutes ou blessures dues aux chutes) par femme à un temps t étaient représentée graphiquement à l'aide de la fonction de moyenne cumulée (mean cumulative function).

L'évolution au cours du temps dans les 2 groupes des capacités physiques locomotrices, de la peur de tomber, du niveau général d'activité physique, et des différents indicateurs de qualité de vie ont été comparés à l'aide d'un modèle marginal (population averaged model) avec un effet aléatoire au niveau du centre.

Par ailleurs, on a examiné les caractéristiques individuelles (socio-démographiques, facteurs de risque de chute, santé perçue, comportements liés à la prévention, activité physique et sociale) et les facteurs liés à l'implémentation de l'intervention (distance domicile-atelier, type de lieu d'entraînement proposé, saison) qui sont associées au fait d'accepter de rentrer dans l'essai, parmi les femmes éligibles. En raison de la structure hiérarchique des données (participantes imbriquées dans des centres), l'analyse multivariée a été effectuée à l'aide de modèles de régression logistiques multiniveaux (niveau 1 : participantes, niveau 2 : centres).

Résultats

Revue systématique et méta-analyse

Dix-sept essais totalisant 4305 participants (2195 participants dans le groupe exercice) de plus de 60 ans, dont 77% de femmes, ont été sélectionnés pour la revue et inclus dans la méta-analyse. La moyenne d'âge des participants était de 76.7 ans. Toutes les interventions évaluées comprenaient des exercices spécifiques de stimulation de l'équilibre. La durée moyenne de l'intervention était de 9.4 mois.

Dans 14 études, l'intervention était effectuée en groupe, parmi ces interventions, les ateliers étaient supplémentés avec des exercices à domicile dans 6 cas. Dans les trois autres essais, l'intervention consistait en des exercices individualisés livrés à domicile uniquement. Deux essais ont examiné le Tai Chi uniquement comme interventions; toutes les autres interventions comprenaient un composant d'entraînement de la marche, de l'équilibre et de l'entraînement fonctionnel. De nombreuses études comprenaient également des exercices de musculation. La durée des programmes d'exercice varie de 5.5 semaines à un an et demi, avec une moyenne d'environ 8.5 mois d'intervention.

Les résultats de la méta-analyse montrent que l'exercice est associé à une réduction du taux de chutes traumatiques dans chacune des catégories de chutes traumatiques considérées, avec un ratio des taux d'incidence estimé ('pooled RaR' et 95% CI) de 0.63 (IC 95% : 0.51 - 0.77, $I^2=50\%$ $p=0.03$) pour l'ensemble des chutes traumatiques (10 essais). Le RaR était de 0.70 (IC 95% : 0.54 - 0.92, $I^2=20\%$ $p=0.27$) pour les chutes ayant entraîné le recours à des soins médicaux (8 essais), de 0.57 (IC 95% : 0.36 - 0.90 $I^2=46\%$ $p=0.09$) pour les chutes accompagnées d'un traumatisme grave (7 essais), et de 0.39 (IC 95% : 0.22 - 0.66 $I^2=0\%$ $p=0.96$) pour les chutes accompagnées d'une fracture, spécifiquement (6 essais). Cependant, ces résultats doivent être interprétés avec une certaine prudence car la qualité méthodologique de plusieurs essais n'a pas pu être déterminée avec certitude dans plusieurs domaines, et une hétérogénéité statistiquement significative a été observée entre les études incluses dans l'analyse des chutes traumatiques totales.

L'essai Ossébo

Il y avait un total de 55 perdus de vue dans le groupe d'intervention au cours du suivi (dont 65% dans la première année), comparé à 42 perdus de vue dans le groupe témoin. Au cours de 2 ans de suivi, on a recensé 397 chutes traumatiques dans le groupe control (C) (temps de suivi total=703 ans), et 305 dans le groupe intervention (I) (temps de suivi total=677 ans), ce qui correspond à une réduction significative de 19% du taux de chutes traumatiques dans le groupe intervention par rapport au groupe témoin (HR= 0.81 (0.67 - 0.99), $p=0.02$). La réduction du taux des chutes traumatiques les plus graves (C: 87 - I:68) est du même ordre, bien que non significative (HR= 0.83 (0.60 - 1.16), $p=0.16$).

A 2 ans, les femmes du groupe intervention ont des performances significativement meilleures que les femmes du groupe témoin sur l'ensemble des tests physiques (par exemple, différence moyenne inter-groupes de temps en équilibre monopodal à 2 an est de 2.1 sec ; $p=0.0009$ -

différence moyenne inter-groupes de temps mis pour se lever d'une chaise à 2 an est de 1.7 sec ; $p < 0.0001$); elles ont également une meilleure perception de leur santé sur le plan physique et fonctionnel (différence moyenne inter-groupes de 5.3 points sur le score 'Physical function' du SF36; $p = 0.01$).

En moyenne, 95 séances d'atelier d'exercice était offertes par centre. Environ 16% ($n = 58$) femmes du groupe intervention n'ont jamais commencé les ateliers. Parmi les femmes qui les ont commencés, la médiane des séances suivies est de 53 (étendue interquartiles 16-71), et la médiane de la durée de participation aux ateliers est de 79 semaines (étendue interquartile 32-97).

Les femmes éligibles qui ont accepté de participer à l'essai étaient plus jeunes, avaient davantage tendance à vivre seule et à avoir fait une coloscopie au cours des 5 dernières années que les femmes éligibles qui n'ont pas accepté de participer à l'étude. En plus, la probabilité d'accepter de participer était plus grande lorsque les ateliers proposés se déroulaient dans des locaux municipaux ou associatifs que lorsqu'ils avaient lieu dans des résidences pour personnes âgées. Également, la participation était plus importante lorsque les ateliers ont débuté pendant les mois d'hiver.

Discussion

Les résultats de la revue systématique de la littérature et de la méta-analyse des essais de prévention des chutes suggèrent que les programmes d'exercice destinés à améliorer l'équilibre et à prévenir les chutes sont également efficaces pour réduire les traumatismes causés par les chutes, y compris les plus graves.

Par ailleurs, les résultats de l'essai Ossébo montrent qu'il est possible de mettre en place à large échelle un programme d'exercice de longue durée qui est efficace vis-à-vis de la réduction des chutes traumatiques, y compris chez des personnes très âgées (> 75 ans). Le programme Ossébo améliore non seulement les capacités physiques mesurées par des tests cliniques, mais aussi la perception que les personnes ont de leur santé sur le plan physique fonctionnel. Cette amélioration des fonctions physiques explique probablement, au moins en partie, l'effet bénéfique du programme d'exercice Ossébo sur la prévention des chutes et les blessures dues aux chutes. Un autre mécanisme qui peut expliquer l'effet plus important sur la réduction des blessures dues aux chutes que sur la prévention des chutes est l'amélioration du temps de réaction, la force musculaire, la marche, la coordination, et ainsi que les fonctions cognitives par l'exercice.

L'analyse des facteurs associés à la participation à l'essai a indiqué que le type de lieu de l'intervention, l'âge, le fait de vivre seul, et les comportements liés à la prévention indépendamment associés à la participation. Par contre, les facteurs liés au risque de chutes (capacités fonctionnelles, antécédent de chute, etc...) n'étaient pas associés à la participation à l'essai. C'est peut-être parce que les femmes éligibles étaient déjà assez homogènes concernant ces facteurs. Alternativement, c'est peut-être dû à une sous-estimation du risque personnel de chute, connu chez les personnes âgées. Ces éléments peuvent aider dans la conception et l'implémentation des futures interventions.

Une des forces principales de ce travail réside dans son approche fondée sur des preuves, et l'utilisation de procédures méthodologiques et statistiques recommandées. Les essais contrôlés randomisés représentent l'étalon-or dans l'évaluation des interventions de soins de santé, et les revues systématiques d'essais randomisés est la méthode recommandée pour identifier et évaluer les preuves existantes sur des interventions en santé publique.

L'utilisation d'une classification bien définie des blessures dues aux chutes dans la revue systématique et l'essai Ossébo est une autre force de ce travail. Cette classification pourrait être reproduite, permet la comparabilité entre les différents essais et est basée sur des critères de jugements cliniquement pertinents.

L'ensemble de ces résultats apporte des preuves scientifiques de haut niveau concernant l'intérêt des programmes d'entraînement de l'équilibre pour prévenir les traumatismes liés aux chutes et contribuer à améliorer la qualité de vie des personnes âgées. D'autres études sont maintenant nécessaires pour déterminer les stratégies les plus efficaces pour améliorer la participation des personnes âgées à ce type de programme

Mots-clés :

Prévention, chutes, prévention des chutes, épidémiologie des chutes, exercices physiques, chutes traumatiques, essai randomisé contrôlé, revue systématique de la littérature, méta-analyse, médecine fondée sur les faits, personnes âgées, capacité locomotrices, peur de tomber, essai pragmatique, participation dans les essais, géolocalisation.

Abstract

Context

Exercise programmes can prevent falls in older community-dwellers. However, evidence that these programmes can also prevent injurious falls was poor.

Objectives

Systematic review of evidence of the effect of exercise interventions on injurious fall prevention from randomised controlled trials (RCT).

Evaluate the effectiveness of ‘Ossébo’, a multi-centre RCT assessing the effectiveness of a 2-year injurious fall prevention balance training programme.

Methods

Systematic review

The definitions of injurious falls from included studies were classified into more homogeneous categories. This allowed the estimation of a pooled rate ratio for each injurious falls category based on random effects models.

Ossébo trial

706 women aged 75-85 years; home-living with diminished functional capacities were included. The 2 groups were compared for rates of injurious falls with a frailty model. Other outcomes included physical functional capacities, and quality of life indicators.

Results

Systematic review

17 trials involving 4305 participants were included. Four categories were identified: all injurious falls, falls resulting in medical care, severe injurious falls, and falls resulting in fractures. Exercise had a significant preventive effect in all categories.

Ossébo

There were 305 injurious falls in the intervention group and 397 in the control group, for a HR of 0.81 (0.67 to 0.99). At 2 years, women in the intervention group had significantly better performances on all physical tests and a better perception of their overall physical function.

Conclusion

Fall prevention exercise programmes are effective in preventing injurious falls, and are feasible for long-term, wide-spread dissemination.

Keywords:

Falls, prevention, accidental fall, fall prevention, epidemiology of falls in older adults, exercise, fall, injurious falls, home-dwelling old people, exercise, systematic review, meta-analysis, evidence-based medicine, frailty model, hazard ratio, exercise intervention, pragmatic trial, participation in trial, geo-localisation, geodetic distance.

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10th Annual Meeting and 5th Conference of HEPA Europe

27-29 August 2014 -University of Zurich, Switzerland

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10 octobre 2013 - Paris

Invited speaker

- “Comment prévenir la chute? Efficacité des programmes d’exercices physiques.” (How to prevent falls? Efficacy of exercise programmes)

Fabienne El-Khoury

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- “Évaluation d’un programme d’exercice pour la prévention des chutes traumatiques: l’essai ‘Ossébo’.” (Evaluation of the efficacy of an injurious fall prevention exercise programme : the Ossébo trial).

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1. General introduction

1.1. Context

1.1.1. An aging population

Longer life expectancy is arguably one of humanity's biggest achievements. Medical progress, public-health efforts, rising standards of living, better education, healthier nutrition and a more hygienic lifestyle in the past century lead to a substantial increase in life expectancy worldwide (Oeppen and Vaupel 2002).

In developed countries, around 30 years in life expectancy have been gained since 1900, and the oldest-old group – i.e., those aged 80 and over – have been the most rapidly expanding segment of the population over the past decades (Rau et al. 2008; Lutz, Sanderson, and Scherbov 2008). It is expected that by the year 2050, the worldwide population of older adults (more than 65 years old) may grow to nearly 2 billion, with 80% of that population living in developing countries (Bremner et al. 2010).

However, humanity's big achievement has its pitfalls; the years gained in life expectancy might be years with disability, since disability increases with age. Although people are living longer, they are experiencing morbidity and disability over a longer period of time (Christensen et al. 2009). Worldwide, the trend toward longer life has been accompanied with an increasing prevalence of diseases in older adults, and decline in mobility, independence and other functions that are essential for a good quality of life (Freedman et al. 2004). The WHO estimates that 10% of the world's population has some form of a disability, 20% of those aged 70+, and 50% of those aged 85+ (Heikkinen 2003; WHO- Disability and rehabilitation (DAR) team 2014), with women experiencing more disability in old age than men (Jagger et al. 2007).

One major source of disability is falling, the leading cause of both fatal and nonfatal injuries among older adults (Rockett et al. 2012). A fall is defined as 'unintentionally coming to rest on the ground, floor, or other lower level' (Lamb, Jørstad- Stein, et al. 2005). Falls are very common (Rubenstein 2006; Stevens et al. 2008; Weisenfluh et al. 2012), cause considerable health care utilisation, long-term pain, and functional impairment among older adults (Hartholt et al. 2011). They also substantially increase the risk of dependency and discharge to a nursing home (Gill et al. 2013), moreover their treatment and complications result in high healthcare costs (Davis et al. 2010b).

1.1.2. Research in geriatric falls

Due to the high incidence and serious consequences of falls, accidental falls have been the subject of many medical and epidemiological studies that aim to characterise them, prevent their occurrence and minimise their consequences. Hence, the scientific literature about geriatric falls and their prevention is now ample. Notably, the Cochrane collaboration recently published 2 different systematic reviews of randomised controlled trials to prevent falls: the first review concerns interventions targeting community dwelling older adults (159 included randomised controlled trial (RCT)), (Gillespie et al. 2012) and the second one concerns interventions targeting older adults living in care facilities and hospitals (60 included RCTs) (Cameron et al. 2010).

Interestingly though, the ‘preventability’ of falls had not always been conceivable in the scientific and medical community. Around the start of the second half of the 20th century, falls were considered as an ‘inevitable aspect of ageing’ (Sheldon 1960). Research was initially scarce and consisted mostly of clinical descriptions of falls among older adults, until the 1990s when many epidemiological studies quantifying the incidence of falls and their consequences were published (M E Tinetti, Speechley, and Ginter 1988; O’Loughlin et al. 1993; Stephen R. Lord et al. 1993). These studies also identified several potentially modifiable risk factors for falling. Therefore, the stage was set for trials testing interventions to prevent falls by targeting the newly identified risk factors, where many different fall prevention interventions were conceived and evaluated. And thus evidence of the preventability of falls started growing, with some type of interventions proving to be effective (Chang et al. 2004), notably exercise programmes.

This dissertation endeavours to further expand and develop the current knowledge about fall prevention exercise programmes among older community-dwellers. It will begin by summarising the current knowledge on the epidemiology of falls and injurious falls.

1.2. Epidemiology of falls in older adults

1.2.1. Incidence of falls among older adults

Falls are a frequent and recurrent problem among older adults, and their incidence increases with age (Berry and Miller 2008; Rubenstein and Josephson 2002). Prospective studies conducted in community-dwelling older adults, unselected for a special condition such as dementia or stroke patients, have reported that around one in three adults older than 65 years fall at least once a year. The rate of falls can differ from a population to another, it is been reported that fall incidence among Chinese older people is approximately half that of Caucasian populations (Kwan et al. 2011). Table 1 presents fall incidence data, among community-dwelling older adults, extracted from recent prospective epidemiological studies.

Almost half of those who have fallen will experience another fall in the following year (Berry and Miller 2008). Furthermore, the rate of falls increases with age, with 50% of individuals over 80 falling at least once each year. A Swedish prospective cohort among women aged 75 years and over (mean 80.8 years), found that half of women (50.5%) fell at least once during the one-year follow-up.

Table 1: Fall incidence among older adults as reported in recent prospective studies.

Reference	country	Age group	no. of participants	Length of follow-up	% of fallers	Rate of falls (fall/p.y.)
(G. Li et al. 2014)	Canada	Mean: 69.4 (sd=8.9)	3985 (all women)	one year	32%	-
(Vries et al. 2013)	Netherland	Median: 75.6	1509	one year	31%	-
(Faulkner et al. 2009)	USA	Mean: 71 (sd=3)	8378	4 years	59.6% (in 4 years)	0.46
(Duckham et al. 2013)	USA	Mean: 78 (sd=5)	743	4.3 years	-	0.81
(Woo et al. 2009)	China	65-69	1304	2 years	23% (in 2 years)	-
		70-74	1344		26% (in 2 years)	
		75+	1242		29% (in 2 years)	
(Berdot et al. 2009)	France	Mean: 73.7 (sd=5)	6343	4 years	42.1% (in 4 years)	

1.2.2. Physical consequences of falls

Falls are associated with a large diversity of undesired physical consequences among older adults, including death, hospitalisation, fractures and other serious injuries such as lacerations, dislocations, sprains and hematoma (Terroso et al. 2014). Around 30% of falls result in injury, and 10% of falls lead to serious injurious falls; such as a fracture, joint dislocation, soft tissue damage, or traumatic brain injury (O'Loughlin et al. 1993; Stevens et al. 2008; M E Tinetti, Doucette, and Claus 1995; WHO- Ageing and life course unit 2008). Falls are responsible for about 40% of unintentional injuries in older adults, that represent the fifth leading cause of death in that age group (Rubenstein 2006). Most fractures in older individuals are the result of a fall, such as a trip or a slip (Bergström et al. 2008).

1.2.2.a. Hospitalisation

Falling is also a major cause of hospitalisation among older individuals (Stevens et al. 2006). In Australia, one in every 10 days spent in hospital by a person aged 65 years and older in 2009–10 was attributable to fall-induced injuries, with an average length of hospital stay per fall injury case of 15.5 days (Bradley and Australian Institute of Health and Welfare 2013).

1.2.2.b. Mortality

The WHO estimated that around 424 000 individuals die from falls globally each year all age groups combined, with adults older than 65 suffering the greatest number of fatal falls (WHO- Ageing and life course unit 2008). In 2012 in France, falls were responsible of 76.6% of deaths due to unintentional accidents in the 70-74 age group, and 90% in persons older than 75 years. In total 23 438 deaths was caused by a fall among French older adults aged 65 and older in that year (INVS 2014).

1.2.3. Psychological consequences of falls

Even when the fall does not yield physical consequences, a fall at old age can have devastating psychological outcomes such as the post-fall anxiety syndrome, in which the faller down-regulates activity in a perhaps overcautious attitude due to fear of falling; this in turn further contributes to deconditioning, weakness and abnormal gait and in the long run may actually increase the risk of falling again (J and M 2007; J. Murphy and Isaacs 1982).

1.2.3.a. Fear of falling

Fear of falling has been one of the most widely investigated and reported psychological consequences of falling (Scheffer et al. 2008). It is a key symptom of the so-called ‘post-fall syndrome’, that manifests itself by an intense fear and walking disorders (J. Murphy and Isaacs 1982). Noteworthy, it can also be commonly found among older persons who had not yet experienced a fall; it has been reported to occur in 12% to 65% of community-dwellers aged 60 years and older and who do not have a history of falling (Legters 2002; Mendes da Costa et al. 2012). Whereas fear of falling is reported in 29% to 92% of older adults who have fallen (Legters 2002). Fear of falling is a potential threat to the physical and mental well-being of older persons; it is thought to have a range of consequences, from increased caution during performance of daily activities, to an excessive restriction of activities which may contribute to a loss of independence and depressive symptoms (S. L. Murphy, Williams, and Gill 2002).

1.2.4. Decline in physical function and loss of independence

Falls, especially injurious falls (whether moderate or serious), often lead to decline in functional status among older adults. Falls were found to be associated with increased difficulty with functional activities: climbing stairs, dressing oneself, rising from a chair, cutting toenails, walking outside and using own or public transport (Mary E. Tinetti and Williams 1998; Laird et al. 2001; Stel et al. 2004). Moreover, those with declined motor functions tend to limit their physical and social activity leading to further loss of functional capacities and increased risk of admission to nursing homes (Mary E. Tinetti and Williams 1997).

1.2.5. Cost of falls

Falls are a major contributor to the economic burden of injuries in developed countries (Roudsari et al. 2005; Stevens et al. 2006). However, the cost of falls is relative to a country and its health system. The majority of the data available come from American studies, whereas the American health system has significantly different characteristics than the French or other European health systems. Therefore the cost estimates of fall in different countries will be presented, in order to illustrate more globally the economic burden of falls.

In 2000, the direct medical cost of fatal falls among older adults aged over 65 in the United States was estimated to be around \$0.2 billion, whereas the direct cost of non-fatal fall-related injuries

(N=2.6 million) was \$19 billion (Stevens et al. 2006). Hospitalisation contributed to 63% of the costs of non-fatal fall injuries, while emergency department visits contributed to 21% of that cost.

In 2001-2002 in Australia, the mean direct cost of an injurious falls was \$1049. The estimated total cost of falls among older adults for the health care system was 86.4 million Australian dollars, with more than half of this cost attributable to hospital inpatient treatment and a projected costs of 181 million Australian dollars in 2021 (Hendrie et al. 2004).

More recently in the Netherlands (2007-2009 period), the mean cost per fall was €9370, and fall-related medical costs were estimated at €675.4 million annually. Fractures contributed to 80% (€540 million) of the fall-related healthcare costs (Hartholt et al. 2012).

Regardless of differences in the average cost of an injurious fall between different countries, it is clear that fall-related injurious falls inflict a substantial burden on health systems and social services especially in ageing populations.

1.2.6. Causes and risk factors for falls

Most falls are multifactorial in origin, and do not result from a single intrinsic or extrinsic cause, but from the interactions between different factors (Soriano, DeCherrie, and Thomas 2007).

Some falls can be linked to specific intrinsic causes; a person's physical condition or a medical problem, such as dizziness, postural hypertension, syncope, etc..(Cronin and Kenny 2010; Rubenstein and Josephson 2002; Olsson Möller et al. 2013). Falling rates are also increased in those with Parkinson's disease and stroke (Stolze et al. 2004). Others are 'accidental' or related to environmental hazards in the person's home or community neighbourhood environment, such as poor lighting, slippery floors, inadequate shoes or clothes and uneven surfaces (Vladutiu et al. 2012). But experts argue that the majority of falls, including those attributed to accidents really stem from the interaction between predisposing factors and acute medical or environmental precipitating factors precipitating factors in a person's environment (Rubenstein 2006; Berry and Miller 2008; Mary E. Tinetti 2003).

The multifactorial nature of fall is also partly due to the multi-dimensional nature of balance.

1.2.6.a. Balance and postural control

Balance is a multidimensional concept referring to the ‘ability of a person not to fall’ (Pollock et al. 2000). Balance is also referred to as postural stability or postural control; a complex motor skill allowing to control the centre of mass (the centre of the total body mass) in relationship to the base of support (area of the body in contact with the support surface) (Horak and Macpherson 2010).

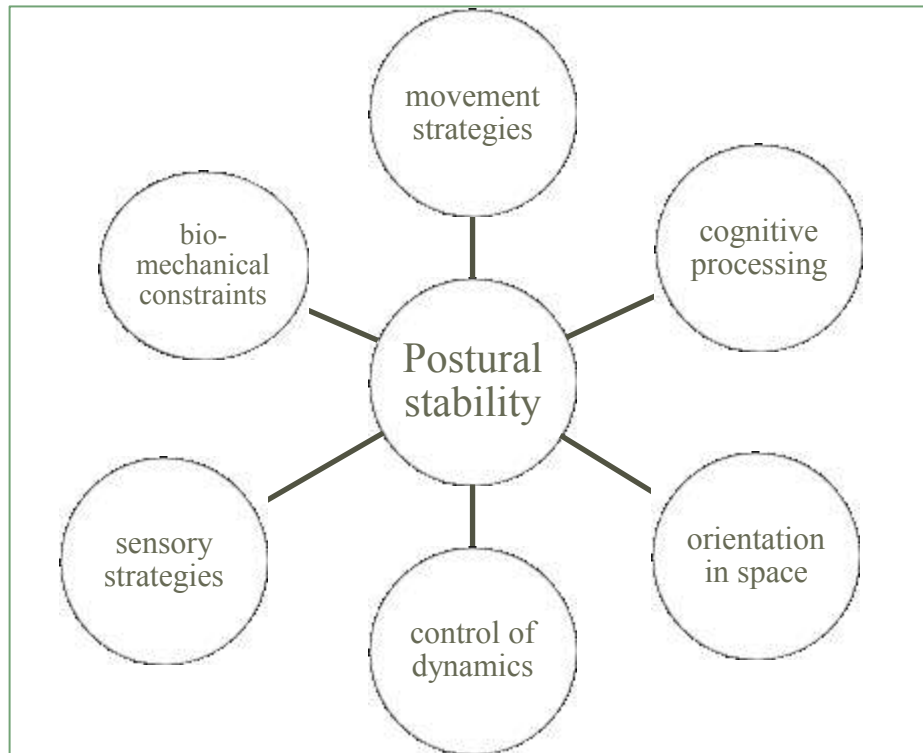


Figure 1: resources required for postural stability (adapted from Horak, 2006)

Fay B. Horak enumerates six different resources required for postural stability and orientation (Horak 2006), underlying an individual’s ability to stand, to walk and to interact with the environment safely and efficiently (Figure 1):

- Biomechanical constraints, notably the size and quality of the base of support: the feet.
- Movement strategies that can be used to return the body to equilibrium (ankle or hips strategies).
- Sensory strategies, information from somatosensory, visual, and vestibular systems.
- Orientation in space, orienting the body with respect to gravity, support, visual and internal feedbacks.
- Control of dynamics, or controlling balance while changing from one posture to another.

- Cognitive processing, like reaction time.

Any disorder in any of those resources may be the cause of balance disorders and therefore increase the risk of falls in older adults. Aging is associated with loss of muscle strength and decline in muscle mass, (Goodpaster et al. 2006) which can affect the base of support and balance. Aging is also linked with reduced vision, vestibular sense, proprioception and reaction time (L. Sturnieks, St George, and R. Lord 2008), which all contribute to increase the risk of falling.

‘The WHO Global Report on Falls Prevention in Older Age’ classified fall risk factors into 4 different categories: behavioural, biological, environmental and socio-economical (WHO- Ageing and life course unit 2008).

In another review of the literature, authors identified ‘lack of balance during gait’ (33%), ‘musculoskeletal and sensory degradation’ (27%), ‘functional dependence in the mobility’ (25%), ‘cognitive impairment’ (24%), age (20%) and being female (18%), as the most common cited **biological causes** in the literature. (Terroso et al. 2014)

The same review found that the **behaviour causes** most referenced were ‘overdose of medication’ (32%) and fear of falling without having ever fallen (30%) or after the first fall (23%), as well as ‘reduction of physical activity’ (16%) along among other causes.

With respect to **environmental causes**, unsafe domestic (17%) and outdoors (16%) environments were found to have the highest incidence. Home hazards include narrow steps, slippery surfaces, and insufficient lighting. (Vladutiu et al. 2012) Outdoor hazards include slippery floor, cracked or uneven sidewalks, and poor lightening in public places.

The **socio-economical causes** cited in the literature included ‘limited access to health and social services’ (2%), ‘low income and low educational level’ (2%) and ‘lack of social interactions’ (1%). This category had the lowest number of references in the reviewed literature, compared to the other categories of causes and risk factors.

1.3. Exercise to prevent falls among community-dwelling older adults

At the end of the 20th century, many studies had shown that certain fall risk factors such as impaired balance, abnormal gait patterns, and muscle weakness can be improved by exercise, even among the very old (Stephen R. Lord, Sherrington, and Menz 2001). Tinetti et al had famously stated back then: ‘falling is a health condition meeting all criteria for prevention: high frequency, evidence of preventability, and high burden of morbidity’ (Mary E. Tinetti and Williams 1998).

It started most notably at first with the FICSIT trials (Frailty and Injuries: Cooperative Studies of Intervention Techniques), consisting of linked randomised clinical trials evaluating the benefits of exercise among frail older adults (Buchner et al. 1993). In 1995, a pre-planned meta-analysis of the seven FICSIT trials showed a 10% reduction in the risk of falls by programmes including general exercise, and a 17% reduction in time to falls by programmes including balance (Province et al. 1995).

Subsequently, evidence of the effectiveness of exercise programmes in preventing falls started growing. In 2000, a systematic review of the literature, that examined 11 fall prevention interventions that included an exercise component, showed that these programmes can be effective (Gardner 2000). However, the evidence was weak due to heterogeneity between the different programmes and targeted population. In 2008, Sherrington et al published a systematic review and meta-analysis of 44 randomised controlled trials that examined the effectiveness of exercise programmes on the reduction of fall rates in older people, most of them living in the community (Sherrington et al. 2008). The reported pooled estimate of the effect of exercise was a 17% reduction in the rate of falling. They also performed a meta-regression in order to see ‘what works’ since intervention components were dissimilar, and found that the greatest relative effect was seen in trials where the exercise programme challenged balance and had a ‘higher total dose of exercise’ a dose of more than 50 hours of exercise, typically 2 x 1 hour sessions for six months. Their findings suggested that effective challenge to balance is provided with exercises that are conducted whilst standing, and in which participants:

- Narrow their base of support, for example by standing with their feet closer together or by standing on one leg.
- Minimise upper limb support (minimising use of their hands to assist balance), for example by holding onto a bar with one hand instead of both hands, or resting one finger on a table for support, rather than the entire hand.

- Practice controlled movements of the body's centre of mass, for example by shifting their body weight from one leg to the other or by standing on a step.

Sherrington et al also found that exercise interventions are less effective in reducing falls when they include a walking component. This may be due to many factors: the increased exposure to hazards that increases fall risk while walking, the possibility that walking could take time away from high level balance-challenging training. This association, between the inclusion of a walking component and decreased efficiency of fall prevention exercise programmes, could also be confounded by the fact that walking programmes were more likely to be prescribed in high risk populations (participants in residential care and not community-dwellers). Actually, the beneficial effects of exercise in these at higher risk population were less marked in the review.

In 2012, the Cochrane collaboration published a systematic review of fall prevention interventions in older people living in the community (Gillespie et al. 2012). Most of the 59 identified studies where the intervention consisted of exercise training had a balance-challenging component; these interventions were found to reduce the rate of falling of around 30%. This is in agreement with findings from Sherrington et al where having a balance component was associated with a more important effectiveness of fall prevention exercise programmes. The preventive effects of strength and balance training are to be expected because they can improve many risk factors of falling, such as muscle strength, flexibility, balance, proprioception, coordination, reaction time, and gait—even in very old and frail people (Kannus, Sievänen, et al. 2005; Tracey E Howe et al. 2012).

Given the multifactorial nature of falls, multicomponent intervention programmes have been considered in reducing fall risk among older people. Earlier clinical practice guidelines even recommended multifactorial interventions for older adults who are at risk of falling (National Collaborating Centre for Nursing and Supportive Care (UK) 2004). However, multicomponent interventions are usually based on comprehensive patient assessment and diagnosis and are staff and resource intensive. Moreover, exercise interventions have been proven to be as effective as multifactorial interventions, with the added advantage of being more cost-effective, more acceptable and generalisable (A. John Campbell and Robertson 2007). Additionally, at least two recent systematic reviews of economic evaluations of falls prevention interventions trials, concluded that single factor interventions, such as the Otago programme, can be cost-efficient, and

are the best value of money compared to other reviewed multifactorial interventions (Davis et al. 2010a; Petridou et al. 2009).

The Otago exercise programme is an individually tailored programme of muscle strengthening and balance-retraining designed to prevent falls in older people living in the community. The Otago programme involves five home visits over a six month period by a health professional to prescribe the exercise programme and monitor compliance and progression. It has been shown to reduce the rate of falls by 35% (M Clare Robertson et al. 2002). This extensively tested programme is now much recommended and used worldwide (Sherrington, Lord, and Close 2008). Similarly, another programme with proven efficacy is the 'Life style integrated Functional Exercise' (LiFE), a balance and strength training programme (Clemson et al. 2012). It is a validated, partially supervised, home-based fall prevention exercise programme that has been shown to reduce fall rates by 31%. Furthermore, since the LiFE exercise programme includes exercises that are embedded into daily activity, it may be easily adopted and maintained by older people. Many other programmes have been proven to effectively prevent falls among older community-dwellers: Tai-chi, group-based, home-based, as well as a mix of group and home based exercise (Gillespie et al. 2012). The latter presenting the advantage of expanding the exercise programme from a once or twice weekly occurrence (group exercise) to a global integration of exercise into daily lives.

Therefore, based on substantial evidence, best practice guidelines and public health statements now recommend exercise programmes as an effective method to prevent falls among community-dwelling older adults (Michael et al. 2010; Kenny et al. 2011; Tiedemann et al. 2011).

Fall prevention exercise programme design should, however, meet the needs and abilities of the target population to ensure it provides exercise that is acceptable, challenging, and safe (Rose 2008). Moreover, evidence of the effectiveness of exercise programmes on injurious falls as well as among care facilities residents is less clear (Cameron et al. 2010).

1.4. Present research: questions and objectives

1.4.1. Research questions

1.4.1.a. Effect of fall prevention exercise programmes on fall induced injuries

As discussed above, systematic reviews and meta-analyses of randomised controlled trials have established that well-designed exercise programmes can prevent falls in older adults living at home (Gillespie et al. 2012; Sherrington, Lord, and Close 2008). However, evidence that these programmes can also prevent injuries caused by falls is poor.

Furthermore, most fall prevention trials usually include between 100 to 300 participants, and thus are underpowered to examine the effect of exercise on injuries caused by falls, in particular the most severe ones that are also the least common. Some studies, however, did report fewer injurious falls in the intervention group compared to control group (Lin et al. 2006; Barnett et al. 2003b; M C Robertson et al. 2001). But the definition of traumatic falls varies greatly depending on the study: some studies only reported falls leading to health care utilisation or specific injuries, such as fractures, while others collapsed multiple fall-related consequences and symptoms into a single definition.

In fact, a reduction in the number of falls does not necessary translates into a reduction in injuries due to falls. Although falls and injurious falls have many risk factors in common, some factors such as muscle mass and bone density, only affect the severity of the consequences of a fall and not its initial occurrence (Fleming, Brayne, and and the Cambridge City over-75s Cohort (CC75C) study collaboration 2008). Furthermore, there is evidence that more active older people tend to have more outdoor falls than indoor falls, with healthy, active people having an increased risk of outdoor falls, especially during walking and vigorous activity (Kelsey et al. 2010). A recent prospective study found that participants with fast, as opposed to normal, gait speed, had an increased risk of having an outdoor fall during vigorous activity, and that serious injury were more likely to occur from an outdoor fall while walking outside compared to falls within 1 km of their home (Kelsey et al. 2012). Thus exercise may not have the same effect on injurious fall prevention that it has on all fall prevention; with more active people falling less but probably suffering more serious consequences when they do fall.

The risk of injury from a fall depends on factors such as velocity of the fall, the energy-absorbing thickness of soft tissues of the part of the body receiving the impact, the protective responses of

the faller, the injury threshold of the tissue (fragility of bone tissue), and the direction and the location of impact (Melton 1985; S. R. Cummings and Nevitt 1989). Low bone mass is a major determinant of the risk of fracture once a fall has been initiated. Exercise may increase bone mineral density among older adults (Marques, Mota, and Carvalho 2011), but in order to do so, the exercise must exert considerable mechanical stress on bone tissue (such as high-impact exercise, vigorous jumping, and resistance training). This type of exercise seems unfit for the oldest sub-groups who are at higher risk of fractures.

In addition, epidemiological studies (case-control and prospective) show that more active women have fewer fractures of the proximal femur (Heesch, Byles, and Brown 2008). But the association with other types of fractures is less clear (Gregg et al. 2003). A prospective study among community-dwellers aged over 75 years, showed that the most active and the most 'functionally vigorous' individuals were at lower risk of falling than the more fragile individuals, but they were also more likely to suffer a severe injury after a fall. Probably because they are more likely to engage in risky activities and fall with increased momentum (Speechley and Tinetti 1991). If this is the case, exercise may have a lesser, or even a null, preventive effect on injurious falls compared to all falls.

1.4.1.b. Effect of exercise on fall risk factors and overall quality of life

Designing effective optimised fall prevention exercise programmes requires a prior understanding of the underlying mechanisms by which physical exercise prevents falls. There is some evidence that some types of exercise (gait, balance, co-ordination and functional tasks; strengthening exercise) are effective in improving clinical balance outcomes in older people, but the effects seem modest (Tracey E Howe et al. 2012). Furthermore, physical exercise may also act by decreasing the fear of falling, restoring self-confidence, improving mental health status and feeling of well-being, and increasing general activity level. The effect of interventions on these psycho-social variables and general indicators of quality of life has rarely been reported, although this assessment is considered to be very important for clinical decision making as well as comparative effectiveness, and health policy (Calvert et al. 2011).

1.4.1.c. Factors influencing participation to fall prevention exercise programmes

Reporting on barriers and facilitators to participation to fall prevention exercise trials has been scarce in the scientific literature, even when the latter comprises numerous trials. This undermines the transition from evidence to practice and the optimisation of the design of trials. Some studies did report on older people's perceptions of facilitators and barriers to participation in fall prevention exercise interventions (Bunn et al. 2008). Nevertheless, they either examined factors associated with attendance to exercise or to general activity avoidance, and therefore did not evaluate factors associated with initial participation to the trial. Or, they had a qualitative approach limiting adjustment for factors usually linked with uptake of general activities such as age and general health status (Booth et al. 2000). Moreover, no other study evaluated factors linked with implementation factors such as intervention settings and distance to intervention. Even though, these factors could be easily modifiable in the design phase of trials and public health interventions.

1.4.2. Research objectives

The main objective of this thesis is to examine the effect of exercise intervention on injurious fall prevention among older community-dwelling adults. It is organised in two parts:

- A **systematic review** of the literature and meta-analysis of randomised controlled trials of fall prevention exercise programmes in order to evaluate and synthesise the evidence regarding the effect of those programmes on the reduction of injuries caused by falls.
- The analysis **of the 'Ossébo' randomised controlled trial** that has been specifically designed to evaluate the effectiveness of a 2-year balance training exercise programme on the prevention of injurious falls among community-dwelling older women aged over 75 years. This analysis had three objectives:
 - . To assess the effect of the 'Ossébo' exercise programme on the prevention of injurious falls.
 - . To assess the effect of the programme on physical and psychological fall-related factors as well as on health-related quality of life.
 - . To examine the individual and programme-related characteristics associated with participation to the trial.

2. Part I:

The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials

2.1. Background and objectives

As discussed beforehand, injurious fall outcomes are very frequent and can have important medical, psychological and economic consequences. Most published randomised controlled trials (RCTs) are underpowered to examine the effect of exercise on injurious falls.

In a supplementary analysis, the 2012 Cochrane review of randomised controlled trials for preventing falls in older adults living at home examined the effect of exercise intervention on fractures prevention (Gillespie et al. 2012). This review was published as I was starting my doctoral research. The supplementary analysis, which is based on six trials, showed that fall-prevention exercise programmes are associated with a significantly lower risk of fractures.

However, besides fractures, other injurious falls outcomes are common and can also have important physical and psychological consequences. All falls leading to medical care ought to be considered since their cost for society is high and their burden on the health care system heavy (Shumway-Cook et al. 2009; Davis et al. 2010b). Even falls causing relatively minor injuries are important to consider, as they too may have serious consequences such as diminished self-confidence, social isolation, and activity restriction, which in turn will accelerate functional decline and increase the risk of nursing home placement (Hartholt et al. 2011).

Accordingly, we sought out to systematically review, with a meta-analytic approach, the current evidence from randomised controlled trials about the effect of exercise interventions designed to prevent falls among community-dwelling older adults on different types of injurious falls.

The first hurdle on the way was related to the lack of a consensus about the outcomes of fall related injuries that should be evaluated in controlled trials, and to the fact that published trials reporting injurious falls used quite different definitions (Schwenk et al. 2012). Consequently, an essential first step of our work was to group definitions of injurious falls found in the studies selected for this review into more homogeneous categories to allow pooling of data.

The systematic review, presented below, was conducted in accordance with the PRISMA guidelines (Liberati et al. 2009).

2.2. Methodology

2.2.1. Systematic review: definition

“A systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review”(Liberati et al. 2009). Accordingly, a systematic review endeavours to provide an exhaustive summary of current literature relevant to a research question, by reviewing and combining all the information from both published and unpublished studies and then summarising the findings. It is a form of *secondary* study that reviews *primary* studies or the identified original research papers.

Systematic reviews have become increasingly important in health care, and systematic reviews of randomised controlled trials are regarded as the strongest level of medical evidence (Khan et al. 2011). A Meta-analysis is a subset of a systematic review, it's a statistical procedure that integrates, or 'pools' the results of several studies identified in the review (Haidich 2010). The result of the meta-analysis is usually a more precise estimate of the effect of treatment or intervention, than any individual study contributing to the pooled analysis.

2.2.2. Study selection criteria

It was decided that the included studies should have a randomised controlled design, in order to minimise bias that could derive from the other types of comparison. As randomised controlled trials are considered as the gold standard for comparing and evaluating different treatment, and for determining whether a cause-effect relationship exists between an intervention and a health outcome (Kendall 2003).

Also, to be included, it was decided that trials should compare exercise designed to prevent falls with 'no intervention' or a 'sham intervention', not designed to alter the risk of falling (for example a programme designed to closely replicate virtually all of the elements of the exercise condition but without the required intensity). Trials that compared two different interventions and did not have a control were excluded; because we wanted to determine the effect of exercise interventions and not compare exercise interventions between them.

Moreover, in order to decrease heterogeneity between different participants and exercise programmes in the different included interventions; intervention trials aimed for a specific population such as older adults with dementia or other mental diseases were excluded. The

programmes used in these types of interventions are usually altered and adjusted specifically for the participants that are usually at a high risk of falling and therefore these programmes are not comparable with programmes administered to a population not selected for a special disease or condition.

Evidently, to be included our review, a study had to have reported or disposed of quantitative data on injurious falls, serious falls, fall related injuries, or fall induced fractures. It should have also been primarily aimed at preventing falls; exercise interventions aimed to prevent or treat other health outcomes, and where falls and injurious falls were simply presented as a secondary outcome, were excluded.

Hence, to be included the study had to be:

- a)* A randomised controlled trial of fall prevention exercise intervention.
- b)* Published in English or French.
- c)* Targeting community-dwelling adults over 60 years of age.
- d)* Providing quantitative data on injurious falls, serious falls, fall-related injuries or fall-induced fractures.
- e)* comparing exercise with ‘no intervention’ (usual activity/care) or a “placebo” control intervention (eg, general health education classes, social visits or a low intensity exercise programme that is not designed to modify the risk of falling)

Exclusion criteria were:

- a)* Exercise was part of a multifactorial programme where participants received other interventions (eg, home management, visual treatment) in addition to exercise; this was in order to determine the ‘true’ effect of exercise.
- b)* Participants were selected for a specific neurodegenerative disease or any other characteristic or condition that greatly affects the risk of falling but is not correctable by exercise (such as severe visual impairment).

In order to identify and report all available published exercise prevention trials, a pre-determined search strategy was carried out, searching in four different search engine/ data bases.

2.2.3. Search strategy

Once the study question had been well defined and the criteria for the studies to be included had been specified, the next step was to conduct a thorough, exhaustive and reproducible literature search to identify relevant studies.

Since there is no single database that covers all publications from all healthcare journals, several electronic databases were searched, supplemented by examining other pertinent resources. This comprehensive search of a range of sources minimises selection bias and is one of the major differences between systematic reviews and other reviews.

Thus The Cochrane Library, Pubmed, Embase, and CINAHL databases were searched in order to identify relevant studies published in peer-reviewed journals through June 2013.

The Cochrane library is a collection of databases in medicine and other healthcare subjects, provided by the Cochrane Collaboration and other organisations. It contains among other databases ‘The Cochrane Central Register of Controlled Trials (CENTRAL)’; a database listing the details of articles of Controlled trials and other studies of healthcare interventions from bibliographic databases and other published and unpublished sources. A subscription is needed to access this library.

The search terms used in the Cochrane Library were: (fall) and (exercise or tai chi or training or physical activity) excluding (Alzheimer or Parkinson’s or dementia or nursing home or protocol or athletes) in the title or abstract of trials, with the word ‘prevention’ in the text and the word variations option enabled.

Pubmed is a subscription-free search engine maintained by the United States National Library of Medicine (NLM) at the National Institutes of Health (NIH).

Using this engine that searches ‘Medline’, a bibliographic database of life sciences and biomedical information, we searched for: (((fall*[Title/Abstract]) AND ((exercise) OR (training) OR "Tai Chi" OR "physical activity"[Title/Abstract])) AND random*[Title/Abstract]) NOT ((parkinson's) OR (asthma) OR (alzheimer) OR (dementia*)) OR "nursing home"[Title/Abstract]), while specifying that search results should have be a ‘clinical trial’ or a ‘controlled clinical trial’ or a ‘randomised controlled trial’, in ‘humans’ and for ‘middle aged: 45-64 years’ or ‘aged:65+years’ or ‘80 and over: 80+ years’.

Embase is an international biomedical database that contains over 25 million indexed records from thousands of peer-reviewed journals. A subscription is needed to access this database.

The search terms for this database were: fall*:ab and (exercise:ab or train*:ab or 'tai chi':ab or 'physical activity':ab) not ('nursing homes':ti or parkinson*:ti or alzheimer:ti or dementia:ti or stroke:ti) and ([controlled clinical trial]/lim or [randomized controlled trial]/lim) and ([article]/lim or [article in press]/lim) and [aged]/lim and [humans]/lim.

CINAHL (Cumulative Index to Nursing and Allied Health Literature) is an index of journal articles about nursing, allied health, biomedicine and healthcare.

The search terms for CINAHL were: AB fall AND AB (exercise OR train OR "tai chi" OR "physical activity») NOT TI ("nursing homes" OR Parkinson OR Alzheimer OR dementia OR stroke). While applying the 'related words' option and restricting the search to randomised controlled trials and for the age groups: 'aged: 65+ years, aged, 80 and over'.

Hand searching: we also screened references in relevant reviews for additional studies. All the references in the latest Cochrane review on 'Interventions for preventing falls in older people living in the community' were manually searched (Gillespie et al. 2012). The references in two other relevant reviews were also hand-searched (Sherrington et al. 2011; Schwenk et al. 2012).

2.2.4. Study selection process

The first step was to merge search results and then to remove duplicate records of the same report, this was done using Microsoft Excel©.

Then, all the titles and abstracts were examined, and noticeably irrelevant reports were removed. At last, the full text of all the remaining papers was retrieved while linking together the studies that reported the same intervention. The retrieved full-text papers were then examined, and their compliance with our eligibility criteria was assessed independently by two reviewers (FEK and PDM) before making a final decision on study inclusion with mutual consent. Reasons for the exclusions was documented in an excel sheet.

2.2.5. Data extraction and outcomes classification

A pre-specified strategy was used in order to collect all relevant information from the included studies.

A digital data collection form (Excel sheet), specifically conceived for this review, was used in order to standardise the extraction of the information. Reviewers had to fill in the following domains: (see also appendix)

- . Participants' characteristics (setting, number, age, % of women ...)
- . Intervention (type of exercise, duration, frequency...)
- . Outcome measures (all available data on falls and injurious falls)
- . Bias assessment
- . Adverse events

The taxonomy for fall prevention interventions developed by the Prevention of Falls Network Europe (ProFaNE)(Lamb, Jørstad- Stein, et al. 2005; Lamb et al. 2011), was used to describe the characteristics of the intervention provided (for example, type of exercises, and intervention procedures). This taxonomy uses internationally agreed criteria to systematically evaluate the content and format of fall prevention interventions. We also extracted the definitions and methods used to collect falls and to classify fall related injuries, as well as the number, rate, or risk ratio of injurious falls and any available data on the nature of the injuries and methods of confirming injuries.

We contacted authors of the included studies, essentially to obtain more detailed data on injurious fall outcomes. For example, in case the number of participants with an injurious fall was presented but not the total number of injurious falls, or if data on falls resulting in fractures was presented but not data on injurious falls.

After collating all the available information presented in the included studies on injurious falls, and reviewing the case definitions used in the selected studies, we sought to group definitions of injurious falls into more homogeneous categories to allow results to be compared across studies and the data to be pooled. This retrospective classification of the definitions of injurious falls found in the selected studies was adapted from two different published classifications: the one proposed by the ProFaNE group (Schwenk et al. 2012), and the standardised classification developed by Campbell and Robertson (A J Campbell et al. 1997a),

which has been used in several reported trials (Elley et al. 2008; M C Robertson et al. 2001; A J. Campbell 2005).

Furthermore, information facilitating assessments of the risk of bias in the included studies (sequence generation, allocation sequence concealment, blinding, and incomplete outcome data) was also collected (see below). Any information on adverse effects associated with the exercise intervention was also noted.

2.2.6. Quality assessment

The Cochrane Collaboration tool was used in this review to assess the risk of bias in included studies (J. P. T. Higgins et al. 2011). This tool was chosen because it presents several advantages:

1/ it focuses on internal validity and hence truly pertains to risk of bias assessment, whereas other ‘quality assessment’ tools used in the literature include other items pertaining to the quality of reporting, external validity or some aspects of trial conduct (such as obtaining ethical approval or calculating sample size) that are not directly related to risk of bias.

2/ specific criteria are used for each quality component to classify studies as ‘high risk’, ‘low risk’ or ‘unclear’; and each assessor is required to explicitly record the specific aspects of the trial conduct on which the judgement was based. Hence, the evaluation process is transparent and the subsequent discussion is facilitated in case final judgement differs between assessors.

The risk of bias was assessed in the following domains:

a) **Selection bias:** refers to systematic differences between baseline characteristics of comparison groups.

- . **Random allocation** (use of a random component in the sequence generation process such as: referring to a random number table, using a computer random number generator, Coin tossing...)
- . Adequate **allocation concealment** (participants and investigators enrolling participants could not foresee group assignment) that prevents selection bias.

b) **Detection bias:** refers to systematic differences between comparison groups in how outcomes are measured.

- . **Blinding of outcome assessors** usually reduces the risk that knowledge of the randomisation group affects outcome measurement.

- c) **Attrition bias**: or “differential dropout”; when dropout rates or reason for drop out differ between comparison groups (J. P. T. Higgins et al. 2011).

We also assessed bias in the recall of falls owing to unreliable **methods of ascertainment**, (J. P. Higgins and Altman 2008) using the criteria developed for the Cochrane review of fall prevention trials.

The methods used to **confirm injurious falls** were also examined: we judged self-reports from participants to be at a high risk of bias, whereas we considered the use of medical records or radiography reports (for fractures) to be at low risk.

Two authors (FEK, PDM) independently assessed the risks of bias and extracted data. We used a standardised form where we documented the reason for each decision along with related extracts from the articles. Disagreement was resolved by consensus or adjudication by a third party (BC).

2.2.7. Summarising the evidence: Statistical analysis

Injurious falls are recurrent events; they can happen to a participant more than once. To account for the number of times these events occur rather than simply whether each participant experienced any event (rather than treating them as dichotomous data) a rate of the events is computed. A rate is the total number of events that occurred in a group, divided by the total number of person-years of observation in that group. The rate ratio (RaR) of injurious falls in the two comparison groups was the outcome of interest in our systematic review. If the rate ratio was not presented in the included study, we calculated it manually using extracted information (number of injurious falls in each group and length of follow-up). In cases where data were available only for people who had completed the study, or where the trial authors had stated there were no losses to follow-up, we assumed that the participants who completed the trial had been followed up for the maximum possible period. We estimated the standard error of the rate ratio by using the formula given in the Cochrane handbook:

$$\text{SE of ln rate ratio} = \sqrt{\frac{1}{E_E} + \frac{1}{E_C}}$$

Where ‘ E_E ’ is the number of events in the exercise group and ‘ E_C ’ is the number of events in the control group.

After extracting or calculating for each study a rate ratio along with its standard error, a pooled effect (meta-analysis) was computed for each outcome (categories of injurious falls). This

pooled effect is a weighted average of the intervention effect. The formula for the weighted measure is:

$$\text{weighted average} = \frac{\text{sum of (estimate} \times \text{weight)}}{\text{sum of weights}} = \frac{\sum Y_i W_i}{\sum W_i}$$

Where Y_i is the natural logarithm of the intervention effect estimated in the i th trial, and the summation is across all studies. W_i is the weight given to the i th trial, it equals the inverse of the variance of the effect estimate. Thus larger studies (with small standard errors) are given more weight than smaller studies (small standard error). This method is called ‘the generic inverse variance method’.

To allow for variability among the participants, type of exercise intervention, and outcome definitions we used a random effect model. A random effect model is recommended when heterogeneity is detected because it assumes that the intervention effect does vary between studies. (Whereas a fixed effect model assumes that the true effect of the intervention is the same in all the included trials, and any detected difference between the studies is due to sampling error).

Results of the meta-analysis were presented graphically using a forest plot: ‘forest of lines’ illustrating the effect estimates and confidence intervals for both (individual) included studies and (pooled) meta-analyses. In this plot, each study is depicted by a block at the point estimate of intervention effect with a horizontal line extending either side of the block. The area of the block indicates the weight assigned to that study in the meta-analysis while the horizontal line represents the confidence interval (typically with a 95% level of confidence). The pooled estimate is presented with a diamond shape, whose width represents the confidence intervals for the overall effect estimate. A rate ratio less than 1 (to the left of the vertical line) signify that the intervention has a protective effect and there were less injurious falls in the intervention group compared to the control group.

2.2.7.a. Investigating heterogeneity

Statistical heterogeneity, (also simply known as heterogeneity) is the presence of variation in true effect sizes underlying the different studies; when intervention effects are more different from each other than one would expect due to random error (chance) alone. It can be due to clinical (different participants and/ or intervention programs), or methodological diversity

(variability in the study design, use of blinding, concealment of allocation...). Therefore, when significant heterogeneity is detected, the pooled estimate should be interpreted with caution.

We assessed the heterogeneity with the Q-test and the I^2 statistic. The Cochran's Q test is the traditional statistical test for heterogeneity, based on the χ^2 test: it tests the null hypothesis that the studies all have the same effect. The test evaluates the differences between observed treatment effects for the included studies and the pooled effect estimate. However, this test may not always accurately detect heterogeneity when it is present. Because of this, the more accurate Higgins I^2 statistic was developed (Julian P. T. Higgins and Thompson 2002). This statistic represents the percentage of variation between the studies estimates as a result of heterogeneity rather than sampling error (play of chance).

$$I^2 = \left(\frac{Q - df}{Q} \right) \times 100\%$$

Where 'Q' is the χ^2 statistic and 'df' is its degrees of freedom.

The I^2 test can vary from 0% to 100%, with 0% signifying that statistical heterogeneity does not exist. Significant heterogeneity is typically considered to be present if I^2 is equal or greater than 50% (Sedgwick 2012).

2.2.8. Sensitivity and subgroup analysis

In order to investigate potential sources of heterogeneity, like the variation of the estimated intervention effect according to some participants' or intervention's characteristics, subgroup analyses were done. These involved comparing different 'sub-groups' of participants or trials. Thus, a pre-specified subgroup analysis based on fall risk at enrolment (a priori) was conducted; that is, trials with participants selected for inclusion based on fall history or other specific risk factors for falling (at higher risk) was compared with trials including non-selected participants. This was done in order to verify that the effect of the intervention in trials that only recruit older adults at higher risk of falls could differ from that in the trials compared with trials that don't recruit participants based on their risk of falls. This difference may be due to clinical difference of the participants but also variability in the type and deliverance of the intervention (adjusted for a more vulnerable population for example), thus possibly changing the effect of the intervention.

Sensitivity analyses were also conducted. Unlike sub-group analysis, they allow the exploration of the possible effect of certain assumptions or decisions (regarding inclusion

criteria for example) on the main results. Therefore, sensitivity analyses involve comparing the results obtained from the meta-analysis of included trials and chosen outcomes including all the trials initially selected, with other pooled results computed under different assumptions (such as stricter or looser selection criteria).

We explored the possible impact of risk of bias on the pooled estimates by removing studies of poorer quality—that is, those for which the risk of bias was unclear for at least three of the quality components considered, or the risk was at least unclear for one category and high for another.

2.2.9. Publication bias

Publication bias is a well-documented phenomenon in medical literature (Thornton and Lee 2000), in which positive or significant results have a better chance of being published and are published earlier, making conclusions exclusively based on published studies often misleading.

One way to explore the possibility of publication bias is to construct a funnel plot, which is a simple scatter plot of the intervention effect estimates from individual studies against a measure of each study's size or precision (standard errors). Commonly, the effect estimates are plotted on the horizontal scale, and the measure of study size on the vertical axis. Small studies have bigger variance, thus their effect estimates will scatter more widely at the bottom of the graph, with the spread narrowing among larger studies. Consequently, in the absence of publication bias the plot should approximately resemble a symmetrical (inverted) funnel (figure 2).

Noteworthy, funnel plot asymmetry may also be due to exaggeration of treatment effects in small studies of low quality, in this case the asymmetry would manifest with a gap in the right bottom side of the graph (for preventative effects) (Sterne et al. 2011).

Other tests (Peters 2006), can be found in the literature in order to test whether there is a linear association between the treatment effect and its standard error; however the funnel plot is the most recommended test (Sterne et al. 2011).

In order to explore publication bias in this review, a funnel plot of effect estimates against their standard errors was plotted for analyses that contained at least 10 data points.

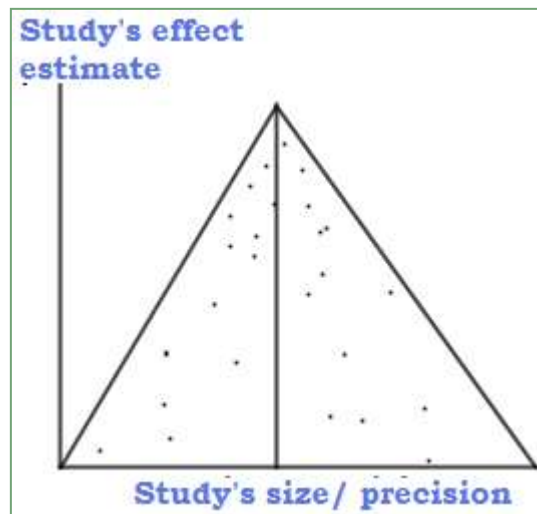


Figure 2: A generic funnel plot

2.3. Results

2.3.1. Literature search results

Figure 3 presents the flow chart of the studies' selection process. We identified 524 potentially eligible titles from searching the Cochrane library, 593 titles from Pubmed, 412 from Embase and 70 from the CINAHL engine. In total, we had collected 1599 titles and abstracts from searching electronic databases. We also identified 59 titles and abstracts through hand-searching references in pertinent reviews. After removing duplicates, the total number of titles and abstracts we examined was 1011 papers, from which 812 papers were excluded after examination.

Thus 199 full-text articles were retrieved and examined for inclusion, from which 172 were excluded:

- 71 papers presented no data on falls.
- 63 papers did not present any quantitative data on injurious falls, even when they had presented data on all falls.
- 9 papers where participants were selected based on a specific disease or handicap that did not meet our inclusion criteria.
- 10 papers where the intervention had multiple components (multi-factorial).
- 4 papers examined the effect of an intervention that did not include exercise.
- 6 papers compared exercise to another intervention that aims to prevent falls, and thus had no control or 'sham intervention'.
- 3 papers examined the effect of an exercise intervention that was not designed to prevent falls, for example the exercise intervention was meant to decrease obesity or cardio-vascular risk.
- 5 papers were about studies that did not have a randomised controlled design.
- 1 paper was in German.

Ultimately, 27 papers were included that correspond to 17 trials (8 of which had 2 or more papers).

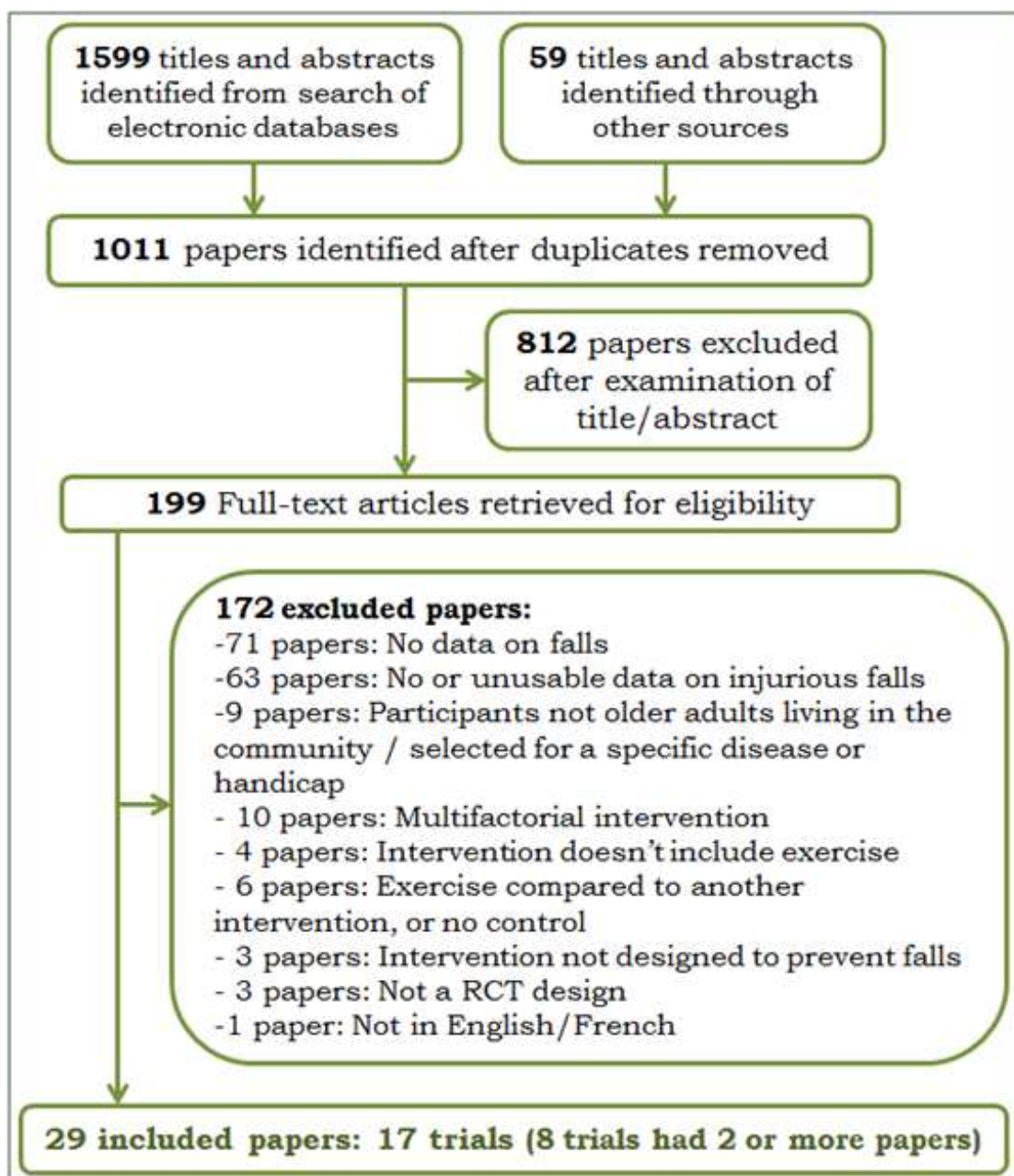


Figure 3: Flow chart of the selection process

2.3.2. Characteristics of included studies

Table 2 presents the characteristics of included studies. The 17 studies in the meta-analysis included a total of 2195 participants randomised in the exercise groups and 2110 randomised in the control groups, with sample sizes in individual studies ranging from 53 to 486 participants (median = 207). The mean age of the overall population was 76.6 years, with a minimum mean age of 69.1 (Kemmler, 2010), a maximum of 88 (Luukinen, 2007) and a median of 74.9. Around 74% (3143) of participants were women, with six studies including only women. Seven studies selected participants based on a higher risk of falls—that is, history of falling, age over 80 years, or physical limitations (as measured by simple functional tests).

Fourteen trials delivered the exercise intervention in a group setting, with six of those supplementing the group sessions with home exercise. In the other three trials, the intervention consisted of individualised exercises delivered at home. Tai Chi was the exclusive exercise intervention in two of the studies; all the other interventions included a gait, balance, and functional training component. Many studies also included strength/resistance training exercises. The exercise programmes duration varied from 5.5 weeks to a year and a half, with an average of around 8 month and a half of intervention, while the average study follow up time was 14 months (minimum 6 months, maximum 30 months).

One study compared two similar multiple component exercise interventions, with the only difference being added endurance training for one arm. These two interventions were compared with a control group. In the analysis, the two exercise groups were combined to create a single pair-wise comparison (intervention versus control).

Most of the trials were carried out in industrialised countries (USA (3), Australasia (5), Europe (7)), with only one trial located in China (Li, 2005). The oldest trials were carried out in the USA (MacRae, Feltner, and Reinsch 1994; Wolf et al. 1996), while the study that included the most subjects was Australian (Fitzharris et al. 2010).

Seven of the included studies had demonstrated a statistically significant effect on fall reduction rates, 2 trials had a borderline positive effect, and all the other except the study done by MacRae et al (MacRae, Feltner, and Reinsch 1994), showed a tendency towards the prevention of all falls.

Table 2: Study characteristics

Study Id	Number of randomised subjects (%women)	Mean age	Participant selection criteria	Type of exercise ^a	Moderate-to high-challenge to balance	Mode of delivery ^b	Exercise sessions frequency ^c	Program-me duration	Follow up period (months)	Rate ratio for all falls (fall rate in controls (person/year))
(Barnett et al. 2003a)	163 (67%)	74.9	65+ 1 or more risk factors for falling	1, 2, 3	Yes	Combined	1 h/wk +HE	One year	12	0.60 [0.36, 1.00] (0.95)
A. J. Campbell et al. 1997a	233 (100%)	84.1	80+	1, 2, 3, 4	Yes	Home exercise	30 min x 3/week	One year	12	0.68 [0.51, 0.89] (1.34)
(Cornillon et al. 2002)	303 (83%)	71	65+ ADL independent.	1	Yes	Group exercise	1 session/wk	8 weeks	12	0.82 [0.58, 1.17] (0.47)
(Fitzharris et al. 2010)	1090 (59.8%)	76.1	70+	1, 2, 3	No	Combined	1 h/wk +daily HE	15 weeks	18	0.79 [0.66, 0.94] (1.14)
(Freiberger et al. 2012)	207 (44%)	76.1	70+ Fell in the past 6 months or fear of falling	1, 2, 6	Yes	Group exercise	1 hx2/wk	16 weeks	24	0.82 [0.62, 1.08] (0.67)
(Haines et al. 2009)	53 (60%)	80.7	65+ Gait instability or use of a mobility aid; discharged from hospital	1, 2, 5	Yes	Home exercise	3 to 7/wk	18 weeks	6	0.72[0.33, 1.57] (1.09)
(Kemmler et al. 2010)	246 (100%)	69.1	65+	1, 2, 3	No	Combined	60 min x2/wk +HE (20 min x2/wk)	18 month	18	0.60 [0.47, 0.76] (0.28)
(Korpelainen et al. 2005)	160 (100%)	73	Low BMD	1, 2, 5	Yes	Combined	1h/wk +HE (20min daily)	18 month	30	0.79 [0.59, 1.06] (0.53)
(F. Li et al. 2005)	256 (70%)	77.5	70+ walks independently	5	Yes	Group exercise	1 hx3/wk	26 weeks	6	0.45 [0.29, 0.69] (0.53)

Results

(Luukinen et al. 2006)	486 (78%)	88	85+ ≥ 1 risk factor for falling Or ≥ 2 falls in previous year	1, 3, 4, 7	No	Combined	Individually prescribed, frequency depends on individuals	16 months	16	0.93 [0.80, 1.09] (1.15)
(MacRae, Feltner, and Reinsch 1994)	80 (100%)	71.1	60+	1	No	Group exercise	1hx3/wk	A year	12	1.28 [0.90, 1.83]* (-)
(McMurdo, Mole, and Paterson 1997)	118 (100%)	64.5	60+ post-menopausal	1, 2	No	Group exercise	45min x3/wk	30 weeks	24	0.53 [0.28, 1.00] (-)
(Means, Rodell, and O'Sullivan 2005)	338 (57%)	73.5	65+ Able to walk at least 30 feet without assistance	1, 2, 3	No	Group exercise	90min x3/wk	6 weeks	6	0.41 [0.27, 0.62] (1.18)
(M C Robertson et al. 2001)	240 (68%)	80.9	75+	1, 2, 3, 4	Yes	Home exercise	Individually prescribed; at least 3 times a week (≈30 min/session+ walking 2x/wk)	A year	12	0.54 [0.3, 0.90] (1.01)
(D. Skelton et al. 2005)	100 (100%)	72.8	65+; ≥ 3 falls in previous year	1, 2, 3, 6	Yes	Combined	1 h/wk +HE (30 min x 2/wk)	36 weeks	9	0.69 [0.50, 0.96] (3.12)
(Smulders et al. 2010)	96 (94%)	71	65+, osteoporosis, ≥ 1 falls in past year; able to walk 15 min unassisted	1, 4, 6, 7	Yes	Group exercise	11 exercise sessions	5.5 weeks	12	0.61 [0.40, 0.94] (1.18)
(Wolf et al. 1996)	136 (81%)	76,2	70+ Ambulatory	5	Yes	Group exercise	45 min/wk	15 weeks	8	0.67 [0.41, 1.09] (1.82)

***: Risk ratio (ratio of the risk of being a faller in the 2 comparison groups)**

α: Types of exercise: 1: Gait, balance, and functional training, 2: Strengthening exercises, 3: Flexibility, 4: General physical activity, 5: 3D (Tai Chi, dance etc), 6: Endurance, 7: Other.

β: Combined: Home exercise + group exercise. **ε:** HE: Home exercise

2.3.3. Classification of injurious falls

The definition and classification of injurious falls varied substantially and most trials did not base their definition on a published reference. Injurious falls usually included diverse consequences, ranging from relatively minor injuries such as bruises or abrasions to fractures or other serious injuries requiring hospital admission. Most often the definition referred to either the presence of symptoms or the use of medical care (Barnett et al. 2003a; A J Campbell et al. 1997a; Cornillon et al. 2002; Haines et al. 2009; F. Li et al. 2005; M C Robertson et al. 2001; Wolf et al. 1996). In other cases, injurious falls were defined as simply any self-reported physical consequence of a fall (Freiberger et al. 2012; Kemmler et al. 2010; Smulders et al. 2010), without any further details on the range of severity or methods of confirmation of the injury. Some definitions made reference to the use of medical care, by using non-specific terms such as “fall for which medical care was sought,” “falls requiring medical care/medical attention,” or “medical consultations/visits” (MacRae, Feltner, and Reinsch 1994; D. Skelton et al. 2005; Cornillon et al. 2002). When serious injuries were distinguished or specifically reported, their definition was more homogeneous across studies. Such injuries usually included fractures, severe soft tissue injuries requiring suturing, or other injuries leading to hospital admission (A J Campbell et al. 1997a; F. Li et al. 2005; Smulders et al. 2010; M C Robertson et al. 2001; Wolf et al. 1996). Some studies only reported fractures due to falls.

Based on our review of case definitions used in the 17 included studies, we distinguished four categories of injurious falls:

A-Those resulting in any reported consequences, including specific symptoms (ranging from bruises and cuts to more serious injuries such as fractures) or medical care

B-Those resulting in medical care

C-Those resulting in serious injuries such as fractures, soft tissue injury requiring suturing, head trauma, or any other injury requiring admission to hospital

D-Those resulting in fractures

These categories represent increasingly specific subgroups of all injurious falls, which can also be considered to correspond to increasing levels of severity (except for those resulting in fracture, which is simply a specific type of serious injury). Depending on the available data, a given study could contribute data relevant to one or more categories of injurious falls.

Table 3 gives the definitions of injurious falls reported in each selected article (as a direct quotation), the category or categories of injurious falls in which it was classified for this

Results

review, and the rate ratio used in the corresponding analysis. For two studies, the rate ratio could not be computed because the authors provided only the number of participants who had an injurious fall (rather than the number of such falls), and our attempts to contact the authors in order to obtain the number of injurious failed. In these cases, we used the ratio of the risk of at least one injurious fall in both groups as an alternative. Of note, the outcomes of injurious fall in those studies were severe injuries and fractures, two outcomes that are relatively rare, so that the risk ratio was likely to be similar to the rate ratio.

Table 3: Injurious falls: extracted definitions and subsequent categorisation with the estimates of intervention-related fall reduction

Study id	Extracted definitions	Rate Ratio of injurious falls			
		A- All injurious falls	B- Falls resulting in medical care	C- Falls resulting in serious injuries	D- Falls resulting in fractures
(Barnett et al. 2003a)	-“Falls that resulted in bruises, strains, cuts and abrasions, back pain and fractures” (A)	0.73 (0.46-1.17)	-	-	-
(A J Campbell et al. 1997a)	- Falls were classified as resulting in “serious” injury if the fall resulted in a fracture, admission to hospital or stitches were required, “moderate” injury if bruising, sprains, cuts, abrasions or reduction in physical function for at least three days resulted, or if the participant sought medical help, -(A=moderate + severe) -(C=severe) -“Falls for which medical care sought” (B)	0.45 (0.30 – 0.67)	0.97 (0.58 – 1.64)	0.82 (0.37 – 1.79)	-
(Cornillon et al. 2002)	-“Cumulative number of medical consultations” (B) -“Falls requiring hospitalization” (C)	-	1.16 (0.57 -2.37)	0.15 (0.02 - 1.16)	-
(Fitzharris et al. 2010)	-“Cut, scrape, gash, bruise or fracture; a head injury resulted or where the fall resulted in hospitalization” (A) -“Falls requiring medical care” (B)	0.85 (0.70-1.04)	0.74 (0.50-1.10)	-	-
(Freiberger et al. 2012)	-“Number of injurious falls” (A)	0.70 (0.46-1.08)	-	-	-
(Haines et al. 2009)	-“Falls with self-reported physical injury” (A) -“Falls resulting in medical review (general practitioner or hospital medical officer if fall took place in a hospital)” (B) -“Falls resulting in fracture” (D)	0.82 (0.32-2.12)	0.34 (0.07-1.62)	-	0.88 (0.08-9.70)

Results

(Kemmler et al. 2010)	-“Subjects who experienced injurious falls” (A) -“Fractures due to falls” (D)	0.65 ^{\$} (0.45-0.92)	-	-	0.49 (0.18-1.30)
(Korpelainen et al. 2005)	-“Fall-related fractures” (D)	-	-	-	0.36 (0.14-0.93)
(F. Li et al. 2005)	-“If falls resulted in fractures, head injuries, sprains, bruises, scrapes, or other serious joint injuries or if the participant sought medical care” (A) -“Medical care visits resulting from a fall” (B) -“Severe falls requiring medical Attention” (C)	0.40 (0.17-0.95)	0.31 (0.11-0.85)	0.28* (0.09-0.88)	-
(MacRae, Feltner, and Reinsch 1994)	-“Fall related injury requiring medical attention” (B)	-	0.18 (0.02 – 1.77)	-	-
(Luukinen et al. 2006)	-“The injuries included fractures, dislocations and soft tissue injuries needing suturing and even more severe injuries” (C)	-	-	0.94 (0.60 - 1.49)	-
(McMurdo, Mole, and Paterson 1997)	-Number of people with fractures (D)	-	-	-	0.22* (0.01-4.59)
(Means, Rodell, and O’Sullivan 2005)	-“Any detectable residual adverse physical change persisting beyond 1 hr after the fall” (A)	0.35 (0.22-0.56)	-	-	-
(M C Robertson et al. 2001)	-“If bruising, sprains, cuts, abrasions, or reduction in physical function for at least three days resulted or if the participant sought medical help (moderate injuries) ; ‘Fall resulted in a fracture, admissions to hospital with an injury, or stitches were required’ (severe injuries) (A=moderate + severe) (C=severe) -“Falls for which medical care sought” (B)	0.80 (0.53-1.21)	0.64 (0.35-1.17)	0.22 (0.04-0.95)	0.28(0.06 – 1.32)
(D. Skelton et al. 2005)	-“Falls requiring medical attention” (B)	-	0.60 (0.33-1.08)	-	-

Results

(Smulders et al. 2010)	-“Self-reported injuries” (A) -Fractures, concussion and wounds that needed suturing (C) -Fractures reported as a consequence of a fall (D)	0.55 (0.32-0.96)	-	0.19 (0.02-1.57)	0.31 (0.03-2.93)
(Wolf et al. 1996)	-“Fall that resulted either in fractures; head injuries requiring hospitalization; joint dislocations; sprains defined as injury to a ligament when joint carried through range of motion greater than normal; other non-specified serious joint injuries; and lacerations required sutures” (C)	-	-	0.69 (0.42-1.12)	-
Pooled rate ratio		0.63 [0.52- 0.77]	0.70 [0.53- 0.92]	0.57 [0.37-0.90]	0.39 [0.23- 0.66]

* Risk Ratio of at least one injurious fall (rate ratio unavailable)

\$ Unpublished data on the total number of injurious falls provided by the authors

2.3.4. Methodological quality

Table 4 summarises the methodological quality judgement. Although few studies were judged at high risk of bias in any of the six domains examined, the quality of some studies could not be judged with any certainty in several domains, because of a lack of detailed description of the methodology.

Study Id	Random sequence generation	Allocation concealment	Methods of ascertaining falls	Blinding of fall outcomes assessment	Incomplete outcome data	Methods of ascertaining serious injuries
Barnett 2003	Unclear	Low	Unclear	Unclear	Low	NA
Campbell 1997	Low	Low	Low	Unclear	Low	Low
Cornillon 2002	Low	Unclear	Low	Unclear	Low	Unclear
Fitzharris 2010	Low	Low	Low	Low	Unclear	NA
Freiberger 2012	Low	Low	Low	Low	Unclear	NA
Haines 2009	Low	Low	Low	Low	Low	High
Kemmler 2010	Low	Low	Low	Low	Low	High
Korpelainen 2006	Low	Low	High	Low	Low	Low
Li 2005	Low	Unclear	Low	Low	Low	Low
Luukinen 2007	Low	Unclear	High	Low	Low	Low
MacRae1994	Unclear	High	Low	Unclear	High	NA
McMurdo 1997	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Means 2005	Low	Unclear	Low	Low	High	NA
Robertson 2001	Low	Low	Low	Low	Low	Low
Skelton 2005	Unclear	Unclear	Low	Low	Low	NA
Smulders 2010	Unclear	Unclear	Low	Low	Low	High
Wolf 1996	Low	Unclear	Low	Unclear	Unclear	Low

Table 4: assessment of risk of bias in included studies

No study was judged at high risk of bias in the random sequence generation domain, with most trials reporting the use of methods that generates a random allocation sequence, such as a random-numbers table or a computer software program that generates the random sequence. Only one study was at high risk of allocation concealment, since the participants were not individually randomised (cluster randomisation), this study was also at high risk of attrition

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bias because of imbalance in numbers and reasons for missing data across intervention groups. Moreover, only one study reported the lack of blinding of an outcome assessor, making it at high risk of detection bias.

Prospective daily fall calendars returned monthly are the preferred method for recording falls, and most of the trials used this method, with only once study using interval recall making it at high risk of fall assessment bias. However, only six of the 11 trials that reported data on serious injuries used medical records to confirm the injury, the others used declaration from patients, thus increasing the risk of classification bias.

2.3.5. Effect of exercise on injurious falls

2.3.5.a. Category A: all injurious falls

Figure 4 shows the forest plots of the exercise effect estimate for all injurious falls. Ten trials, with a total number of 2922 participants, provided data in this category. Participants in the exercise group had fewer injurious falls than participants in the control group in all of these studies; furthermore half of those studies demonstrated a significant effect on injurious fall prevention (A J Campbell et al. 1997b; Kemmler et al. 2010; Means, Rodell, and O'Sullivan 2005; Smulders et al. 2010; F. Li et al. 2005). The pooled estimated rate ratio was 0.63 (0.51 to 0.77, $I^2=50\%$, $p=0.04$).

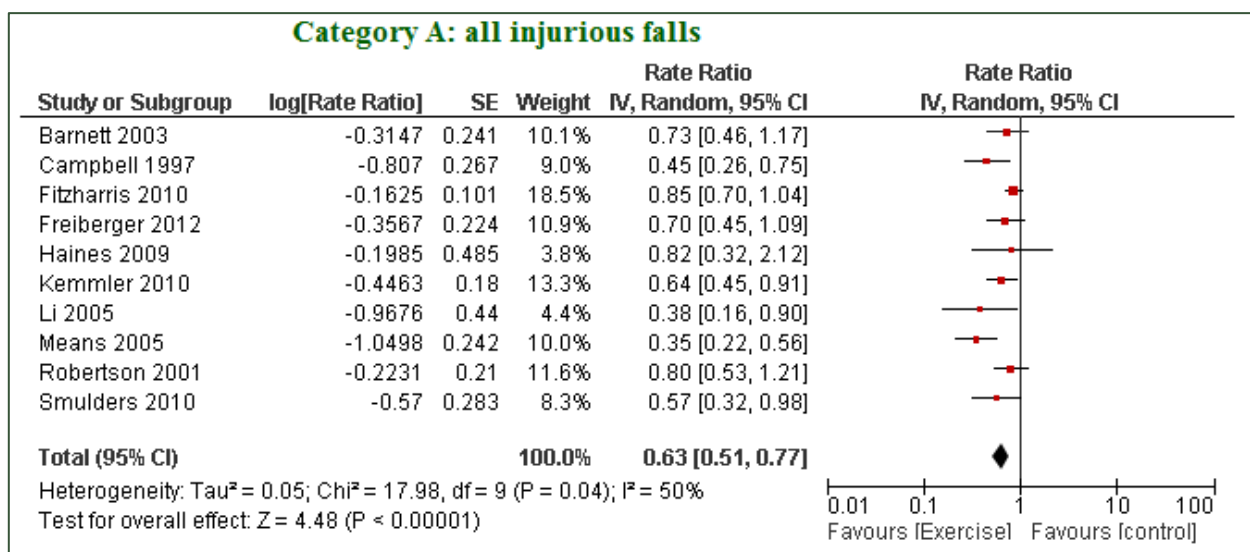


Figure 4: Forest plot of studies for category A analysis (all injurious falls)

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2.3.5.b. Category B: falls resulting in medical care

Eight trials with a total of 2356 participants presented data on falls resulting in medical care (Figure 5). One of those studies had a rate ratio greater than one, with all the others showed a tendency toward the reduction of falls resulting in medical care. The pooled estimate was 0.70 (0.54 to 0.92, $I^2=20\%$, $p=0.27$).

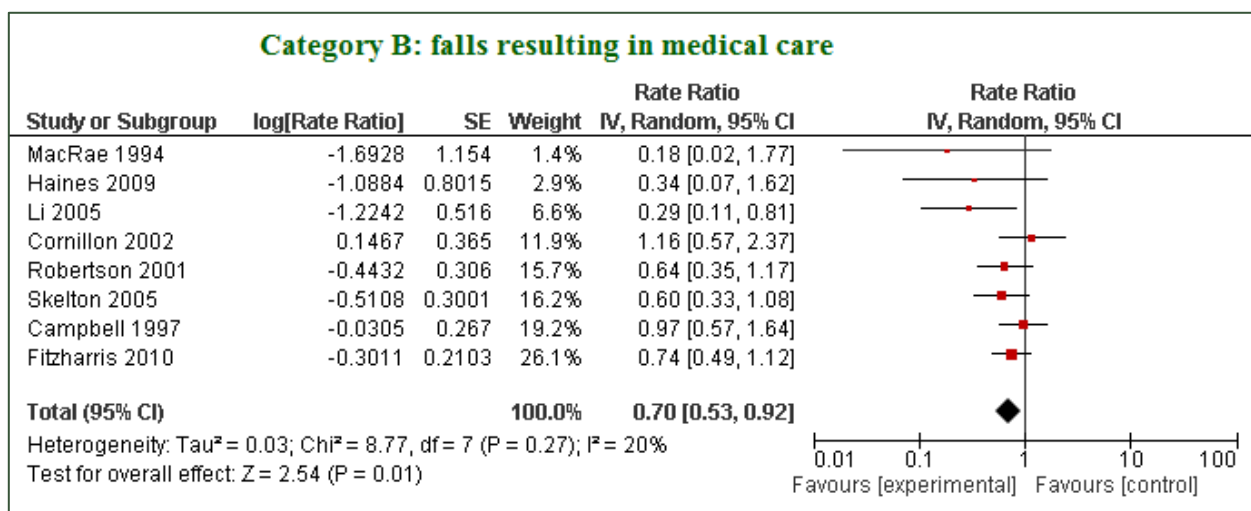


Figure 5: Forest plot of studies for category B analysis (falls resulting in medical care)

2.3.5.c. Category C: falls resulting in serious injuries

For falls resulting in serious injuries, seven trials with a total of 1750 participants had the required information. The pooled effect estimate is 0.57 (0.36 to 0.90, $I^2=46\%$, $p=0.09$). All these studies had individually shown a tendency to reduce serious fall-related injuries, with two of them (F. Li et al. 2005; M C Robertson et al. 2001) showing a significant effect (Figure 6).

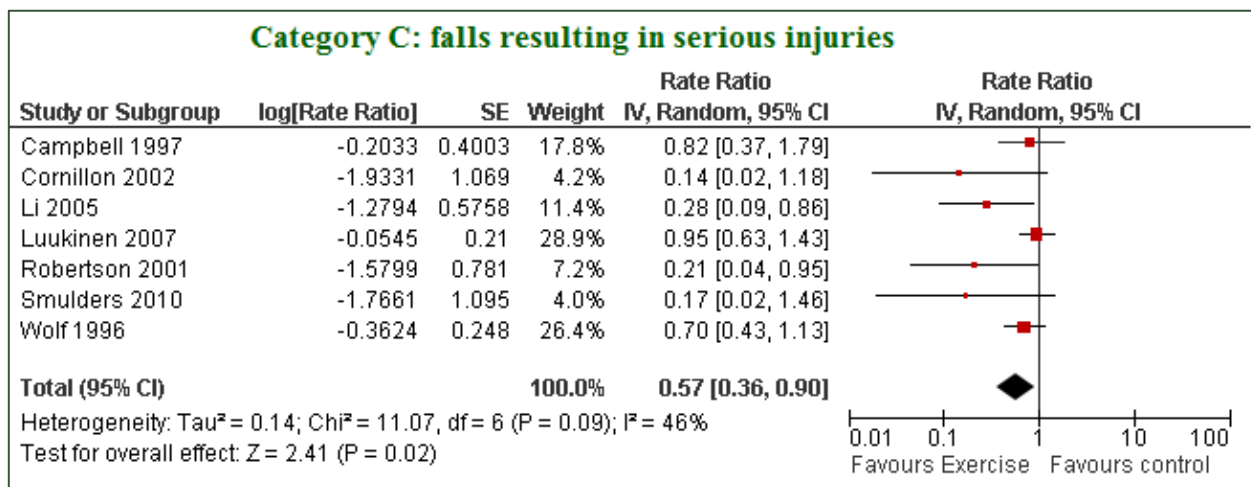


Figure 6: Forest plot for category C analysis (falls resulting in serious injuries)

2.3.5.d. Category D: falls resulting in fractures

Exercise seemed to significantly decrease the rate of falls resulting in fractures as well (category D), with a pooled effect of 0.39 (0.23 to 0.66, $I^2=0\%$, $p=0.96$; six trials). None of the studies had individually shown a significant effect on fall-related fractures reduction even when all of them presented a tendency towards the reduction of fractures (Figure 7).

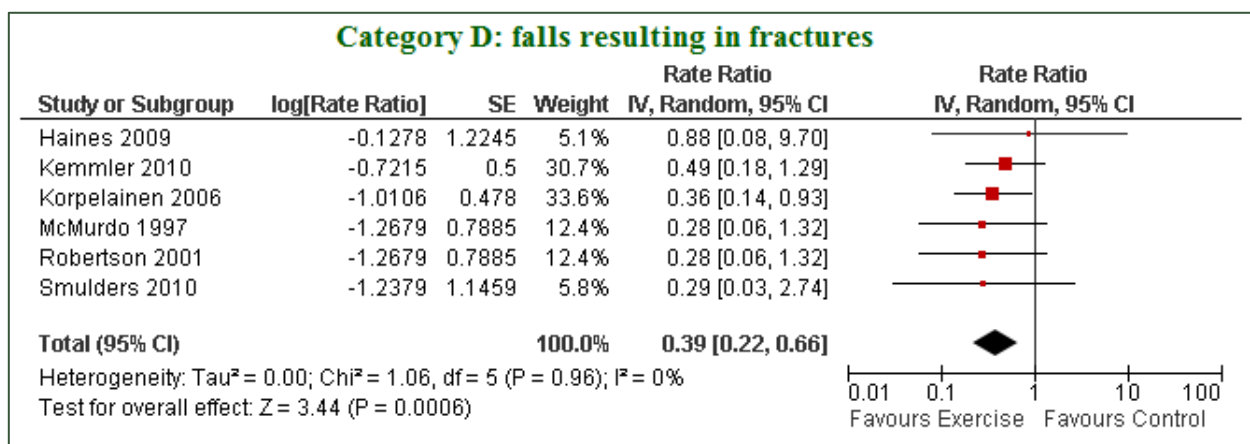


Figure 7: Forest plot for category D analysis (falls resulting in fractures)

2.3.5.e. Effect of exercise on all falls

We had also extracted data on all falls, and computed a pooled estimate for the effect of exercise intervention on the rate of falls for trials included in each analysis described above. These effects were: 0.64 (0.55-0.73) for trials included in category A analysis, 0.74 (0.61-0.89) for trials included in category B analysis, 0.69 (0.56-0.85) and 0.64 (0.55-0.75) for trials included in category C and D analyses.

2.3.6. Sensitivity and subgroup analyses

Studies who had at least 3 unclear risk of bias out of the quality components considered (Barnett et al. 2003a; Cornillon et al. 2002; McMurdo, Mole, and Paterson 1997; Wolf et al. 1996), or at least one unclear risk and one high risk (Luukinen et al. 2006; MacRae, Feltner, and Reinsch 1994; Means, Rodell, and O'Sullivan 2005; Smulders et al. 2010), were considered to be of poorer quality. When these studies were removed from the analysis, the pooled estimate of the effect of exercise on injurious falls became: 0.69 (0.58-0.82, $I^2=26\%$, $p=0.21$) for category A out of 8 studies, 0.64 (0.47 -0.87, $I^2=0\%$, $p=0.35$) for category B out of 4 studies, 0.54 (0.35-0.83, $I^2=44\%$, $p=0.54$) for category C from 3 trials and 0.44 (0.23-0.85, $I^2=0\%$, $p=0.77$) from 3 trials of category D. Thus removing studies with a higher risk of bias

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barely changed the pooled estimate of the effect of exercise in any of the four injurious fall categories; however it greatly reduced the heterogeneity between studies included in the analysis of all injurious falls, that was no more statistically significant ($p=0.22$).

We also carried out a pre-planned subgroup analysis of the effect of exercise in reducing injurious falls (category A) based on falls risk at enrolment (a priori), i.e., comparing trials with participants selected for inclusion based on history of falling or other specific risk for falling such as physical performance impairments or an age superior than 80 year (higher fall risk) (A J Campbell et al. 1997b; Barnett et al. 2003a; Haines et al. 2009; Freiburger et al. 2012; Smulders et al. 2010; Luukinen et al. 2006; D. Skelton et al. 2005) versus unselected (lower fall risk). The effect on injurious falls was very similar between the 2 subgroups: 0.66 (0.53-0.83) for the higher risk subgroup and 0.61 (0.43-0.87) for the other studies.

2.3.7. Publication bias

Publication bias was explored for only the first category of fall outcome (all injurious falls), since it is not recommended to assess publication bias when the analysis include less than ten studies. The funnel plot constructed from the ten trials included in the analysis of all injurious falls showed a barely asymmetrical scatter (Figure 8). However there was no asymmetrical ‘gap in the bottom corner’ that usually corresponds to an over-estimation of the reported pooled estimate cause by the publication bias or “small study effects” (exaggeration of treatment effects in small studies of low quality). In fact all the included studies, regardless of their size seemed to have reported an estimate that’s very close to the pooled one.

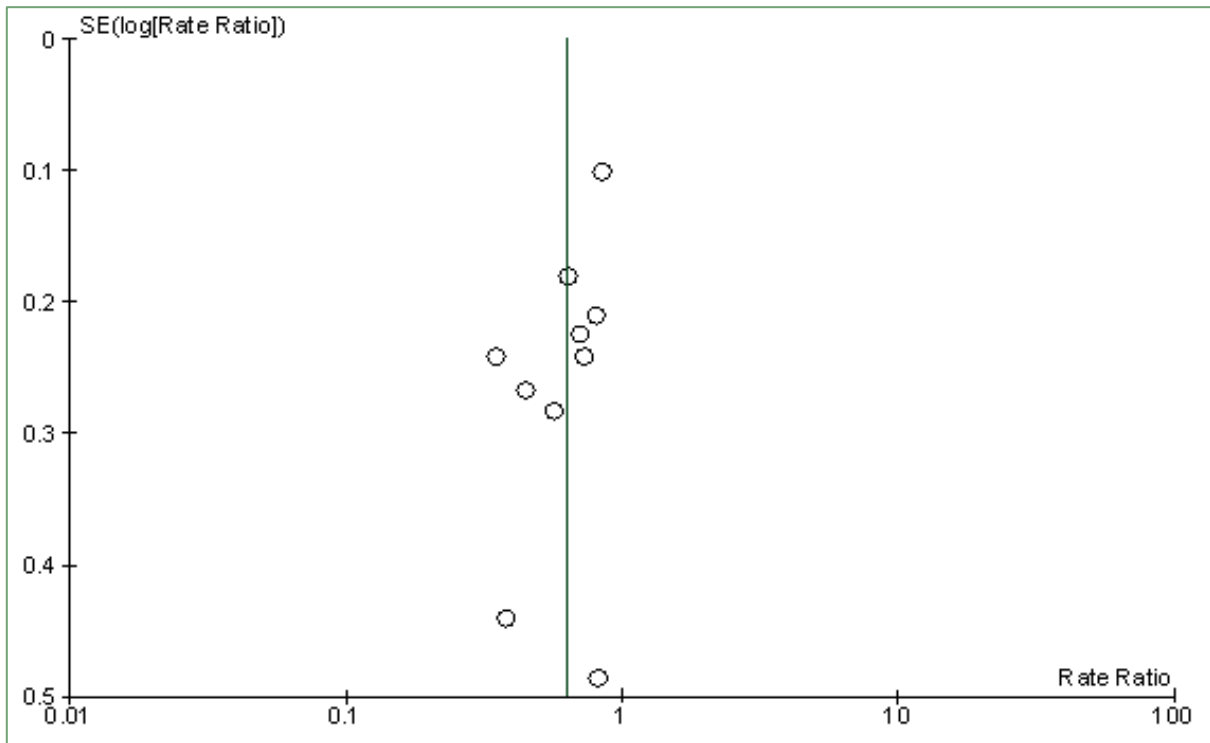


Figure 8: funnel plot of studies included in analysis of all injurious falls (Category A)

2.3.8. Adverse reactions

Only two studies reported adverse effects relating to exercise interventions; a total of eight participants in those two studies were reported as having a brief temporary musculoskeletal discomfort related to the intervention (Haines et al. 2009; Korpelainen et al. 2005). In one study (Haines et al. 2009) five participants reported discomfort (muscle soreness) during the first week of the programme, though this discomfort was decreased in subsequent weeks. In the other study, three women experienced musculoskeletal problems due to the exercise intervention, which led to a minor modification of the training regimen that helped them complete the exercise program without further problems.

No other adverse events, in particular no fall-related injuries occurring during the exercise sessions, were reported in any of the included studies. However, only six trials specifically reported the absence of adverse reactions.

2.4. Discussion

2.4.1. Summary of findings and interpretation

This review provides evidence of the effectiveness of exercise programmes in preventing different categories of injuries resulting from falls in older community dwelling people. The protective effect seems most pronounced for the more severe fall-related injuries: the estimated reduction is 37% for all injurious falls, 43% for severe injurious falls, and 61% for falls resulting in fractures.

Many of the risk factors for falls and fall-induced injuries are similar (Mary E. Tinetti 2003). Impaired balance and gait are correctable by well-designed exercise programmes, even in very old and frail elderly (Iwamoto et al. 2009; F. Li et al. 2005; S R Lord et al. 1995). Exercise programmes that have proven to be effective in preventing falls emphasise balance training, and there is now ample evidence that this type of programmes improves balance ability (Tracey E Howe et al. 2012; A J Campbell et al. 1997b). Similarly, all trials included in this review included a balance-challenging component, which may explain the positive effect on injurious fall prevention.

Additionally, most exercise programmes are in fact multi-component; they also include other types of exercise such as gait and functional training, strengthening exercises, flexibility, and endurance. Thus these programmes could be doing more than simply improving balance; there is evidence that these types of interventions can also improve reaction time, muscle strength, gait, coordination, and overall physical functioning as well as cognitive functions, especially executive function (Fitzharris et al. 2010; Liu-Ambrose T 2010; Barnett et al. 2003a). These factors thus would decrease the risk of injury once a fall has been initiated.

In fact there are many neuromuscular events that occur during a fall (Santello 2005):

- First phase :the preparation for touch down which calls for a preparatory muscle activation.
- Second phase: muscle activity following foot contact (after touch down) that is implicated in the braking and stabilisation of body posture
- Third phase: preparing body segments for impacts with external objects, these motor tasks also being called ‘interceptive movements’.

It is therefore thought that exercise prevents injurious falls not only by improving balance and decreasing the risk of falling, but also by improving cognitive functioning,[41] and the speed and effectiveness of protective reflexes during the different phases of a fall (such as quickly

Discussion

extending an arm or grabbing nearby objects) or the energy-absorbing capacity of soft tissues (such as muscles), thereby better controlling the impact absorption and diminishing the force of impact on the body (Nevitt and Cummings 1993; Quant et al. 2001). Hence, for any given initial energy of a fall, improved protective responses should decrease the severity of the resulting injury, which may explain why the estimated protective effect of exercise is stronger for severe injuries than for all injurious falls, the latter including severe but also minor and moderate injuries.

It may be unexpected to find that although exercise reduces the severity of injury, the pooled effect of exercise on preventing all injurious falls (37%) is larger than the effect of exercise on falls resulting in medical care (30%) which are presumably more severe. However, medical care-seeking behaviour is not solely influenced by the nature and severity of the injury but also by the type and availability of care and socio-demographic characteristics as well as by other personal factors including personality, pain tolerance, and anxiety (P. Cummings, Koepsell, and Mueller 1995; Babitsch, Gohl, and von Lengerke 2012). Accordingly, the mere fact that medical care was sought does not necessarily indicate that an injury was more severe, although this might've been the case when different categories of injurious falls are examined within the same population. Of the ten studies included in the 'category A' analysis of all injurious falls, five also contributed to the analysis of falls resulting in medical care (category B), (A J Campbell et al. 1997a; Fitzharris et al. 2010; Haines et al. 2009; F. Li et al. 2005; M C Robertson et al. 2001) and three also contributed to the analysis of severe injurious falls (category C) (A J Campbell et al. 1997a; F. Li et al. 2005; M C Robertson et al. 2001). Within these studies, the pooled estimate of the effect of exercise decreased from category A to category B for all studies but one, and from category B to category C for all studies. These results support the argument that exercise reduces the severity of the injuries caused by falls.

Other risk factors are specific to the risk of trauma during a fall, and correction of these factors by exercise may also help explain the more important protective effect of exercise on serious injuries such as fractures. In particular, low bone mass is a major determinant of the risk of fracture once a fall is triggered. Besides, impact and resistance exercise has been reported to increase bone mass and attenuate the losses in bone mass associated with aging (Guadalupe-Grau et al. 2009). In three of the five trials included in the analysis of fall-induced fractures, (Korpelainen et al. 2005; McMurdo, Mole, and Paterson 1997; Kemmler et al. 2010)

the intervention in question was specifically designed to improve bone mass and consequently included high intensity impact exercise, as well as balance, gait, and functional exercises. It resulted in a significant positive effect on bone mass at bone sites that varied with the study. However, these exercise interventions were tested in younger relatively active elderly women and may not be suitable for older people aged more than 75 years, who are at the highest risk of fractures, especially hip fractures.

Whereas, the large estimated pooled effect of more moderate-intensity exercise programmes on serious injuries found in this meta-analysis suggests that reducing the risk of falling and improving protective responses during a fall are important and feasible means of preventing fractures and other serious injuries among older adults. This finding is especially important because large epidemiological studies have shown that most fractures in the population occur in people at moderate “bone risk” for their age (Stone et al. 2003; P Dargent-Molina et al. 1996b). Other authors have also argued that fracture prevention strategies should not solely focus on osteoporosis prevention but should also include fall prevention strategies such as exercise training (Kannus, Parkkari, et al. 2005; Jarvinen et al. 2008; Martin 2009; D. A. Skelton and Beyer 2003). Of note, a recent systematic review reported that exercise intervention aiming to prevent fractures among individuals with low bone mass density should include balance components.(61)

Hence, while prescription of anti-osteoporotic drug treatments is currently recommended for older adults with low bone mass, who are at the highest risk of fracture, additional effective strategies that can be proposed to larger segments of the elderly population will be necessary to significantly reduce the burden of fractures in this population (Cheung and Detsky 2008). And more and more evidence is highlighting fall-prevention exercise training as one such strategy.

2.4.2. Comparisons with other reviews

2.4.2.a. The Otago Exercise Programme

The Otago Exercise Programme was conceived by the fall prevention research group at the University of Otago medical school in New Zealand. It is a set of individually-described leg muscle strengthening and balance retraining exercises specifically designed to prevent falls, delivered at home by trained instructors. Four controlled trials, involving 1016 women and men aged 65 to 97, assessed whether this programme reduced falls and injuries in community-

living older people. Robertson et al conducted an individual-level data meta-analysis of the results of these four trials,(M Clare Robertson et al. 2002) and demonstrated a 35% reduction in the risk of an injurious fall (moderate or serious), a result similar to our findings. However they failed to demonstrate a significant reduction in serious fall-related injuries. A more recent review including three additional trials of the Otago exercise programme,(Thomas, Mackintosh, and Halbert 2010) failed to support the previous result that the programme significantly reduced the risk of injurious falls, possibly because of a lack of access to individual-level data, or differences in programme implementation and supervision (as suggested by the significantly lower adherence rates reported in the three additional trials compared with the first four).

2.4.2.b. Cochrane review

The recent Cochrane systematic review of fall prevention interventions carried out a specific analysis to examine the effect of exercise interventions on the risk of fall-related fractures among older adults, and obtained comparable results (pooled relative risk= 0.34 (0.18-0.63) (Gillespie et al. 2012). Of the six trials included in the Cochrane analysis, five are also included in our study. The only exception is that we excluded the study by Bischoff-Ferrari, where participants were recruited in the hospital while in the acute phase of an injury (hip fracture). We judged against including that trial since its results may not be comparable to those of studies not recruiting on the basis of an injury (Bischoff-Ferrari et al. 2010). Inversely, we included the study by Kemmler et al, (Kemmler et al. 2010) that compared an exercise intervention including balance, gait, and strengthening and flexibility exercises to a “wellness” exercise programme designed not to affect the risk of falling, whereas this study was not considered in the Cochrane analysis of fracture risk.

2.4.3. Strengths and limitations of this review

2.4.3.a. Heterogeneity among studies

There was a noteworthy heterogeneity among studies included in the analysis of all injurious falls (category A)($I^2=50\%$, $p=0.04$). Although no significant heterogeneity was detected in the analysis of severe injurious falls (category C), the inconsistency was also moderately large ($I^2=46\%$, $p=0.09$). Pooled data from studies with significant statistical heterogeneity require careful interpretation because heterogeneity indicates the possibility of meaningful differences between these studies. This review examined the effect of interventions based solely on

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exercise and targeting specifically community-dwelling elderly, excluding studies where participants were institutionalised or recruited based on a certain disease or handicap. However, the included interventions are still quite diverse, in particular in terms of intervention components (type of exercises, frequency, intensity, mode of delivery, and total duration) and inclusion criteria for participants. This problem is a common one among systematic reviews and meta-analyses in general and in the field of fall prevention intervention; similar or even larger measures of heterogeneity have also been reported in other meta-analyses of fall-prevention exercise interventions (Gillespie et al. 2012; Sherrington et al. 2008).

To explore possible reasons for heterogeneity, we carried out pre-planned subgroup analyses based on fall risk at enrolment (whether participants were recruited because of a history of fall or an increased risk of falls). The subgroup analyses showed no difference in pooled estimates between studies with participants selected for their higher risk of falling versus lower risk (unselected), for the four categories of fall-induced injuries.

Among intervention components, the type of exercise appears to be an important factor influencing the effectiveness against falls: it has been established that exercise interventions including a balance-training component appear more effective (Province et al. 1995; Sherrington et al. 2008; Gillespie et al. 2012). Sherrington et al. colleagues reported that the intensity of the balance training component was also important: programmes that include moderate to high challenging exercises (ie, standing exercises in which people sought to stand with their feet closer together or on one leg, to minimize use of their hands to assist, and to practice controlled movements of the centre of mass) are more effective in reducing falls than programmes that include less challenging balance exercises (Sherrington et al. 2011). All interventions included in this review include a balance-training component, hence we performed an additional subgroup analysis by comparing interventions where the exercise programme provides a moderate or high challenge to balance (based on Sherrington's definition), (Barnett et al. 2003a; A J Campbell et al. 1997a; Freiburger et al. 2012; Haines et al. 2009; F. Li et al. 2005; M C Robertson et al. 2001; Smulders et al. 2010; Cornillon et al. 2002; Korpelainen et al. 2005; Wolf et al. 1996; D. Skelton et al. 2005) versus a low challenge. (Kemmler et al. 2010; Means, Rodell, and O'Sullivan 2005; Fitzharris et al. 2010; MacRae, Feltner, and Reinsch 1994; Luukinen et al. 2006; McMurdo, Mole, and Paterson 1997) We found no significant difference in exercise effect between these two subgroups with

regard to the reduction of all injurious falls or falls resulting in medical care (categories A and B). For severe injurious falls and falls resulting in fractures (categories C and D), there were not enough studies to perform subgroup analyses by intensity of balance training.

Moreover, the relatively small number of studies included in this review did not allow us to perform additional subgroup analyses exploring the effect of other components within interventions or other factors related to the way interventions were implemented that might have affected results.

Although we tried to reduce heterogeneity in the extracted definitions of injurious falls as much as possible by grouping them in more homogeneous categories, remaining inconsistency in definitions may also help explain the observed heterogeneity. In the category of all injurious falls (category A), in particular, several studies used imprecise definitions of injurious falls (Freiberger et al. 2012; Haines et al. 2009; Kemmler et al. 2010; Means, Rodell, and O'Sullivan 2005; Smulders et al. 2010) but were nevertheless included in the analysis since by definition this category is the largest, and refers to any types of physical consequences of a fall. We performed a sensitivity analysis excluding from the analysis of this category studies that used imprecise definitions. The resulting pooled rate ratio was similar to that obtained in the main overall analysis (0.69, 0.53 to 0.90, $I^2=49\%$, $p=0.10$) and indicated that our results are robust to differences in outcome definitions between studies.

2.4.3.b. Quality of included studies and Publication bias

Results of the sensitivity analysis excluding trials judged to be at higher risk of bias in all 4 categories of injurious falls barely changed the pooled effect estimates and indicates that our results are also robust to key risks of bias.

The funnel plot of the ten studies contributing to the analysis of all injurious falls showed a barely asymmetric scatter. Asymmetrical funnel plots may indicate publication bias or be caused by an exaggeration of treatment effects in small studies of low quality (J. P. T. Higgins et al. 2011). However, the funnel plot in this analysis does not show any clear evidence of “small study” effects. Note that almost all the studies included in this review were initially designed to prove that exercise has an effect on the fall rate and not on the rate of injurious falls. Among the 17 studies considered in this review, 8 did not demonstrate a significant effect of exercise on fall prevention. Moreover, the pooled effect of the included trials on the rate ratio of falls was 0.68 (0.61 to 0.77), which is comparable to the effect of exercise reported in the Cochrane review (Gillespie et al. 2012). These points suggest that the studies

included in this review, because they presented data on injurious falls, do not represent a distinct selection of fall prevention exercise trials biased towards “positive” trials for all falls. Nonetheless, we cannot exclude the possibility that studies are more likely to report fall-related injuries when there tend to be a positive effect on injurious falls. On the other hand, it is also likely that some studies did not report data on injurious falls simply because the relevant data was not collected.

2.4.3.c. Reporting of adverse effects and other outcomes

Only minor adverse reactions were reported in 2 of the 17 included trials. However, nearly half of the selected papers did not even discuss the issue of intervention adverse effects. It has also been suggested that fall-prevention exercise programmes may have adverse psychological effects that may affect the quality of life (eg, through self-imposed activity restriction) (Laybourne, Biggs, and Martin 2008; Sjösten, Vaapio, and Kivelä 2008). Some trials have reported the effect of the intervention on fear of falling, physical activity levels, or other aspects of quality of life (Barnett et al. 2003a; Haines et al. 2009; F. Li et al. 2005; Smulders et al. 2010; Wolf et al. 1996). Their results either show no effect, or a tendency towards a beneficial effect of the intervention on these outcomes, in particular a lessening of fear of falling. More complete data on adverse physical reactions as well as on psychological and quality of life outcomes would improve our ability to judge the overall benefit of exercise fall-prevention programmes.

2.5. Conclusion and recommendations

The results presented in this systematic review reveal a positive effect of exercise on injurious fall prevention, including the most severe falls and those that result in medical care — that is, those with the greatest consequences for older people's health and resource use. These results should provide useful supplementary evidence for health care providers to encourage participation in exercise fall-prevention programmes, and further justification for decision-makers to fund those programmes.

Systematic reporting of falls and injuries should be implemented in future RCTs, where the different levels of severity of the injury should be standardised and defined in advance, in order to improve the comparison between studies and subsequently the accuracy of pooled estimates for each category of falls. Future trials should also aim to address some of the limitations of published studies, in particular by providing data on other important outcomes (physical and cognitive functional capacities, psychological outcomes, and quality of life) and a thorough description of implementation process.

These findings were published in BMJ (El-Khoury et al. 2013).

3. Part II:
The ‘Ossébo’ multi-
centric randomised
controlled trial

3.1. Description of the Ossébo trial

3.1.1. Background and main objectives

Fall prevention exercise programmes that emphasise balance training have been proven successful in reducing the incidence of falls among community-dwelling older adults. At the outset of the Ossébo trial (~2006), there was limited evidence that these programmes can also prevent injuries caused by falls, especially in the older subgroups that are at higher risk of injury. The results of our recent systematic review and meta-analysis that I just presented suggest that exercise programmes designed to improve balance and reduce falls can also reduce injuries caused by falls, including the most severe. However, these results must be interpreted with caution due to the limits of the review detailed in the previous chapter.

Additionally, most interventions included in our review lasted less than one year, and their long-term benefit is unclear. Few interventions targeted the subgroups of the home-living older adults who are at highest risk of falls and injuries, such as women aged over 75 years with diminished balance and gait capacities – that is those for whom the absolute benefit of the intervention should be greatest (M Clare Robertson et al. 2002). Moreover, the effectiveness of the interventions in real life conditions is unclear. Thus, designing and implementing interventions that are both effective against injurious falls and acceptable over the long term remains a challenge, especially for the oldest and more fragile subgroups (Close 2013; Rose and Hernandez 2010).

To our knowledge, Ossébo is the first long-term (2-years) exercise trial that targets very old (> 75 years) community-dwelling adults at higher risk of falls and injuries, and is sufficiently powered to demonstrate an effect on injurious falls. The trial was conducted in 20 sites located throughout France, and applied a pragmatic approach intended to inform the design and implementation of future community-based intervention programmes. The study also provides comprehensive information on physical as well as psychosocial outcomes (fear of falling and health-related quality of life). It also presents data on adverse outcomes, which were often lacking in previous research despite their recognised importance for assessing the programmes' overall benefits.

Hence, the major aims of the trial were to assess the effectiveness of the Ossébo exercise programme on injurious falls as well as total falls in a very old (>75 years) population, and to

assess the impact of the programme not only on physical capacities but also on psycho-social factors (fear of falling, general activity level and health-related quality of life). An additional aim was to examine the personal and programme-related factors that are associated with participation into the trial.

3.1.2. Study design

The Ossébo study is a multicentre, balanced, two-arm, parallel-group, assessor-blinded randomised controlled trial (Patricia Dargent-Molina, Khoury, and Cassou 2013; Patricia Dargent-Molina and Cassou 2008). Randomisation was stratified for study centre and body weight.

The study protocol was approved by the Ile-de-France IV ‘Committee for the Protection of Persons’ (CPP) (ref 2007/29). It is registered with the CNIL (‘Commission nationale de l’informatique et des libertés’: French data protection authority) under the number 907198. It is also registered on ClinicalTrials.gov under the number: NCT00545350.

3.1.2.a. Study centres

The intervention took place in 20 centres throughout France (Figure 9). The centres were in the following cities: Paris, Reims, Lille, Amiens, Montpellier, Strasbourg, St Etienne, Annecy, Nimes, Rouen, Boulogne, Lyon, Villejuif, Caen, Issy-les-Molineux, and Nantes. There was one intervention site by city except in Paris where five different centres were in place: in the 5th, 16th, 17th, 18th, as well as in the 19th ‘arrondissements’ (administrative districts).

Cities were chosen if SIEL Bleu, the organisation in charge of implementing the intervention, had established activities in the city and if a location and contacts (investigator from geriatric services) for the baseline examination were available.

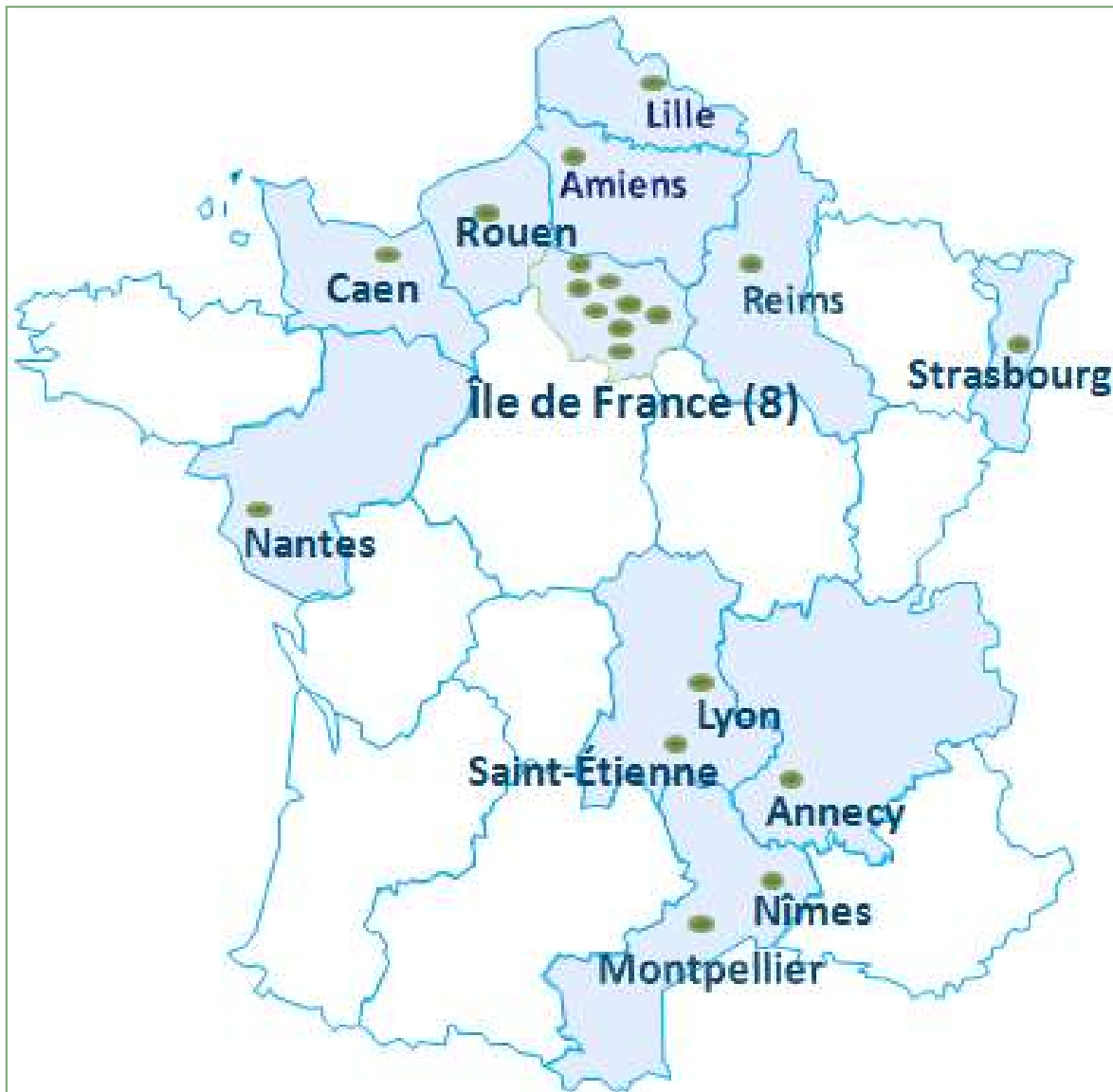


Figure 9: The cities where the Ossébo centres took place

3.1.2.b. Participants

Recruitment process and eligibility criteria

The recruitment was organised in successive waves; 2 to 3 recruitment centres at a time. It took place between December 2007 and April 2011, and was centrally organised (at Inserm CESP-Villejuif).

The Ossébo trial only target older women because they are at a higher risk of injurious falls compared to men of the same age (Stevens and Sogolow 2005). Community-dwelling women aged 75-85 years living near intervention sites were identified through voter registration lists. These women received letters inviting them to a free balance and health examination. Women who replied positively and returned the pre-paid reply coupon were called and a rendezvous

Study design

for the baseline examination was scheduled. The women were also sent a questionnaire on current medical treatments and health-related quality of life (SF36 (Leplège et al. 1998)) to be returned at the time of the examination.

This examination took place in hospital geriatric departments or senior health centres near the intervention sites, and were performed by examiners (nurses most often) specially recruited and trained for the study. It included two functional tests, previously validated for the prediction of hip fracture in the EPIDOS (Epidémiologie de l'Ostéoporose) French cohort (P Dargent-Molina et al. 1996b), that were used to determine eligibility. These tests were time to walk over a 6-m course (measured twice and averaged) and ability to do 4 tandem steps. Women who took ≥ 7 sec for walking 6 m or were unable to do 4 consecutive tandem steps were potentially eligible for the trial. The frailest women with a walking time > 12.5 sec ((95th percentile of the EPIDOS population) or unable to stand for 10 sec with feet together, were excluded from the trial because they were considered to be at high risk of falls and traumas and would probably require specific, individualised and supervised exercises.

Women who had at least one of the medical conditions listed below were excluded from the trial:

- Substantial alteration in cognitive function as assessed with the Pfeiffer test.
- A degenerative neurological condition such as Parkinson's disease.
- Major visual or hearing problems.
- A medical condition involving the neuromuscular, skeletal or cardiovascular system that generally precludes exercising.

Women already partaking in exercise classes, or who expected to move away within the next 6 months, or those who would have difficulty attending exercise classes regularly were also excluded.

Study presentation

If the woman was eligible for inclusion in the trial, the examiner presented the Ossébo trial as a prequel to ask for her consent for participation to the study. Therefore, eligible women were informed that, like many in their age group, they had diminished balance capacities. Also, that physical activity and balance exercise are recommended by medical and governmental authorities, enjoyable and could benefit their quality of life and balance confidence. The objective of the trial, randomisation process, and follow-up were then briefly explained. The

format of the exercise sessions were also described, with emphasis on how they would help maintain and preserve balance and that they would be delivered by a specialised association.

Randomisation

Randomisation was centrally organised (at the Paris-Ouest Clinical Research Unit- 'Unité de Recherche Clinique Paris (URC) Ile de France Ouest'). The randomisation lists were computer-generated, with randomly-sized blocks and an allocation ratio of 1:1. Randomisation was stratified for study centre and body weight (<59 versus ≥ 59 kg). The reason for stratifying on weight was that low body weight had been shown to be a major risk factor for low bone mineral density and fractures in a cohort of older French women with similar recruitment strategies (P Dargent-Molina, Poitiers, and Bréart 2000). Before the beginning of the trial, a biostatistician who had no other involvement in the trial installed the randomisation lists with the examination data entry programf on laptops dedicated to the study. At the end of the baseline examination, the program automatically determined the eligibility of each woman, based on her examination results; if she was eligible and agreed to participate, it randomly assigned her into the experimental intervention or the control group.

3.1.2.c. Intervention

The intervention was conceived and implemented in partnership with SIEL Bleu, a non-profit organisation specialised in delivering physical activity programmes for older people (www.sielbleu.org). The programme is based on a careful analysis of the literature; in particular, description of specific fall prevention programmes that have demonstrated their effectiveness (published or requested from the authors), various published and on-line guidelines, reference articles on exercise for falls management, and on the long (> 15 years) field experience of the SIEL BLEU group with regard to the conception and implementation of fall prevention programmes among older adults in the community.

Care providers

Intervention instructors, all of them graduates in sports science and experienced in exercise groups for older people in both the community and institutions, were SIEL Bleu employees specifically trained for the study and already practicing in the cities where the trial was set up.

General description and objectives of the exercise programme

The 2 years intervention consisted of weekly exercise classes in small groups of 10-15 women, supplemented with home exercises.

The Ossébo exercise programme has three general objectives:

1. Improving physical factors which affect balance and contribute to a higher risk of falls and fall induced injuries. This objective is realised through the improvement of posture and balance control through exercises aimed at:

- Strengthening the hip stabilising muscles, quadriceps, and foot flexor/extensor muscles in an analytical as well as comprehensive way, and any muscle chain intervening in a movement or posture for which balance is a key factor for its realisation or the result of the action.
- Mobilising target joints involved in actions specific to locomotion and in general skeletal reinforcement.
- Sharpening perception of plantar sensations.

2. Raising awareness on the risks of falls and their prevention through behaviours changes, realised through exercises aimed at helping women to:

- Have better general movement (e.g., standing travelling moves, cross over, position changes, floor work)
- Be more attentive (e.g., perform all movements in consciousness, training of peripheral vision)
- Be more aware of one's body in space (e.g., sharpen the reflexes, managing body weight).
- Analyse risk factors (e.g., understand balance mechanisms, lift an object safely, and allocate loads)

3. Fostering long term maintenance of balance training and physical activity. This is realised through the integration of some exercises and behaviours into daily living routine, in order to carry on a healthier lifestyle. A series of home exercises initially thought in collective sessions are selected for individual, self-directed, home-based sessions. The aims are to encourage participants to:

- Memorise the exercises
- Develop the ability to perform the exercises alone correctly
- Practice regularly

Exercise location

The group sessions took place in community settings usually serving for similar activities. Most commonly, it was in associative venues such as senior citizens clubs, in other centres it was in an auditorium or a room in a city hall ('mairie'), or in a hospital.

Specific content of the programme

The exercises were designed to improve muscle extensibility and, to a lesser degree, joint flexibility (eg, calf and hip flexor stretches), balance (eg, knee bends, tandem stance/walk, backward/sideways walking, toe/heel walking, sit-to-stand), reaction time (eg, play in group with balloon), coordination (eg side and front leg swings), muscle strength of muscles critical for posture and balance (eg, hip abductors, knee extensors, ankle plantar flexors) and internal sense of spatial orientation (proprioceptive sense) through plantar sensation stimulation. The exercises were designed to be comfortable and fun. Social interactions were encouraged to facilitate long-term compliance.

The programme was divided into 8 terms. The level of difficulty and intensity of exercises increased progressively over time (eg, through increasing the number of repetitions of a given exercise and going from isolated motor abilities to more global exercises combining several abilities), although priority was always given to consolidation and maintenance of acquired progress. Exercises in terms 1 and 2 were slow-paced, performed on a broad base of support and a chair close by for safety. Terms 3 and 4 included exercises with a decreased base of support, increased speed, and less support from the chair. The second year (terms 5 to 8) was dedicated to consolidating the exercises learned the first year and progressively evolving to more global activity of gymnastics and maintenance.

Home exercises

Subjects were also expected to perform a home exercise programme (at least once a week) based on the content of the exercise class and adapted by the instructor to each participant's physical abilities. Home exercises served the purpose of promoting and optimising subject's compliance and engagement in the intervention, as well preventing sedentary behaviour, and increasing the global 'dose' of the exercise.

Standardisation

Instructors were asked to perform the same exercises and progressions in all centres, guided by a detailed instruction book. They did, however, have some degree of freedom to adapt the

Study design

programme to groups or individuals, for instance, by changing the number of repetitions or presentation of a given exercise (eg, with or without equipment) or the number of exercises (eg, by adding games at the end of the session) while following the general framework of exercises proposed for each term.

One person from SIEL Bleu (D Lutz, programme developer) was in charge of supervising the instructors' activity over the whole intervention period to ensure that the programme was adequately implemented in all centres.

Record of participants' adherence to the intervention

Instructors recorded attendance at group sessions and frequency of home exercising at each group session, and then sent this information to the study coordination centre every week. They also reported any falls or other adverse events that occurred during group exercise sessions to the study clinical coordinator (Bernard Cassou, geriatrician).

Control group

Women randomised to the control group did not receive any intervention. At the end of the baseline examination, participants in both groups were offered brochures about fall prevention (in particular, those published by the French national institute of health prevention and education-‘INPES’), which discussed the importance of physical activity, a balanced diet, and Vitamin D supplementation, and offered suggestions for assessing home hazards and managing medication. Biannual newsletters reminded all participants about major risk factors for falls and prevention measures. At the end of the 2-year follow-up, four free exercise classes were offered to women in the control group.

3.1.2.d. Data Collection

Baseline and follow-up examinations

Known risk factors for falls and injurious falls were assessed at inclusion during baseline examinations (in the same examination that evaluated trial eligibility). These assessments took place in local hospital geriatric departments or senior health centres and were performed by examiners (nurses, most often) specially recruited and trained for the study. The same evaluation was repeated during the follow-up examinations, at 1 and 2 years after inclusion. The examination consisted of series of functional tests, anthropometric and socio-demographic measurements, and a questionnaire about physical activity level and fall and health-related characteristics.

Functional tests of balance and motor function

The physical examinations included the 2 tests used to determine trial eligibility the timed 6-m walk and tandem walk, as well other standardised functional tests of balance and motor function. These tests were chosen because they are simple to use, reliable, are associated with the risk of falling and their results can be potentially modified by exercise. The tests were:

The timed 6-m walk

This test measure the time it takes the women to walk 6 meters. The distance was marked on the ground, and examiners instructed participants to walk the marked distance at their own pace. The test was repeated twice for each examined participant, with the examiner noting the time in seconds with a stopwatch at the end of each test. The average times of both trials was used for the analysis.

Slow gait speed at usual pace is associated with an increased risk of falling among other outcomes such as mortality, disability, and cognitive impairment (Cesari et al. 2005; Kan et al. 2010). This tests shows a good test-retest reliability and predictive of many disabilities in older age including hospitalisation, health deterioration, disability in mobility and in the upper limbs, mortality, cognitive deterioration and hip fracture (Muñoz Mendoza et al. 2010).

Timed up-and-go

For this test, the examiner measured in seconds with a stopwatch, the time it takes for a woman to stand up from a standard arm chair, walk a distance of 3 meters, turn, walk back to the chair, and sit down again.

This test has been proven to be an appropriate tool for clinical assessment of functional mobility (Herman, Giladi, and Hausdorff 2011). It is widely used and is recommended as a clinical assessment tool for fall risk (American Geriatrics Society and American Academy of Orthopaedic Surgeons 2001). An increased time required to perform the test is associated with mobility disorders and increased fall risk.

Sit-to-stand test

For the sit-to-stand, the examiner measured in seconds using a stopwatch, the time it takes for a woman to rise from a chair without armrests, five times, as quickly as possible with her arms folded across her chest. Repeated chair rise test requires lower limb strength, range of motion, and balance. This test has been proven to be predictive for balance disorders and recurrent falls among older adults (Buatois et al. 2008; Whitney et al. 2005).

Static balance tests

During these exams, examiner measured with a stopwatch the time a woman could stay in these different positions (figure 10):

- Semi-tandem: the heel of one foot placed to the side of the 1st toe of the opposite foot (woman chose which foot went forward).
- Full tandem: heel of one foot directly in front of the other foot.
- Standing on one leg.

Inability to stand in those positions is associated with balance disorders. These tests had been proven reliable, valid, and discriminant in measuring balance functions among older adults (Rossiter-Fornoff et al. 1995).

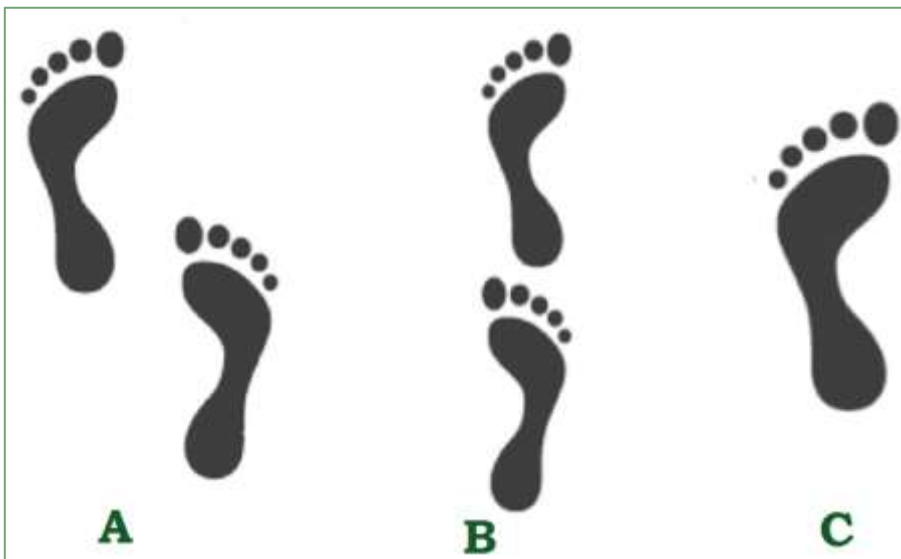


Figure 10: base of support during static balance tests.

(A) Semi-tandem stance, (B) tandem stance, (D) one leg stance (monopodal stance).

The tandem walk test

This test assesses dynamic balance. Participants were asked to walk with the heel of their front foot touching the big toe of their rear foot (tandem walk). The outcome variable was binary, distinguishing between women who were able to do 4 consecutive steps in tandem walk from the others. The inability to perform this test is associated with vestibular disability and an increased risk of falling (Cohen et al. 2012). This test has been proven to be a predictor of fall-related hip fracture in a prospective study with a population comparable of that of the Ossébo's study (P Dargent-Molina et al. 1996a, -).

Physical and socio-cultural activity, and sedentary behaviour indicators

Physical activity level was estimated by a questionnaire suitable for older women, adapted from the questionnaire developed by Lord et al in their fall prevention trials (S R Lord et al. 1995; Stephen R Lord et al. 2003). It assessed the weekly frequency and duration of walking for grocery shopping, walking for exercise, and total leisure-time physical activities. Leisure-time physical activities examined included: swimming, dancing, gym classes, gardening, biking, and yoga. Subsequently, two scores were created that measured the number of times a week the women undertook a physical activity (walking or leisure activities), and the number of times in a week the participant initiated these activities.

The questionnaire also measured weekly frequency and duration of other social and cultural activities: watching a movie or attending an exposition, clubs or associations meetings, card or board games with friends, going to the restaurant, any religious activity, and visiting family and friends.

Physical activity is associated with a reduction in the risk of falling and in fall-related injuries among older adults (Pereira, Baptista, and Infante 2014; Moayyeri 2008), it is also associated with a better quality of life (Acree et al. 2006; Rejeski and Mihalko 2001).

Sedentary behaviour was measured by asking women how many hours a day they spend sitting down, including sitting doing for activities such reading, sewing and watching TV. A sedentary lifestyle was associated with an increased risk of recurrent falls among women in a cross-sectional Brazilian study (Pinheiro et al. 2010). Also, sedentary behaviour is independently associated with a decrease in the health-related quality of life of older adults (Balboa-Castillo et al. 2011).

Fear of falling

Measured by the validate 'Falls Efficacy Scale' (FES-I) (Yardley 2005). This questionnaire contains 16 items (figure 11) about fear of falling in every day activity with 4 possible responses (1: not worried to 4: very worried). Missing data was handled as recommended by PROFANE ("Prevention of Falls Network Europe" 2015). When data was missing on more than four items then the score was not used (considered 'missing'). When data was missing on no more than four of the 16 items then the sum of the items that have been completed was divided by the number of items completed, and then multiplied by 16. The score ranged from 16 to 64, a higher score corresponding to a more important concern about falling.

Study design

The FES-I has been reported to have an excellent internal and test–retest reliability, and has good validity to discriminate differences in concern about falling between groups (Yardley 2005).

	Items	Not at all concerned (1)	Little concerned (2)	Concerned (3)	Very concerned (4)
1	Cleaning the house (e.g., sweep, vacuum, or dust)				
2	Getting dressed or undressed				
3	Preparing simple meals				
4	Taking a bath or shower				
5	Going to the shop				
6	Getting in or out of a chair				
7	Going up or down the stairs				
8	Walking around the neighborhood				
9	Reaching for something above your head or on the ground				
10	Going to answer the telephone before it stops ringing				
11	Walking on a slippery surface				
12	Visiting a friend or relative				
13	Walking in a crowded place				
14	Walking on an uneven surface (e.g., rocky ground, poorly maintained, pavement)				
15	Walking up or down a slope				
16	Going out to a social event (e.g., religious service, family gathering, or club meeting)				

Figure 11: the 16 items of the FES-I score

Health indicators

Women filled the validated French version of the ‘SF-36’, the Short Form (36) Health Survey, which is a self-reported generic health status measure (Leplège et al. 1998). Four different health subscales were evaluated: physical functioning or limitations in physical activities because of health problem (10 items), general health perceptions (5 items), vitality (4 items), and general mental health (psychological distress and well-being) (5 items) (Figure 12). All items are scored so that a high score (of the subscale) defines a more favourable health status. Items in each subscale were linearly transformed so the final subscale score ranged from 0 to 100.

When they were less than half of the items in one subscale missing, the average of the answered items were imputed to each of the missing values. Otherwise, the score was treated as ‘missing’.

Health scale	Item	Abbreviated item content
Physical Functioning (PF)	PF1	Vigorous activities, such as running, lifting heavy objects, strenuous sports
	PF2	Moderate activities, such as moving a table, vacuuming, bowling
	PF3	Lifting or carrying groceries
	PF4	Climbing several flights of stairs
	PF5	Climbing one flight of stairs
	PF6	Bending, kneeling, stooping
	PF7	Walking more than a kilometre
	PF8	Walking half a kilometre
	PF9	Walking 100 metres
	PF10	Bathing or dressing yourself
General Health (GH)	GH1	Is your health: excellent, very good, good, fair, poor
	GH2	I seem to get sick a little easier than other people
	GH3	I am as healthy as anybody I know
	GH4	I expect my health to get worse
	GH5	My health is excellent
Vitality (VT)	VT1	Feel full of life
	VT2	Have a lot of energy
	VT3	Feel worn out
	VT4	Feel tired
Mental Health (MH)	MH1	Been a very nervous person
	MH2	Felt so down in the dumps that nothing could cheer you up
	MH3	Felt calm and peaceful
	MH4	Felt down
	MH5	Been a happy person

Figure 12: the 4 examined subscales of the SF36 questionnaire.

Fall outcomes

Falls were defined as “unexpected event[s] in which the participant comes to rest on the ground, floor, or other lower level” (Lamb, Jørstad- Stein, et al. 2005). The main outcome of the study was the rate of injurious falls (severe and moderate).

Monitoring

The occurrence of falls during follow-up was centrally organised (at Inserm CESP- Villejuif) and based on the calendar card method, a recommended method to monitor falls.(Lamb, Jørstad- Stein, et al. 2005) Women were asked to return at the end of each month pre-addressed, pre-paid monthly calendar postcards on which they could mark the exact date of any fall.

Study design

Women who failed to return their monthly fall calendars were contacted by a blinded investigator, encouraged to fill in and send their postcards, and asked about whether they fell in the previous month. If the investigator was not able to reach the participants, a person from her contact network (family or friends that each participant indicated at the time of the baseline examination) was called.

Whenever a fall was reported, an investigator blinded to allocation group called the woman to conduct a standardised fall interview to confirm the fall and collect further information on its consequences and circumstances. If a fracture or hospitalisation was reported, a copy of the radiologist's report or any other medical record was requested to confirm the severity of the injuries.

Classification

Falls were then classified by an expert geriatrician blinded to group assignment into one of three categories: (a) falls with no consequences, (b) falls resulting in moderate injuries, and (c) falls resulting in serious injuries. The definition of severe fall-related injuries was adapted from that of the FICSIT trials (Buchner et al. 1993): falls that resulted either in fractures; head injuries requiring hospitalisation; joint dislocations; sprains accompanied by a reduction in physical function; other non-specified serious joint injuries; lacerations requiring sutures. The definition of moderate fall-related injuries was adapted from the one used by Campbell and Robertson (A J Campbell et al. 1997a): “if the fall resulted in bruising, sprains, cuts, abrasions, or reduction in physical function for at least 3 days, or if the participant sought medical help”. The ‘fall survey’ was designed to facilitate the subsequent classification of falls and limit confusion with clear simple binary questions listing different symptoms and injuries. When there was a doubt as to whether the fall should be classified as moderate or serious, the case was reviewed between researchers, also blinded to group allocation, and the decision was reached by consensus.

Data management

Completed fall surveys were digitised by an independent data entry company. Separately, the investigator who called the woman registered the event on the study's data management software. This password-protected software was specially developed by the URC (Unité de Recherche Clinique Paris-Ouest, developers: O. Thierry and A. Cindy) for the Ossebo study and could only be accessed through the servers of the CESP in Villejuif.

At the end of the follow-up, records from the digitised fall surveys were compared and verified with exported registers from the study software using the SAS software to ensure that all falls were included in the analysis and validate the records used for analysis.

Sample size calculation

Initially, the objective was to examine the effect of exercise intervention on the risk of having a severe injurious falls, and the plan was to recruit 1000 women per group. However, about 8 months after the beginning of the recruitment process, recruitment targets were revised because of delay in the implementation of the recruitment process in some centres and because fewer women than expected met the inclusion criteria and accepted to participate. Therefore the main outcome was expanded into the rate of all injurious falls, that is, those resulting in severe as well as moderate injuries, and the sample size was recalculated accordingly. This change was approved by the institutional review board of the study sponsor (Direction de la Recherche Clinique – Assistance Publique – Hôpitaux de Paris). Seven-hundred women in each group followed for 2 years were therefore needed to be able to show a 25% reduction in all injurious falls (hypotheses: 30 injurious falls per 100 women-years; $\alpha=0.05$; $\beta=0.80$; dropout rate=15%).

3.1.3. Participants and follow-up

Figure 13 describes the recruitment process. Around 11% of the women who received the invitation to a free balance examination responded positively. Among the 4221 women examined in the 20 centres, around one third (N=1137) met the eligibility criteria, and almost two thirds of those eligible (N=706) agreed to participate and were randomised to either the intervention (352) or the control group (354). The mean age of the participants at recruitment was 79.7 (SD=2.8), and about 40% had fallen at least once in the year before the study (Table 5). Most of the participants (68%) lived alone, about 41% of them used psychotropic medication, and notably, 40% of them had a high school diploma ('Bac'). The two comparison groups were comparable in terms of socio-demographic, health-related characteristics and major risk factors for falling at baseline (Table 5).

Table 5: Characteristics of the two randomised group at baseline

	Control N=354	Intervention N=352
	Mean(SD) or Percentage (n)	
Age, in years	79.6 (2.8)	79.8 (2.8)
BMI (kg/m ²)	27.0 (4.6)	27.1 (4.6)
Fell at least once in the last year	159 (44.9%)	137 (38.9%)
Used psychotropic medication	140 (39.5%)	149 (42.3%)
Lived alone	230 (65.3%)	248 (70.7%)
Finished high school (Bac)	131 (38.0%)	151 (43.8%)
Visual acuity ^a	6.9 (2.2)	6.9 (2.1)
‘Timed Get Up and Go’ (s)	12.4 (3.1)	12.4 (2.7)
Time to walk 6 m (s)	7.5 (1.7)	7.4 (1.7)
Unable to do 4 tandem steps	83 (23.5%)	79 (22.4%)
Time for the five chair stands (s)	15.5 (4.6)	15.5 (4.4)
Time spent walking for casual activities ^b (h/week)	3.1 (2.4)	2.8 (2.3)
Time spent walking for exercise (h/week)	2.1 (2.8)	1.9 (2.9)
Time spent doing physical leisure activities (h/week) ^c	2.4 (2.9)	2.3 (3.2)
Time spent sitting down (h/day)	4.4(1.4)	4.3(1.4)
Fear of falling score ^d	26.0 (7.0)	25.5 (7.1)
Physical functioning score ^e	57.5 (20.7)	59.4 (21.6)
General health score ^e	54.7 (16.0)	57.0 (15.8)
Psychological health score ^e	60.7 (18.2)	61.3 (18.1)
Vitality score ^e	46.6 (16.1)	48.44 (16.3)

^a visual acuity was measured at a distance of 5 m with a Snellen letter test chart (decimal scale).

^b Activities such as walking to general practitioner, pharmacy or store

^c Activities such as walking, swimming, dancing, gym classes, gardening, biking, and yoga

^d based on the fall efficacy scale (FES-I)

^e based on the SF-36 Short-Form questionnaire.

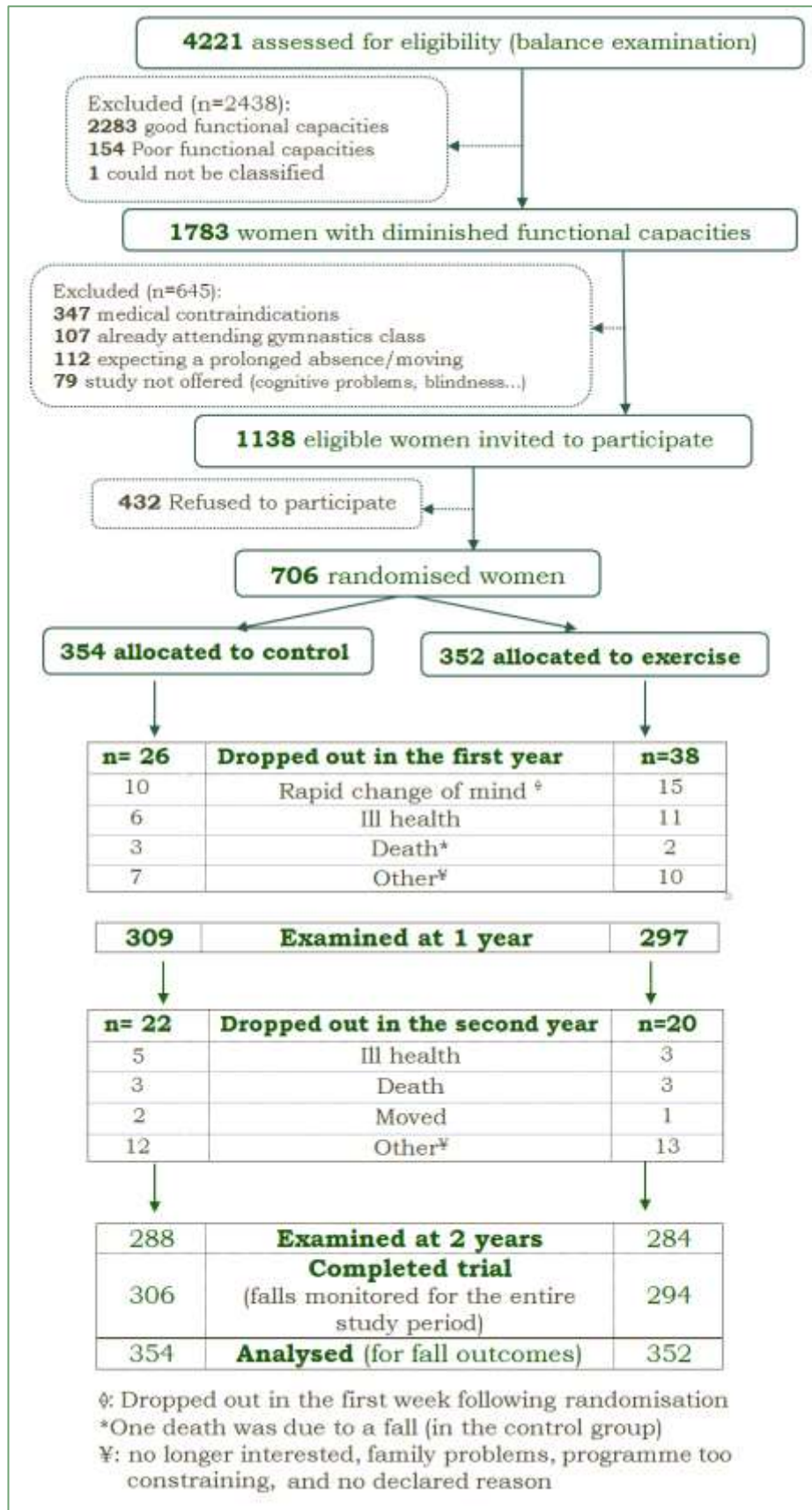


Figure 13: Participants flow

3.1.3.a. Follow-up

There were a total of 55 lost to follow-up in the intervention group during the study period compared to 42 in the control group. In both groups, the number of dropouts was larger during the first year than during the second year. In the intervention group, 65% of dropouts occurred in the first year of the study, with 15 women dropping out immediately after randomisation.

Eleven participants died during the study, 6 of them in the control group. Only 3 of the 11 women fell in the 3 months before their deaths, 2 of those falls did not result in any consequences, and the death in those cases was not due to falls. The third fall resulted in a serious injury leading to the death of the woman (in the control group).

Falls were monitored for the entire study period for 306 women in the control group and 294 women in the intervention group.

There was information available from 609 (Intervention group: n=299) women for the first follow-up examination, and from 573 (I=284) participants for the examination at the end of the study (figure 13). For the first examination at 1 year after inclusion, 602 (I=297) women undertook the physical examination and completed the auto-questionnaire. Five women (I=1) completed the physical examination but did not return the questionnaire, while 2 women (I=1) only returned the auto-questionnaire. For the second examination at the end of the trial, data from the physical examination and auto-questionnaire was available for 570 (I=283) participants, while the other 3 women (I=2) only returned the auto-questionnaire.

Table 6 presents reasons for drop out in the two groups.

Table 6: Reasons for drop out in the two groups

Reasons	Control	Intervention	Total
No longer interested	14	18	32
Rapid change of mind	10	15	25
Ill health	11	14	25
Death	6	5	11
family problems	1	3	4
No declared reason	3	1	4
Moved	2	1	3
Programme too constraining	1	1	2
Total	48	58	106

3.1.4. Intervention implementation

On average, participants were offered 94.9 (SD=11.6) exercise sessions over the entire intervention period. A total of 26 instructors participated in administering the intervention in the 20 centres. There were 1 to 3 groups of exercise by centre.

As intended, the intervention took place in a community-based location such as municipal, animation and associative settings in 12 centres. However, in other centres the exercise took place in hospital settings (5 centres: Boulogne-Bilancourt, Paris 05, Paris 16, Saint Etienne, and Villejuif), or in homes for older adults (3 centres: Issy-les-Moulineaux, Paris 20, and Montpellier).

The exercise programme's implementation was largely performed according to the protocol, except in 3 centres that did not complete the 8th term.

3.1.5. Adherence to the intervention

Fifty-eight (16.5%) women randomised in the intervention group never started the programme, including 15 who dropped out completely from the study while the others accepted to have their falls monitored (mean time of follow-up: 658 days (SD=225)). Among women who started the programme, 38 women (11%) attended less than 5 sessions. For these women who started the intervention, the median number of attended sessions is 53 (Q1 – Q3: 16 - 71); the median length of participation into the programme is equal to 78.5 weeks (Q1 –

Q3: 31 - 97). Overall 259 women reported doing home exercises with an average of 52 (SD=32) declared home sessions. Among women who started the intervention, around 60% (205) stayed in the intervention until the start of the second year, and 125 (42.5%) stayed beyond the 18th month of intervention. Figure 14 presents the average number of offered group sessions as well as the average number of attended sessions per centre. Figure 15 presents the number of participants in the exercise group who definitely stopped going to the exercise sessions over time.

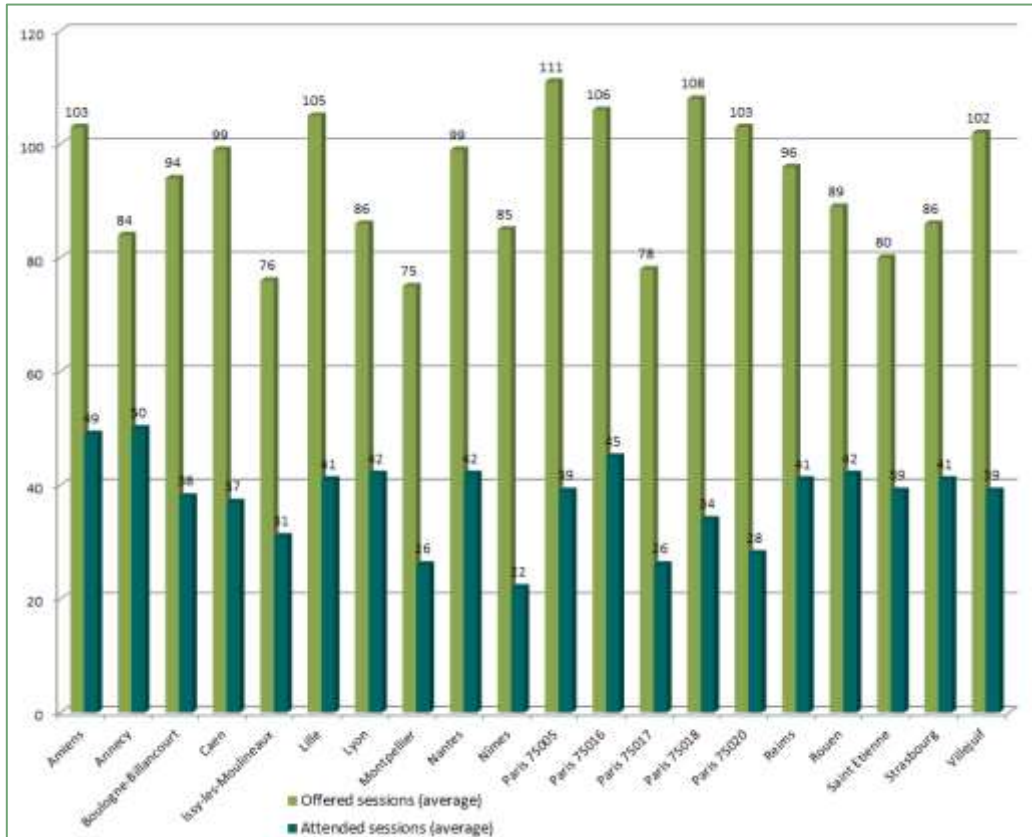


Figure 14: Mean number of offered and attended group sessions

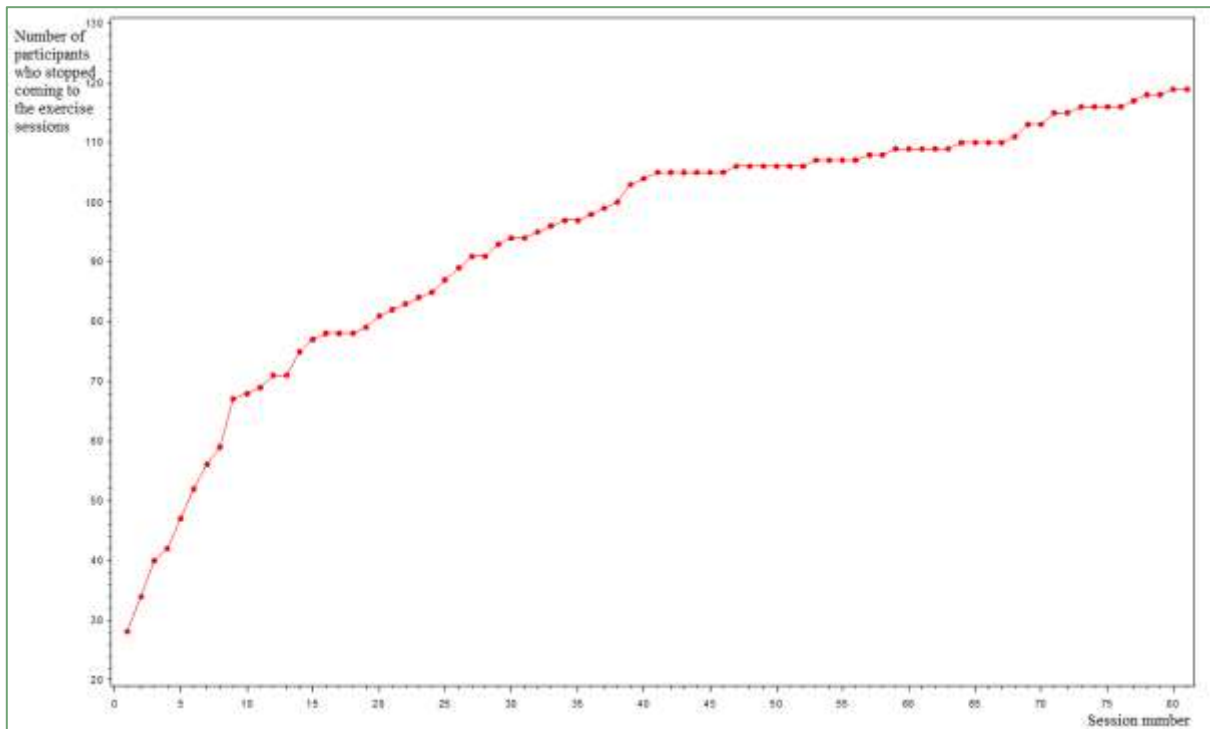


Figure 15: Number of participants who withdrew from the exercise session

3.2. Effectiveness of the Ossebo exercise programme on fall-related injuries prevention

This section will present the main results of the ‘Ossébo’ trial, concerning the effectiveness of the intervention on the reduction of falls and fall-related injuries.

3.2.1. Methods

3.2.1.a. Outcomes

The primary outcome was the rate of all injurious falls (moderate and severe) as detailed above. The effect of the intervention on the most serious of those falls as well as on total falls (whether or not they had any consequence) were also examined.

3.2.1.b. Analysis

Outcome definition

Falls due to traffic accidents or specific medical conditions (stroke, cardiac problem) were excluded from the analysis. Women who dropped out within the first month after randomisation (no calendar card) were censored with a follow up =1 day. For participants not lost to follow-up, follow-up was censored the day of the last intervention class in each centre, because after that date women in the control group were offered intervention classes.

Statistical analysis

Data were analysed according to the intention-to-treat principle. Falls, and injurious falls are recurrent events that may occur more than once over the follow-up time for a given participant. Thus methods used to model these events should account for the dependence between falls occurring in the same individual.

Many modelling approaches has been suggested in order to analyse recurrent events data (M Clare Robertson, Campbell, and Herbison 2005; Kuramoto, Sobolev, and Donaldson 2008), with the negative binomial regression being the most commonly used model in published data on falls analysis.

For the analysis of the effectiveness of the Ossébo trial, 2 recommended statistical approaches were employed: the shared frailty model and the mean cumulative functions. In a

complementary analysis, I also analysed data with the negative binomial regression, in order to compare our results with published results. These models allow the use of all available data (events) and not just the first event, until the end of follow-up or drop out.

Mean cumulative function

The MCF was first introduced in 1995 (W. Nelson 1995, 199), as a method to model censored recurrence data, it is mainly used on product repairs analysis or ‘reliability’ analysis. But it can also be applied in other fields, notably epidemiology, since it allows the computation of the average number of events occurring in one individual within a certain time period in a population exposed to censoring events such as loss to follow-up or non-occurrence of outcome event (assuming that the time to events is independent from the time of censoring) (W. B. Nelson 2003).

If we apply this method to a cohort with recurrent events, every participant in the cohort would have a cumulative function representing the number of recurrences up to time t ; a staircase function that tracks the accumulated number of events (thus has unequal step rises). The MCF would therefore represent the mean curve of all staircase functions at a time t (figure16).

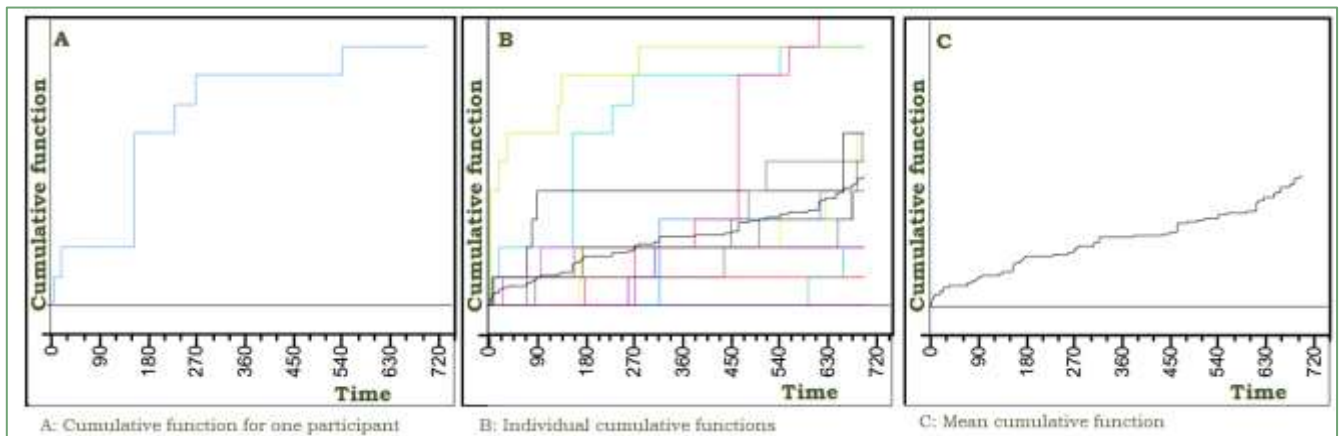


Figure 16: Mean cumulative function MCF (t): an average of the cumulative number of recurrences of events for each individual at a time t

This method has been recently recommended as a useful tool in the analysis of fall events, especially in fall prevention trials as it can illustrate the average number of falls per individual that the intervention has prevented at a certain time by computing the difference in MCF curves between the intervention and control group, therefore it can detect differences between

groups that had varying intensities of subsequent fall outcomes over time (Donaldson et al. 2007).

To examine the effectiveness of the Ossébo intervention, we started by graphically comparing the intensity of events between the two groups by a mean cumulative function, $MCF(t)$; plotting the population mean of the cumulative number of events (falls or injurious falls) per woman that occurred up to time t (Donaldson et al. 2007). The difference between the 2 MCFs corresponds to the mean number of preventable events by participant. A log-rank type test of equality of the rate functions was used to test the equality of the 2 MCFs, assuming the weight functions are constant through time (events that occur at different times has the same weight) (Joseph C. Gardiner 2014). This analysis was done for every fall outcomes: injurious falls, all falls, and severe injurious falls using the ‘reliability’ procedure in SAS (Gutierrez, n.d.).

Frailty model

The notion of ‘frailty’

It is worth noting that in geriatrics the term ‘frailty’ is commonly used, independently of an statistical connotation, it indicates an age-associated biological syndrome, a certain phenotype of older adults with ‘excess vulnerability’ (Walston et al. 2006).

Whereas, the term ‘frailty model’ was introduced by Vaupel et al. in 1979 (Vaupel, Manton, and Stallard 1979). They noted that demographic life tables published at the time ignored how some individuals are more at risk of dying than others. These “frail” persons tended to die at earlier ages than their more robust peers. Therefore, estimates of population-level hazards of dying would underestimate individual-level hazards for frailer individuals. Population mortality rates might be over-estimated for certain age groups, because the frail individuals die earlier. To account for this heterogeneity in the risk of dying, Vaupel et al. suggested the introduction of a ‘frailty factor’ in modelling hazards and survival. The frailty factor modifies the hazard multiplicatively. For example, an individual with a frailty equalling 2, has twice the hazard as the “standard” individual with frailty equalling 1. Likewise, an individual with a frailty of $\frac{1}{2}$ has one-half the hazard of the standard person. It adjusts for unobserved covariates that operate on the individual (for example nutrition) or unobservable factors of the individual (for example hereditary factors). Later on, several authors cited the work of Vaupel et al. and used the term ‘frailty’ to extend survival model accounting for heterogeneity in term of

susceptibility to death or other diseases between individuals (Dobson 1988; Oakes 1989; Aalen 1988).

Model definition

Frailty models are time-to-event, or survival models with a random effect. They are an extension of the Cox proportional hazards model that introduces a ‘frailty term’, an unobserved random effect, which defines how likely a subject is to experience the event compared to the average rate (Duchateau and Janssen 2007). Therefore, frailty is an unobserved random proportionality factor that modifies the hazard function of an individual and thus can account for correlation between events and heterogeneity between individuals.

In fall prevention trials, included participants might be at different risk of falling and having injurious falls at baseline, even after controlling for known risk factors, because of unobserved covariates. The frailty parameter models these unknown covariates. In a frailty model, events from the same participant share the same frailty value which generates dependence between those events, thus accounting for heterogeneity of the risk of falling between different participants.

Formula

In a Cox proportional hazards model, the hazard function for the i th individual is:

$$\lambda_i(t) = \lambda(t; \mathbf{Z}_i) = \lambda_0(t) \exp(\mathbf{Z}_i' \boldsymbol{\beta})$$

where $\lambda_0(t)$ is an unspecified baseline hazard function, \mathbf{Z}_i is the vector of explanatory variables for the i th individual, and $\boldsymbol{\beta}$ is the vector of unknown regression parameters associated with the explanatory variables. $\boldsymbol{\beta}$ is assumed to be the same for all individuals.

In a frailty model, all events (j) of the same individual (i) are clustered together in order to model correlation between these events, the hazard rate for the j th event of the i th individual is:

$$\lambda_{ij}(t) = \lambda_0(t) e^{\boldsymbol{\beta}' \mathbf{Z}_{ij}(t) + \gamma_i}$$

\mathbf{Z}_{ij} is the vector of (fixed-effect) covariates, $\boldsymbol{\beta}$ is the vector of regression coefficients, and γ_i is the random effect for participant i . Frailties ($e^{\gamma_1} \dots e^{\gamma_n}$) are the exponential transformations of the random components ($\gamma_1, \dots, \gamma_n$), and the frailty model can be written as:

$$\lambda_{ij}(t) = \lambda_0(t) e^{\gamma_i} e^{\boldsymbol{\beta}' \mathbf{Z}_{ij}(t)}$$

Application to fall outcomes analysis

In the Ossébo intervention analysis, the event hazard rates in the two groups over the entire study period were modelled and compared with the frailty model, via the SAS procedure ‘phreg’ while introducing participant unique identification in the ‘random’ statement (Amrhein 2014). The ‘random’ statement of the ‘phreg’ procedure adds a normally distributed random effect for participants, therefore fall outcomes from the same participant are no longer uncorrelated but instead they have a covariance that depends on the variance of the random effect. A larger variance implies greater heterogeneity in frailty across participants and a greater correlation between events of the same participants.

The corresponding data are organised as one record per subject per event. The table included a variable for the recurrence status, the value for this variable was ‘1’ for events, and ‘0’ for censure (lost to follow-up, death or end of the study). Other variables included indicators for interval start time and interval stop times (‘tstart’ and ‘tstop’), group, centre, and other variables used for adjustment.

For every pre-defined category of injurious falls, a hazard rate ratio (hazard rate in the intervention / hazard rate in the control group) and 95% confidence interval was therefore computed. All analyses were adjusted for centre. In complementary analyses, the estimated hazard rate ratios were further adjusted for baseline risk factors for falls and injuries: age, BMI, use of psychotropic medications (Y/N), falls during the previous year (Y/N), visual acuity, and time for the “get-up-and-go” test.

Negative binomial regression

Negative binomial regression is a generalisation of Poisson regression (modelling count outcome variables), with an added multiplicative random effect to represent unobserved heterogeneity (overdispersion) and allow variation of the event rate among subjects (Cook and Lawless 2002). Like the Poisson models, negative binomial assume that the recurrent events are occurring independently of each other. However, it also assumes that events rates are constant over time, a major limitation of this model, and the reason why the frailty model was chosen over it.

The SAS procedure ‘genmod’ was used to model and compare the rate of fall outcomes between the two groups (incidence rate ratio), with negative binomial regressions. The corresponding data files had one record per participant.

3.2.1.c. Sensitivity analysis

To assess the potential impact of attrition (incomplete outcome data due to attrition) on the intervention effect estimates, we performed a sensitivity analysis using a worst case scenario based on the method proposed in the Cochrane review of interventions to prevent falls (Gillespie et al. 2012). At first the ratio of two rate ratios of falls were computed: the first one (RaR1) is calculated by dividing the rate of injurious falls in the intervention group by the rate of injurious falls in the control group, using all available data. These rates were not computed with a statistical model but by dividing the total number of injurious falls by the number of person-years in each group (to use the same computation method as for the second rate ratio). The second ratio (RaR2) is calculated for all participants by using the conservative assumption that participants with missing data in the intervention group had the same rate of falls as observed in the control group (during their “lost” follow-up time), and vice versa. Then the two rate ratios were compared. A ratio of these rate ratios (RaR2/RaR1) greater than 1.15 or less than 0.85 usually indicates the possibility of clinically important bias.

3.2.2. Results

3.2.2.a. Number of falls and their consequences

Table 7 presents data on follow-up and incidence of fall outcomes in both groups. There were 640 falls in the control group, and 533 falls in the intervention group. More than half of fallers (59%) fell more than once during the follow-up. Concerning fall-induced injuries, there were 397 injurious falls (by 189 women) in the control group versus 305 (170 women) in the intervention group. Of all injurious falls, 14% were fractures and 8% other serious injuries, while 78% had less severe consequences and were classified as moderate injurious falls (table 7). Table 8 presents the consequence of injurious falls in both groups.

Table 7: Incidence of fall outcomes in both groups

	Control	Exercise	Total
No. of participants	354	352	706
Total number of women-years of follow up	703.09	677.13	1380.22
No. of falls (rate ^a)	640 (0.92)	533 (0.79)	1173 (0.85)
No. of injurious falls (rate ^a):	397 (0.56)	305 (0.45)	702 (0.51)
Moderate injuries	310 (0.44)	237 (0.35)	547 (0.40)
Serious injuries	87 (0.12)	68 (0.10)	155 (0.11)
Fractures	56 (0.08)	49 (0.07)	105 (0.08)
No. of fallers	222	208	430
No. of women with at least one injurious falls	189	170	359
No. of women with at least two falls/two injurious falls	139 /95	115/70	254/165
No. of women with at least one serious injurious fall/two serious injurious falls	73/12	59/7	132/19

^a- Rate = total number of events (fall outcomes) divided by the total length of follow-up (women-years).

Table 8: Consequences of moderate and serious injurious falls

Consequences		Control	Exercise
Moderate (N=547)	Hematoma or wound	284	208
	Sprain	5	4
	Head trauma	19	18
	Falls with medical care ¹	56	58
	Falls with disability ² >48 h	73	50
Serious (N=155)	Fracture (major osteoporotic fractures ³)	56 (33)	49 (22)
	Lacerations requiring sutures	23	10
	Head trauma with hospitalisation	5	3
	Severe sprain ⁴	7	11
	Joint dislocation	5	4
	Other serious injuries ⁵	18	7

¹Rate = total number of events (fall-related outcomes) divided by the total number of women-years of follow up within a given group.

¹: Falls resulting in a medical consultation, visit to the emergency room, or hospitalisation.

²: Reduction in physical function (difficulties in any of the following activities: moving indoor or outdoor, getting dressed, bathing, cooking, and shopping) for at least 3 days.

³: Neck, femoral, tibia, wrist, proximal humerus and vertebral fractures

⁴: Sprains that were confirmed by medical records or accompanied with disability for >48 h

⁵: Tendon rupture (shoulder, fingers), hemarthrosis, knee hyarthrosis, rhabdomyolysis, articular hematoma.

3.2.2.b. Estimated effects of the intervention

Injurious falls

Result from the frailty model

Over the 2-year intervention period, the injurious fall hazard rate was 19% lower in the intervention group than in the control group. Similar hazard ratios were obtained after adjustment for centre (HR=0.81 [0.67–0.99], p=0.02), as well as other covariates (HR=0.82 [0.70–0.96], p=0.01). The covariance of the random effect in the unadjusted model was 0.53 (SE=0.09), the coefficient for participant was significant (type III test) [p<0.0001], indicating inter-individual correlation. After adjusting for other variables this variance decreased (0.01 (SE=0.05)), as well as the association between participants and the rate of injurious falls (p=0.29).

Results from the MCFs

The MCF curves of injurious falls for the two groups are presented in figure 17, and the difference between the MCFs of the two groups, or the average number of prevented injurious falls, is presented in figure 18. The two curves began to separate between 3 and 4 months. The average number of prevented injurious falls (difference between the two MCFs) increases steadily until approximately 9 months (day 300, MCFs difference = 0.19 (0.06 to 0.31), and then tends to plateau or increase more slowly over time. By the end of the intervention, the average number of prevented injurious falls per participant was about 0.25 (95% CI: 0.03-0.47). The test of equality of the rate functions indicated that the two groups are statistically different ($p=0.02$).

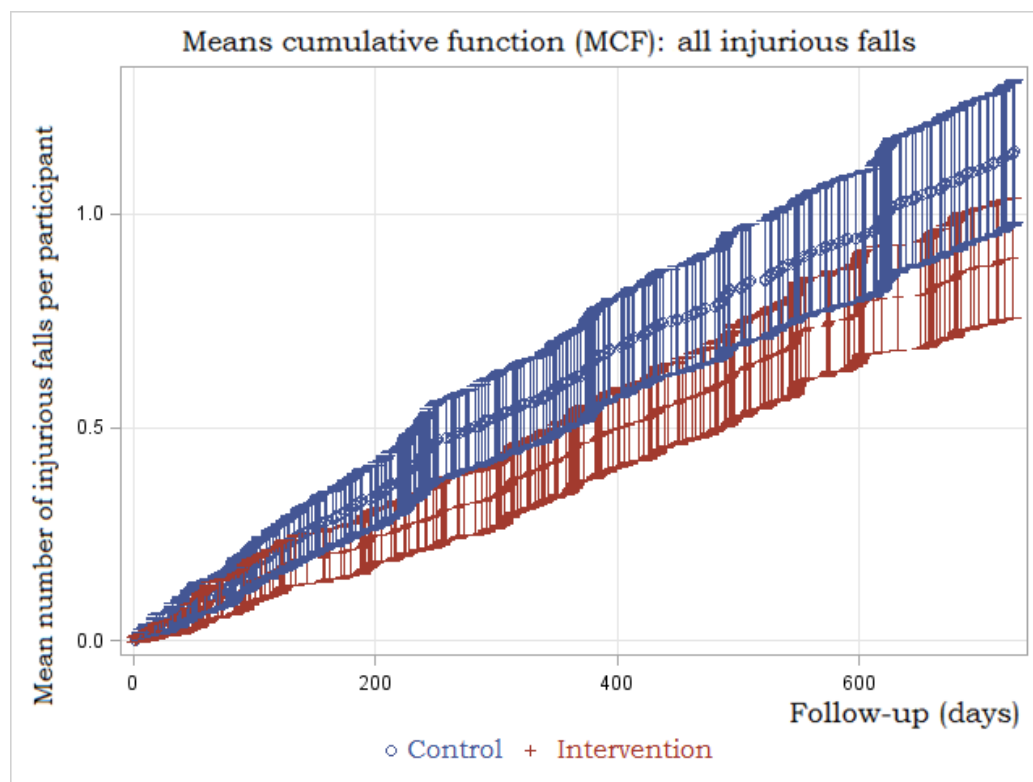


Figure 17: MCF- all injurious falls

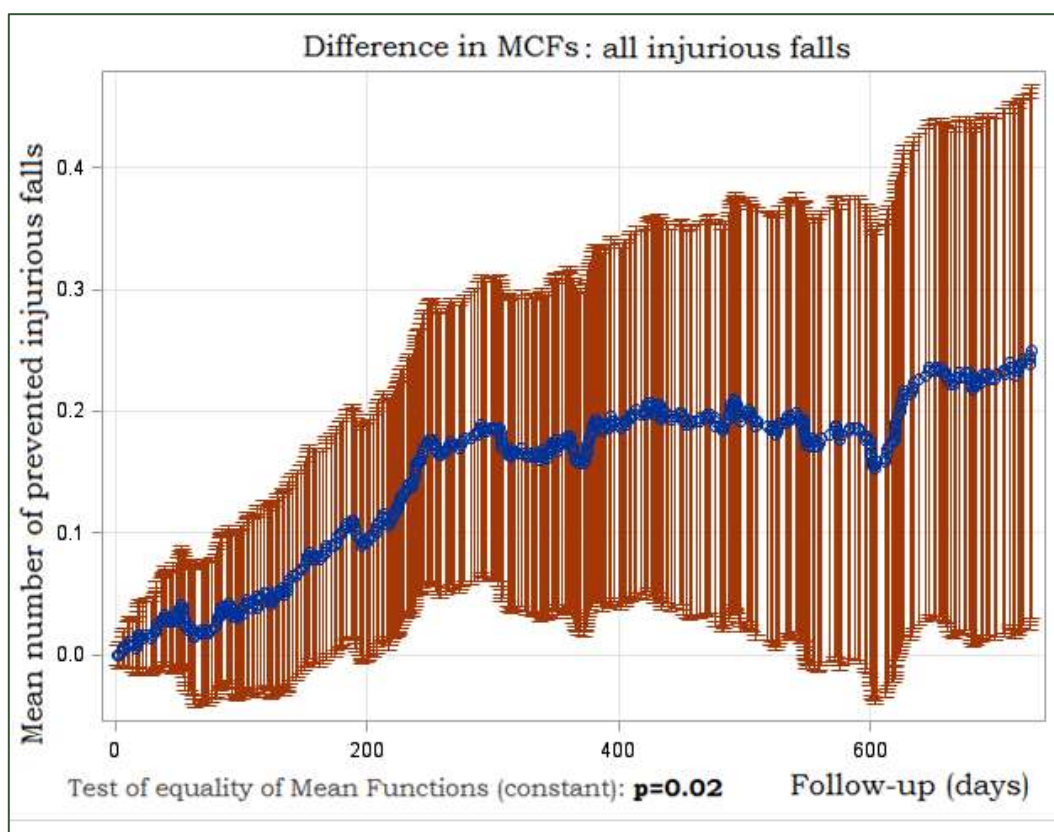


Figure 18: Difference in MCFs between the 2 groups- all injurious falls

Result from the negative binomial regression

Results from the negative binomial model were comparable with those from the frailty model. They indicate that women in the exercise group fell at a rate 20% lower than the women in the control group. The computed incidence rate ratio (IRR) was 0.80 (95% CI: 0.64 to 0.98, $p=0.035$). Adjusting for centre (IRR=0.80 [0.66 to 0.98, $p=0.032$]) and risk factors for falls didn't change the effect (IRRa=0.81 [0.67 to 0.99, $p=0.035$]).

Serious injurious falls

Result from the frailty model

As computed from a shared frailty model, the hazard rate ratio was 0.83 [0.60 to 0.99], $p=0.16$). Comparable hazard ratios were obtained after adjustment for centre (HR=0.84 [0.60 to 1.17], $p=0.29$) and other covariates (HR=0.85 [0.61 to 1.18], $p=0.32$). The random effect covariance estimate in the unadjusted model was 0.33 (SE=0.25), indicating some correlation between events of the same individual, however the random term was not significant (type 3 tests $p=0.30$).

Results from the MCFs

Figure 19 presents the MCF curves for serious injurious falls, while figure 20 presents the difference between these MCFs between the two groups (the average number of prevented serious injurious falls). Because severe injurious falls are considerably less frequent than other analysed fall outcomes, their MCF curves are more difficult to interpret. However they show the same pattern as the other events, with the average number of prevented severe injurious falls increasing until it seems to stabilise. Notably, at day 55 that number equalled 0.015 (0.002 to 0.027), increased to reach 0.07 (0.014 to 0.04) at day 301 and at the end of the intervention it was 0.20 (0.027 to 0.26)). The difference between the rate function between the two groups was not significant ($p=0.23$) probably because of a lack of power.

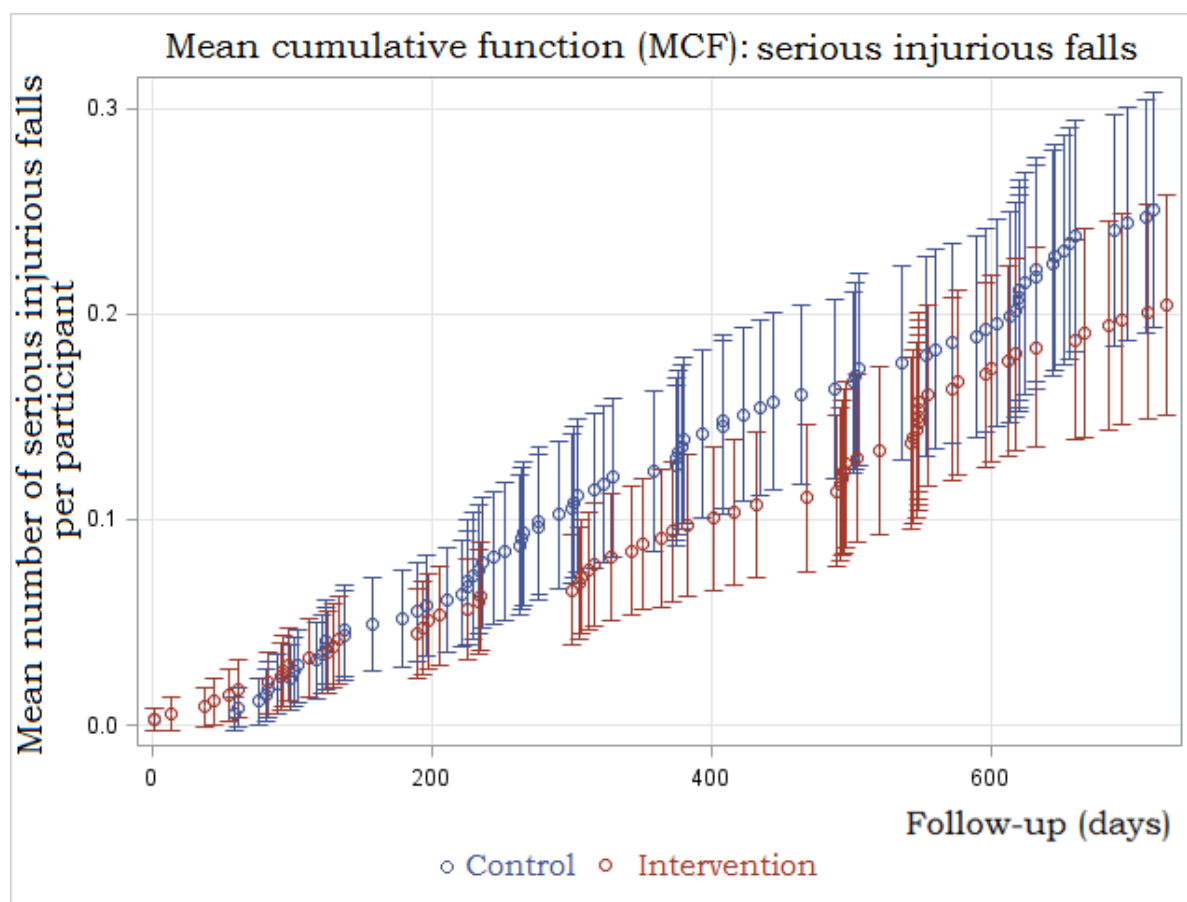


Figure 19: MCF- serious injurious falls

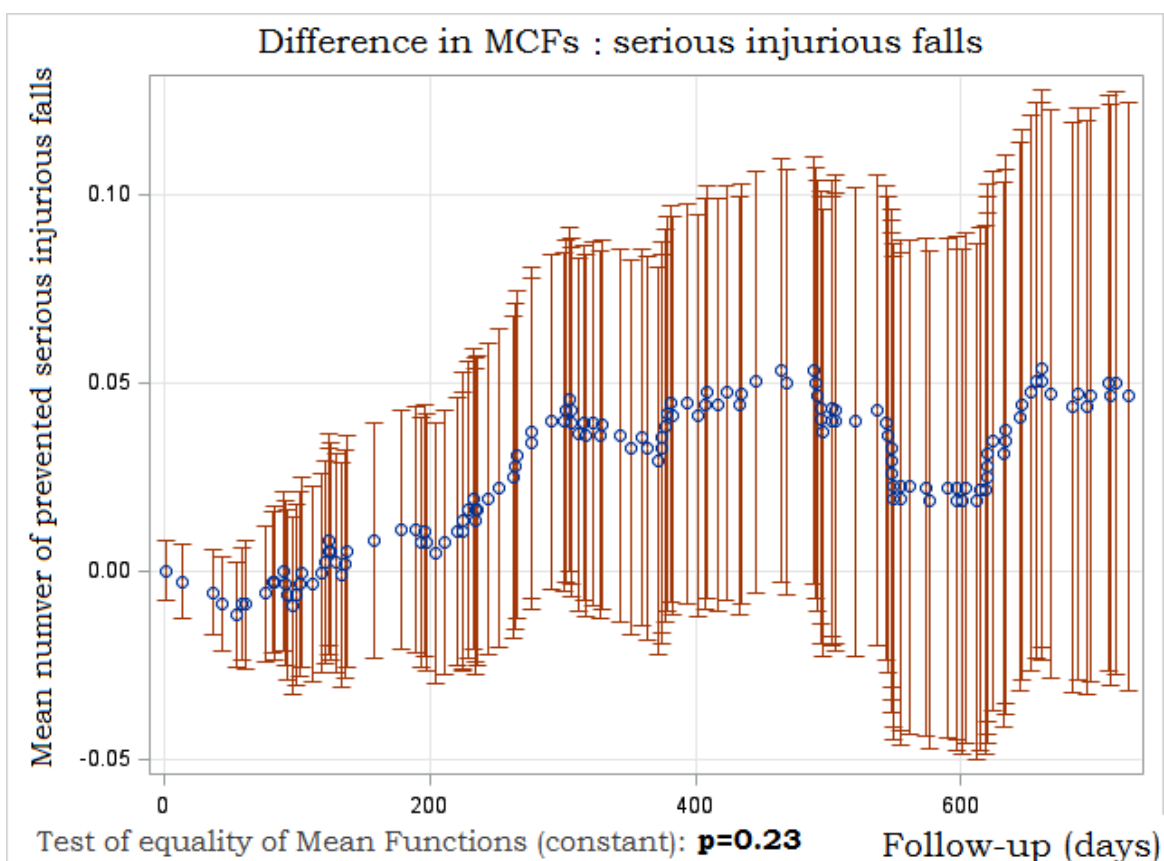


Figure 20: Difference in MCFS between the 2 groups- serious injurious falls

Result from the negative binomial regression

The incidence rate ratio (IRR) of serious injurious falls computed from a negative binomial regression was 0.81 (0.58 to 1.14, $p=0.22$). The percentage of the reduction (19%) is comparable to that of injurious falls however unlike the later, it is not significant.

All falls

Result from the frailty model

Over the 2-year intervention period, the hazard rate of all falls was 12% lower in the intervention group than in the control group ($HR=0.88$ [0.77 to 0.99], $p=0.33$) as computed by a shared frailty model. Comparable hazard ratios were obtained after adjustment for centre ($HR=0.88$ [0.77 to 1.00], $p=0.38$) and other adjustment variables ($HR=0.87$ [0.77 to 0.98], $p=0.017$). The random effect covariance estimate in the unadjusted model was 0.17 ($SE=0.04$), the coefficient for participant was significant (type III test) [$p<0.0001$], indicating inter-individual correlation. After adjusting for other variables this correlation decreased

Results

(0.005 (0.03)), but the association between participants and the rate of all falls remained significant ($p=0.03$).

Results from the MCFs

The MCF curves of all falls for the two groups are presented in figure 21, and the difference between the MCFs of the two groups (the average number of prevented falls), is presented in figure 22. The MCF curves for all falls had the same pattern as for injurious falls, with the two groups beginning to separate between 3 and 4 months; the MCFs difference at day 90 after the start of the intervention had a value of 0.02 (95% CI: -0.08 to 0.12), whereas on day 120 the difference was 0.05 (95% CI: -0.07 to 0.17). This difference, albeit not significant, increased until approximately the 9th month after the start of the study where it stabilised: day 270, MCF-difference= 0.18 (-0.01 to 0.37). By the end of the intervention, the average number of prevented falls per participant was 0.30 (95% CI: -0.07 to 0.67). The rate functions of the two groups were not significantly different ($p=0.11$).

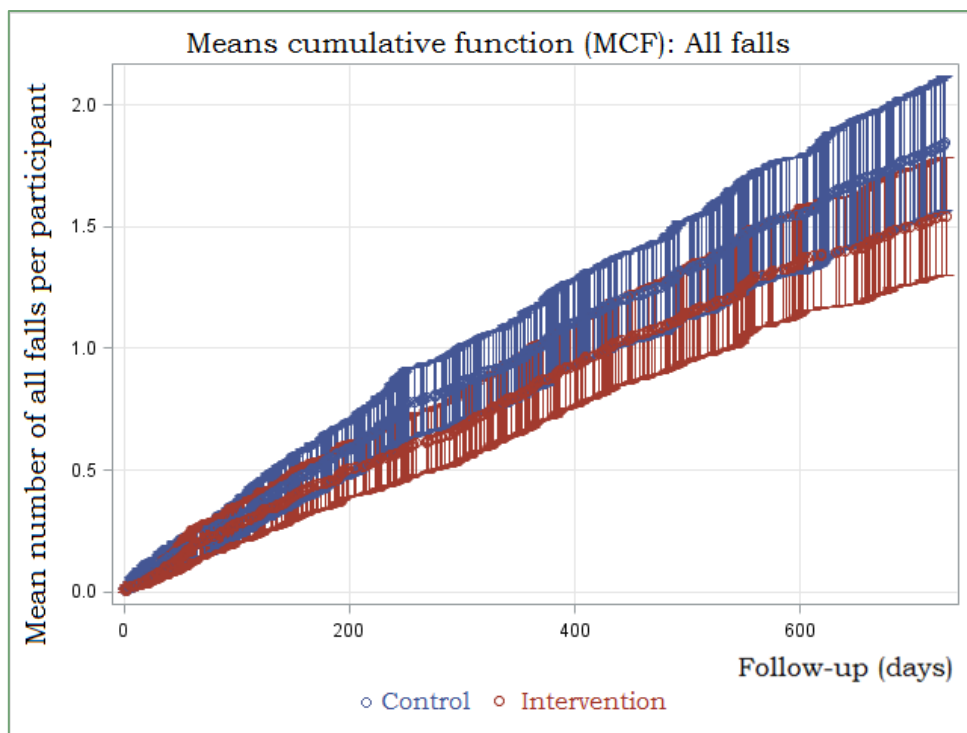


Figure 21: MCF- all falls

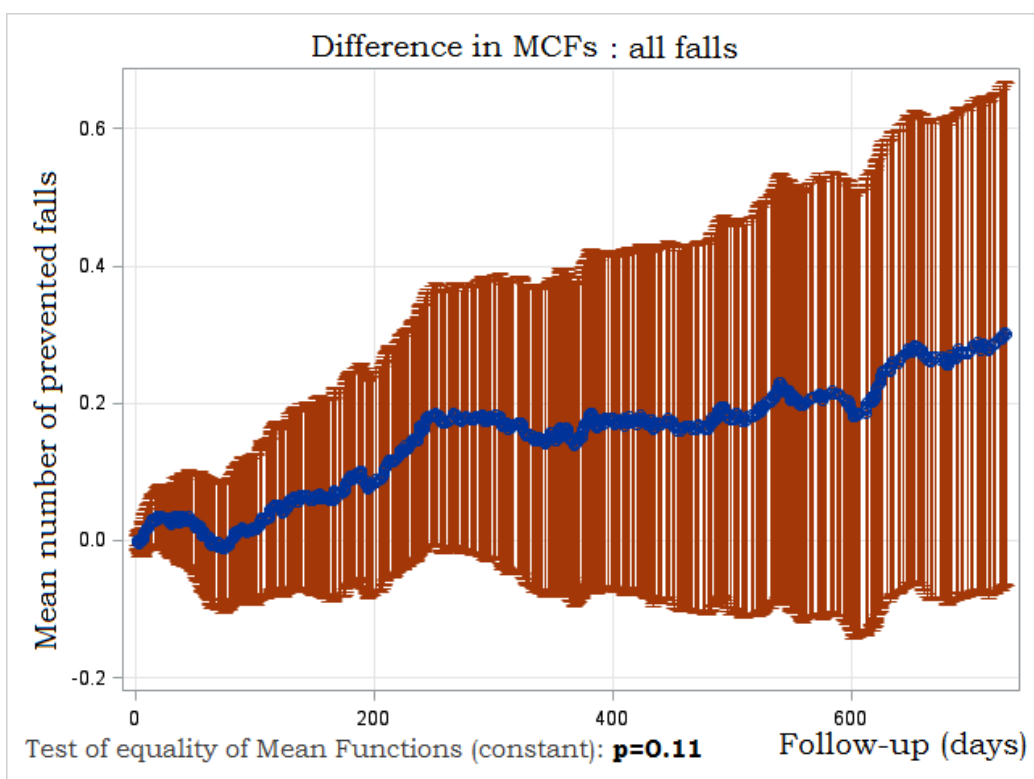


Figure 22: Difference in MCFs between the 2 groups- all falls

Result from the negative binomial regression

The incidence rate ratio (IRR) computed from a negative binomial regression was 0.89 (95% CI: 0.71 – 1.11 , $p=0.29$). Adjusting for centre (IRR=0.89 [0.72 to 1.10, $p=0.27$]) and risk factors for falls (IRRa=0.91 [0.75 to 1.11, $p=0.35$]) gave analogous results.

Table 9: Results from shared frailty models for the three fall outcomes

Fall outcome	Non adjusted		Adjusted for centre	
	HR (95%CI)	Random effect: covariance (SE), p value	HR (95%CI)	Random effect: covariance (SE), p value
Injurious falls	0.81 (0.67 to 0.99)	0.53 (0.09)- [$p<0.0001$]	0.81 (0.67 to 0.99)	0.54 (0.08)- [$p<0.0001$]
All falls	0.88 (0.77 to 0.99)	0.17 (0.04)- [$p<0.0001$]	0.88 (0.77 to 1.00)	0.17 (0.04)- [$p<0.0001$]
Severe injurious falls	0.83 (0.60 to 1.16)	0.33 (0.25)- [$p=0.30$]	0.84 (0.60 to 1.17)	0.34 (0.24)- [$p=0.30$]

Sensitivity analysis

In the sample, RaR1 (rate ratios of falls computed without missing data) for injurious falls is equal to 0.80 (0.44/0.56). There were a total of 58 dropouts in the intervention group and 48 in the control group, these accounted for 84.6 and 59.33 ‘lost’ person-years, respectively. After applying the rate of falls of the other group to these lost person-years, the new RaR2 equals =0.84 (table 10).

Thus, the ratio $RaR1/RaR2 = 0.80/0.84 = 0.96$. Which, according to the Cochrane judgment rules, indicates that the potential for bias related to missing data on falls due to attrition may be considered limited.

Table 10: Calculation sheet for the attrition bias sensitivity analysis.

	Intervention	Control
Number of injurious falls (sample)	305	397
Person year (sample)	686.5	711.93
Rate Ratio 1 (sample)	0.44	0.56
Mean time of follow up for (sample)(years)	2.194	2.196
Lost to Follow up (n of LFU)	58	48
Actual follow-up time for the LFU (years)	41.39	40.98
Total lost time of follow-up* (years)	84.610	59.330
Number of added injurious falls ^Υ	47.18	26.36
Number of injurious falls (2) ^ϣ	352.18	423.36
New person-year (2) [†]	771.11	771.26
Rate Ratio 2	0.46	0.55
RAR1/RAR2	0.957	

*: Sum of individual ‘lost time of follow-up’= time between the date of drop-out until the end of the intervention

Υ: Total lost time of follow-up*rate of injurious falls (sample) in the other group

ϣ: Number of injurious falls (sample) + number of added injurious falls

†: Total lost time of follow-up + Person year (sample)

3.2.2.c. Adverse events

Four women fell during an exercise class, another fell on her way back home after class. These events resulted in 4 moderate and 1 serious (wrist fracture) injurious falls. Three of those women returned to the intervention after the incident (table 11). These falls were included in the analysis. Another woman twisted her ankle during an exercise session; another woman reported back pain after a session and consequently decided to drop out of the study. No other adverse events were reported.

Table 11: Adverse events reported in the trial

Participant	Type of the adverse event	Location	Type/ severity of the injury	Subsequent adherence to the intervention
1	fell on her forehead	the exercise group session	moderate injury (bump on the head)	returned to the intervention
2	fell on her left side	the exercise group session	moderate injury (swollen eye, bump on her head, cut on her face)	incident occurred 2 sessions before the end of the intervention
3	fall	waiting room, right before the exercise session	moderate injury (reduction in physical function)	abandoned after the incident
4	fall	the exercise group session	wrist fracture	returned to the intervention
5	fall	fell as she was leaving the exercise session	moderate injury	returned to the intervention the next week
6	tripped and twisted her ankle	the exercise group session	did not fall on the ground (trainer caught her)	incident occurred a couple of sessions before the end of the intervention
7	back pain	Not available	back pain	abandoned after the incident

3.2.3. Discussion

3.2.3.a. Principal findings

A 2-year pragmatic programme of balance retraining and muscle strengthening significantly reduced the rate of injurious falls by 19% in at-risk women aged 80 years on average. The reduction of the most serious of those falls, such as those leading to a fracture and hospitalisation, was of the same order of magnitude although not statistically significant. The intervention also reduced the rate of total falls albeit somewhat less than the rate of injurious falls. The effect of the intervention on fall outcomes prevention appear to begin between the 3rd and 4th month after the start of the intervention, increasing around the 9th month, then tended to plateau or increase in a slower rate over time (as shown by the MCF curves).

3.2.3.b. Interpretation

The programme's estimated effects on injurious falls (19% reduction), and falls (12% reduction) appear lower than the pooled average effects of exercise found in the meta-analysis described above (37% reduction in injurious falls). Multiple reasons could've contributed to the lower effectiveness of the Ossébo, including its length (2 years), its population of 'very old' older adults (>75 years), whereas most of the interventions included in the meta-analysis lasted less than a year (average: 9.4 months), and some included older adults older than 60 years. During the first year, the Ossébo's programme was designed to ensure a progressive increase in the level and intensity of training. During the second year, however, the programme evolved from essentially focusing on balance improvement and fall prevention to more general gymnastics and maintenance, although long-term fall prevention remained the primary objective of the intervention. The inflection of the difference between the MCF curves of the two comparison groups starting towards the end of the first year of intervention might suggest that the second part of the programme should be re-adjusted to continue reducing falls. There may be limits, however, to the extent to which balance and strength can be improved in older at-risk subgroups, and the inflection of the difference between the MCFs may reflect these limitations. In any case, the maintenance of a positive difference between the MCFs over time attests to the effectiveness of the programme in maintaining achieved progress.

Another possible explanation may be related to the larger size of the Ossébo trial and its multicentre character, with 20 different study centres. A recent meta-epidemiological study

found that single-centre RCTs showed larger treatment effects than did multicentre RCTs, even after controlling for their sample size (Dechartres et al. 2013). A possible explanation presented in that study is that intervention implementation process or participants' profile may be less homogeneous in multicentre studies than in single-centre studies. This is especially true in a pragmatic long-term trial like Ossébo where the intervention was delivered in real life conditions. For instance, there may have been longer breaks during the programme in some centres because the premises where classes were taking place was closed during the 2-month summer school vacations, or because of instructors' illness or pregnancy leaves that could not be replaced immediately, etc.

Incomplete participation in the exercise programme may also have contributed to the lower effect of the Ossébo programme compared to the pooled effect of exercise found in the meta-analysis. In particular, a rather large number of women randomised in the intervention group never started the exercise programme (16,4% of women in the intervention group), also 11% of women in that group attended only a few classes and then abandoned the programme during the first month. Even women who participated for more than a year in the intervention did not attend all the classes.

Similarly to the results of the meta-analysis, the benefit of the Ossébo programme seems larger for injurious falls than for all falls. There is evidence that multicomponent programmes, like Ossébo, can improve balance as well as reaction time, gait, muscle strength, coordination, and overall physical and cognitive functioning (Sherrington and Henschke 2012; Liu-Ambrose et al. 2012). It is therefore thought that exercise prevents injurious falls not only by improving balance and decreasing the risk of falling, but also by improving the speed and effectiveness of protective reflexes or the energy absorbing capacity of soft tissues, thereby diminishing the force of impact and hence the severity of the resulting trauma.

3.2.3.c. Limitations

Several limitations of this study must be acknowledged and are listed below.

There were missing (incomplete) data on falls for 105 (14.9%) participants who either died (n= 11) or withdrew from the study (n= 94) at various times during the 2-year study period.

In both groups, the number of dropouts was larger during the first year than during the second year (9% overall at 1 year, which is equivalent to the median 12-month attrition rate reported in other fall prevention exercise trials (Nyman and Victor 2012). This was especially true in the intervention group (38 versus 26 during the 1st year), with quite a few women rapidly

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changing their mind and withdrawing from the study within a few days following their inclusion. This may not be surprising since women had to decide if they wanted to participate at the end of the baseline examination, but a number of them may have realised later on the extent of needed commitment and engagement, moreover they did not chose the day, the location nor the time of the long-term weekly group sessions.

As noted in the Cochrane review (Gillespie et al. 2012), the reasons usually put forward for dropping out of studies are diverse (no more interested, no benefit for control participants, too constraining for exercise participants, family problems, too occupied, fatigue, illness unrelated to falls, etc.) and it is difficult to know how these combined (self-reported) reasons might affect the true rate of falls in each comparison group. Hence, we used the criteria used in the Cochrane review for assessing the potential impact that attrition would have on our estimate of the intervention effect on the rate of injurious falls (Gillespie et al. 2012). Sensitivity analysis using a worst-case scenario suggests that the risk of bias due to attrition may be considered limited.

Another limitation of this study is that it is underpowered to demonstrate an effect on the most serious injurious falls. This is partly due to the logistic complexity of setting up large multicentre studies, and to the difficulty of recruiting older people in RCTs and in engaging them in fall prevention programme, especially for the long-term. The original aim was to recruit 2000 women (1000 in each group), which would have allowed to demonstrate a 30% reduction in severe injurious falls in the intervention group with a statistical power of 80% (hypotheses: serious injuries rate = 8 per 100 person-years; 10% drop-outs; risk alpha=0.05). However, recruitment target has to be revised during the trial because of delay in the implementation of the recruitment process or the exercise programme in some centres and because of fewer eligible women than expected, problems that are commonly encountered in clinical trials (McDonald et al. 2006).

Another limitation was the absence of double blinding which could have influenced the reporting of falls among the 2 groups. However this is inevitable in these types of studies. Also, it is difficult to determine in what direction it could've biased the results. The Cochrane collaboration recommends that falls in fall prevention trials should be monitored and verified by a researcher blind to group allocation (Gillespie et al. 2012), which was the case for this study.

3.2.3.d. Strength

Ossébo is one of the few fall prevention trials large enough to be able to show a clinically significant effect of exercise on the less frequent injurious falls. It is also one of the few trials with a long-term intervention and follow-up.

Furthermore, a well-defined classification of injurious falls, determined before data collection, was used. Incident falls were classified by a blinded investigator, and a large proportion (73%) of the serious injuries was validated by obtaining radiographs or hospital records. The main outcome, injurious falls, is less likely to be biased because of under-reporting than is the outcome of total falls, since recalling and recognising a fall is linked to the severity of the consequences (Freiberger and de Vreede 2011).

Moreover, the trial had a pragmatic approach: the selection criteria were simple and can easily be used by general physicians as well as health or physical activity practitioners providing care for older people. Moreover, the intervention was implemented through a network of care-providers already largely present in the field, in many (unspecialised) centres throughout France, which should facilitate generalisation of the programme. The intervention took place in community-based settings such as municipality halls, as it is done in usual care.

Additionally, for the analysis of fall outcomes, which are recurrent events, two different recommended methods were employed (frailty and MCF). As well as the negative binomial (NB) regressions that were only used in this analysis to compare our results with other results, since NB are frequently used in the reporting of fall prevention trials (M Clare Robertson, Campbell, and Herbison 2005). Shared frailty models, unlike the more commonly used negative binomial regression, model time-to-events and don't assume that event rates are constant over time, therefore they are more appropriate to model recurrent events (Box-Steffensmeier and De Boef 2006). While mean cumulative functions allow for an easy interpretation of the average number of events expected in one participant at a certain time and are also useful in interpreting fall outcomes results (Donaldson et al. 2007).

3.2.3.e. Conclusion

It is feasible to put in place a large-scale, long-term exercise fall prevention programme for very old at-risk adults, with the programme being safe and effective in reducing costly injurious falls. However, for the Ossébo programme to have optimum effectiveness and a larger public health impact there is a need to find strategies to increase participation and improve long-term adherence. Also, it is important to see whether the intervention has an impact on physical function as well as other health-related and psychological measures such as fear of falling and the perceived health-related quality of life.

3.3. The effect of the Ossébo exercise programme on physical and psycho-social fall- and health-related factors

The aim of the ensuing analysis is to evaluate the impact of the ‘Ossébo’ exercise programme on physical functions, as assessed by clinical tests, and on psychological factors and health-related quality of life indicators.

3.3.1. Methods

3.3.1.a. Outcomes

The outcomes used in this analysis were measured at the baseline, and follow-up examinations described above. They include functional tests of balance and motor function (‘Timed Get Up and Go’, 6 m walking test, 5 chair stands test, static balance tests...), physical activity and sedentarity indicators, fear of falling score, and indicators of health-related quality of life (SF36: physical function, mental health, general health and vitality).

3.3.1.b. Analysis

Data were analysed according to the intention-to-treat principle. To model the results of the tandem walk test, a dichotomous outcome, the generalised estimating equation (GEE) model was applied. This model is commonly used for repeated categorical response, where the within-subject observations are likely to be correlated, whereas between-subject measurements are likely to be independent. Therefore, the GEE extends generalized linear model (GLM) to account for correlated responses (Burton, Gurrin, and Sly 1998). It disregards within-subject covariance structure, and simply models the mean response.

Regarding continuous variables, the first step was to examine their distribution. Then the respective means of each score at the 3 the time points (examinations) were graphically plotted according to group of randomisation, in order to visualise the evolution of the scores through the different examinations. Then a population-averaged model (marginal model) was used to analyse the effect of the intervention on these repeated measures.

The marginal model adjusts for within-subject co-variability by modelling the within-patient covariance structure (Verbeke and Molenberghs 2009). In other words, observations from the same individual are not assumed to be independent. This is done by assuming that the residuals from a single subject are related: their covariances are non-zero. The term ‘marginal’ is used to

Methods

emphasise that the mean response modelled is conditional only on covariates and not on other responses or random effects.

To choose the best covariance structure, the different available structures in SAS (variance component, autoregressive, Toeplitz, compound symmetry, and unstructured) were compared using the Akaike Information Criterion (AIC). Therefore for each variable, the covariance structure of the model with the lowest AIC was chosen. A random effect for study centre was also added to the model.

All analyses were conducted with SAS 9.4 (SAS Institute, Inc). The analysed data set had one examination per observation (maximum 3 rows per women). The ‘poc Genmod’ procedure was used for GEE modelling, along with the ‘repeated’ statement for subject identification. The statement ‘estimate’ was used to compute a relative risk and confidence intervals by using robust error variances.

The marginal model was run with the ‘proc mixed’ procedures, using the ‘repeated’ statement for subject identification, and the ‘random’ statement for adjusting for centre. At each follow-up the fixed effect of the intervention was extracted using the ‘lsmeans’ statement that presented the estimated mean difference along with its 95% confidence interval between the two groups.

3.3.2. Results

3.3.2.a. Functional tests of balance and motor function

Tandem walk

The results from the tandem walk tests are presented in table 12. More women in the intervention group that were not able to complete 4 steps in the tandem walk at baseline were successful at 1 and 2 years compared to the control group (1 year: 40% vs 26%, 2 years: 37% vs 21%). Moreover, among women who were successful in completing the test at baseline, fewer women in the intervention group were unsuccessful at repeating the feat in the follow-up examinations compared to the control group (1 year: 6% vs 10% , 2 years: 5% vs 9%).

Table 12: Results of the tandem walk test at the 3 examination

Tandem walk test	Baseline	First follow-up (N=539)			Second follow-up (N=547) (vs baseline)		
	Able (N (%))	Improved (N (%))	Stable (N (%))	Declined (N (%))	Improved (N (%))	Stable (N (%))	Declined (N (%))
Exercise	79 (22.4%)	107 (39.6%)	146 (54%)	17 (6.3%)	99 (36.5%)	159 (58.6%)	13 (4.8%)
Control	83 (23.4%)	70 (26%)	171 (63.5%)	28 (10.4%)	57 (20.6%)	193 (69.9%)	26 (9.4%)

The relative risk of failing the test as estimated by the GEE is 0.62 (0.56 to 0.67, $p < 0.0001$), indicating that women in the intervention group were significantly more likely to pass the test compared to women in the control group.

Tests with quantitative measurements

Figures 23 and 24 present the crude mean results of functional tests for both groups at the 3 examinations. Additionally, table 13 presents results from the functional tests with quantitative measurements. For each examination, the number of participants that performed each test and the group mean average are presented. Also, the between group mean difference for functional tests, estimated by the marginal model is also presented for each outcome.

Results

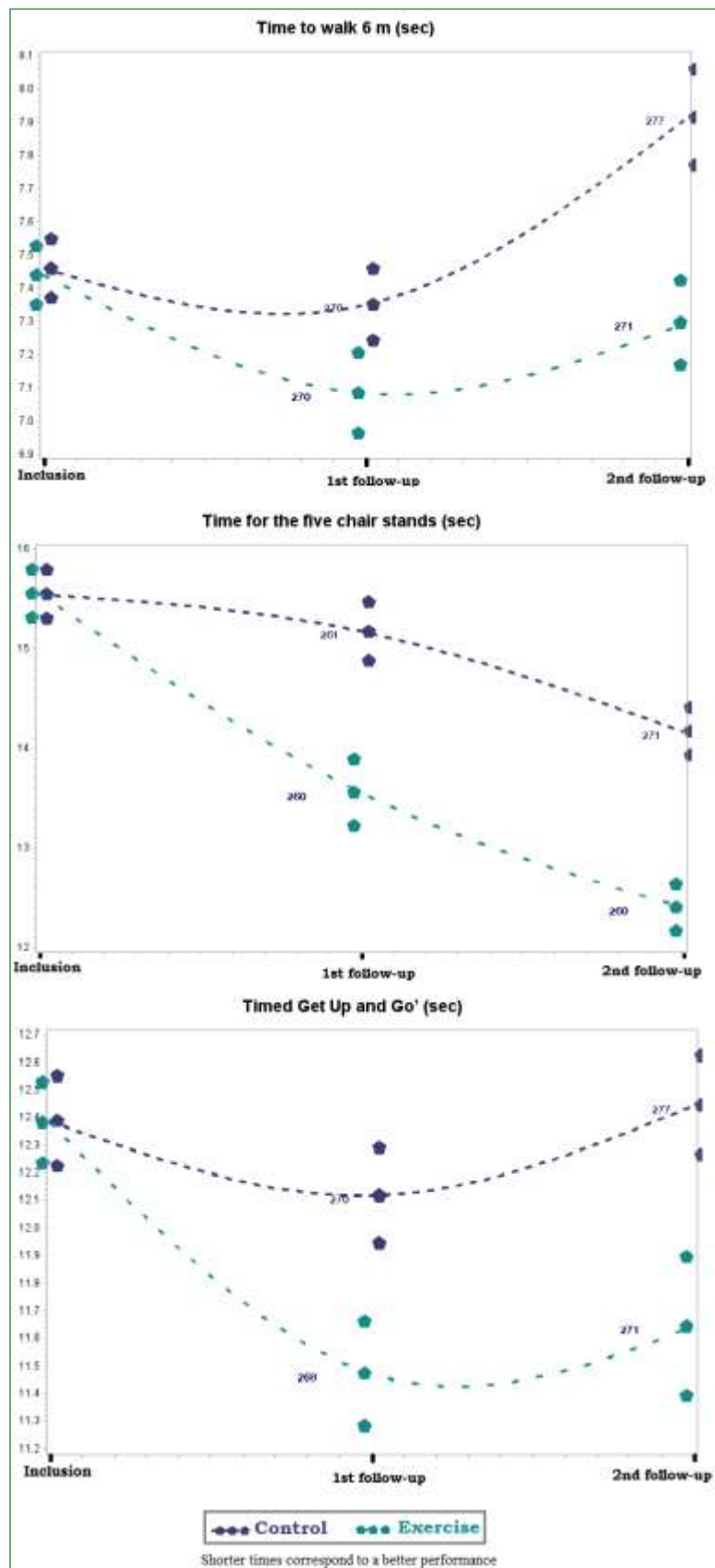


Figure 23: Results from the functional tests performed at the three examinations

Results

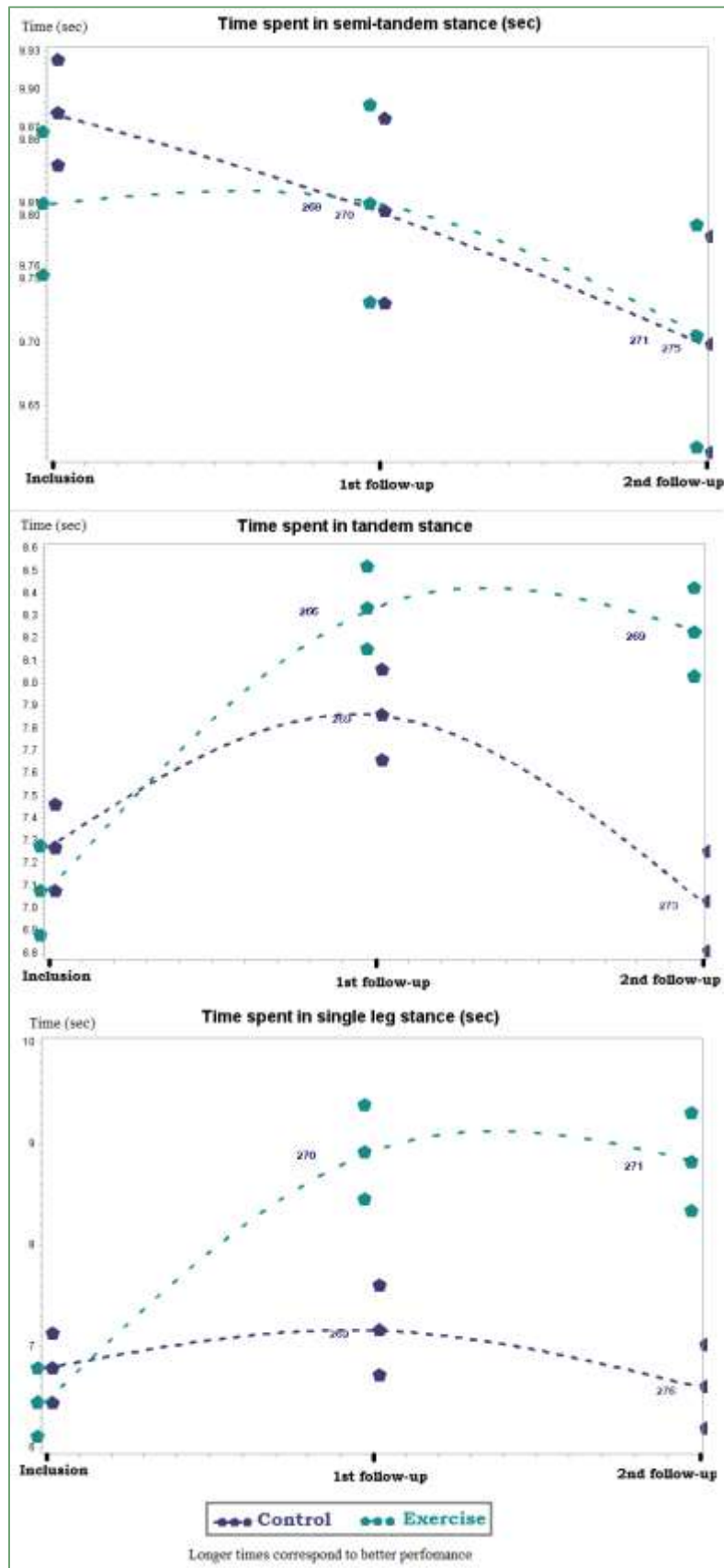


Figure 24: Results from static balance tests performed at the three examinations

Table 13: Results of the functional tests from the 3 examinations

Outcome	Control (C) Mean (SD)			Intervention (I) Mean (SD)			Estimated mean difference C v I (95% CI) ¥	
	Baseline n=354	1 year n=309	2 years n=288	Baseline n=352	1 year n=297	2 years n=284	1 year	2 years
‘Timed Get Up and Go’ (s)	12.39 (3.1)	12.12 (2.9)	12.44 (3.0)	12.38 (2.8)	11.47 (3.1)	11.69 (4.1)	0.53 (0.06-1.01)	0.68 (0.10 - 1.27)
Time to walk 6 m (s)	7.46 (1.7)	7.35 (1.8)	7.91 (2.4)	7.44 (1.7)	7.08 (2.0)	7.30 (2.1)	0.27 (-0.03 - 0.57)	0.54 (0.16 - 0.91)
Time for 5 chair stands (s)	15.55 (4.6)	15.23 (4.7)	14.17 (3.9)	15.55 (4.4)	13.55 (5.4)	12.40 (3.8)	1.51 (0.67 - 2.35)	1.70 (1.08 - 2.33)
Time spent in single leg stance (s)	6.78 (6.5)	7.16 (7.3)	6.60 (6.9)	6.44 (6.3)	8.92 (7.7)	8.82 (8.0)	-1.72 (-2.95 - -0.50)	-2.07 (-3.29 - -0.85)

¥: computed from an unadjusted marginal model. Statistically significant findings ($p < 0.05$) are displayed in bold

A positive mean difference presented for the Timed Up and Go (TUG), time to walk 6 m and time for the 5 chair stands, and a negative mean difference for time spent in single leg stance indicate better performance by the intervention group than the control group.

Results from the marginal model

Results from the marginal model indicate that the intervention group fared significantly better in most balance and gait performance tests compared to the control group at 1 and 2 years (table 13). On average, participants in the exercise group were around one second and a half faster in performing the five chair stands tests at both followup examination. They were also faster in performing the 6m walking test, and the ‘timed get up and go’ test in these examinations. Women in the exercise group also spent more time on one leg during the static balance test at both follow up examination, and they also stayed significantly longer in the tandem position at 2 years compared to the control group. No between-group difference could be detected for time spent in semi-tandem stance.

For the ‘Timed Get Up and Go’ test the between group difference at 1 and 2 years is explained by an improvement in the exercise group: the exercise group were 0.69 seconds faster at 1 year compared to inclusion, $p < 0.0001$), while the control group’s result did not change in the follow up examinations compared to inclusion.

Regarding the time to walk 6m test, the intervention group was slightly faster at 1 year compared to inclusion, while the control group did not exhibit any change. At 2 years, the control group was significantly slower compared to baseline, while the intervention group had similar speed than baseline results.

Women in the intervention group were significantly faster in performing the five chair stands tests in the followup examination compared to baseline, at 2 years they gained 2.95 seconds ($p < 0.0001$). While the control group only manifested a slight gain in speed at 2 years in a lower rate. Women in the control group had similar results than baseline concerning the time spent on one leg, while women in the exercise group lasted longer compared to the first examination in the 2 subsequent examinations. They also spent more time in tandem stance in the follow up examinations (at one year they spent around a second more in this position, $p < 0.0001$), whereas women in the control group has slightly better times at the one year examination compared to baseline (-0.50 , $p = 0.03$).

Participants in the exercise group did not improve their time standing in semi-tandem stance in the follow-up examinations, similarly to their counterparts at 1 year. At 2 years women in the control group had slightly worse results compared to inclusion but it did not translate into a between-group difference as seen above.

Physical activity and sedentarity indicators

Table 14 presents physical activity level for examined women at the three examinations according to group, as well as the results from the repeated measures model. The intervention does not seem to have an effect on physical activity level as measured by the time and the frequency women spent walking and doing other leisure activities per week. Likewise, no difference between the 2 groups was detected at one or at 2 years for the sedentary behaviour indicator (daily hours spent sitting) was found.

Table 14: Physical activity level at the three examinations

Outcome	Control (C) Mean (SD)			Intervention (I) Mean (SD)			Estimated mean difference C v I (95% CI) ¥	
	Baseline n=354	1 year n=309	2 years n=288	Baseline n=352	1 year n=297	2 years n=284	1 year	2 years
Walking for casual activities (no./week) ♦	4.77 (2.2)	4.42 (2.3)	4.28 (2.4)	4.33 (2.2)	4.10 (2.3)	4.21 (2.3)	0.31 (-0.05 - 0.67)	0.10 (-0.29 - 0.48)
Walking for casual activities (hr/wk)	3.06 (2.4)	3.23 (2.7)	3.40 (2.7)	2.78 (2.3)	2.85 (2.4)	3.39 (2.7)	0.39 (-0.01 - 0.79)	0.04 (-0.40 - 0.48)
Walking for exercise (no./week)	4.09 (2.3)	4.13 (2.4)	4.11 (2.4)	3.80 (2.5)	3.73 (2.4)	4.15 (2.3)	0.36 (-0.11 - 0.84)	0.12 (-0.40 - 0.64)
Walking for exercise (h/week)	2.11 (2.8)	2.30 (3.1)	2.16 (3.2)	1.89 (2.9)	2.29 (3.1)	2.03 (3.0)	0.04 (-0.45 - 0.54)	0.13 (-0.36 - 0.63)
Leisure physical activities ☼ (no./week)	1.02 (1.2)	1.35 (1.7)	1.33 (1.8)	0.99 (1.3)	1.32 (1.9)	1.01 (1.3)	0.04 (-0.25 - 0.33)	0.26 (0.00 - 0.52)
Leisure physical activities ☼ (h/week)	2.43 (2.9)	2.83 (3.3)	2.65 (3.4)	2.23 (3.1)	2.76 (3.4)	2.35 (3.2)	0.10 (-0.43 - 0.64)	0.27 (-0.26 - 0.80)
Sitting down (h/day)	4.23 (1.4)	4.44 (1.3)	4.42 (1.4)	4.34 (1.4)	4.36 (1.4)	4.55 (1.5)	0.06 (-0.15 - 0.27)	-0.14 (-0.37 - 0.09)

¥: computed from an unadjusted marginal model; with a random effect for centre

♦: Activities such as walking to general practitioner, pharmacy or store.

☼: leisure activities include: walking, swimming, dancing, gym classes, gardening, biking, and yoga.

Fear of falling

Table 15 presents physical fear of falling as measured by the FES-I. The table also presents results from the repeated measures model. Fear of falling seem to increase in both group with each examination, but more so in the control group. The FES-I score mean difference between groups as estimated by the marginal model was significant at 1 year; this difference was not significant at 2 years.

Table 15: Fear of falling score at the three examinations

Outcome	Control (C) Mean (SD)			Intervention (I) Mean (SD)			Estimated mean difference C v I (95% CI) ¥	
	Baseline n=354	1 year n=309	2 years n=288	Baseline n=352	1 year n=297	2 years n=284	1 year	2 years
Fear of falling (FES-I score)	26.02 (6.9)	26.93 (7.9)	27.29 (8.2)	25.52 (7.1)	25.44 (7.7)	26.10 (7.4)	1.50 (0.23- 2.76)	1.12 (-0.19 - 2.41)

¥: computed from an unadjusted marginal model; with a random effect for centre

Results

Health-related quality of life

Table 16 presents results of the health-related quality of life indicators for examined women at the three examinations as measured by the SF36 questionnaire. The table also presents results from the repeated measures model. All 4 health-related quality of life scores tended to decrease in both groups (health status perceived as worsening over time), but less strikingly in the intervention group. The mean difference between groups was significant for vitality and general health at 1 year, and for physical function at 1 and 2 years.

Table 16: Health-related quality of life indicators at the three examinations

Outcome	Control (C) Mean (SD)			Intervention (I) Mean (SD)			Estimated mean difference C v I (95% CI) ¥	
	Baseline n=354	1 year n=309	2 years n=288	Baseline n=352	1 year n=297	2 years n=284	1 year	2 years
SF-36 Physical function score	57.47 (20.7)	55.17 (22.4)	52.44 (22.8)	59.40 (59.4)	58.71 (23.3)	58.13 (24.5)	-3.90 (-7.51 - -0.30)	-5.27 (-9.06 - -1.48)
SF-36 Mental health score	60.70 (18.2)	60.57 (17.9)	61.16 (17.0)	61.33 (18.1)	62.91 (17.0)	63.12 (16.3)	-2.55 (-5.33 - 0.25)	-1.58 (-4.26 - 1.11)
SF-36 General health score	54.72 (16.1)	55.45 (22.8)	54.6 (16.1)	57.05 (15.8)	57.94 (15.7)	56.43 (15.8)	-2.33 (-4.86 - 0.20)	-1.64 (-4.21 - 0.93)
SF-36 Vitality score	46.62 (16.2)	45.62 (16.4)	45.61 (16.4)	48.44 (16.3)	48.21 (16.3)	48.2 (16.3)	-3.17 (-5.71 - -0.62)	-2.57 (-5.21 - 0.08)

¥: computed from an unadjusted marginal model; with a random effect for centre

3.3.3. Discussion

3.3.3.a. Principal findings and interpretation

The 'Ossébo' exercise programme was successful in improving balance and gait performances among older women; women who were allocated to the intervention group performed better than the control group in different physical functional tests after one year and 2 years of intervention.

This improvement in physical functions probably explains, at least in part, the beneficial effect of the Ossébo exercise programme on injurious falls prevention. As in other studies recently reviewed by Cochrane (T E Howe et al. 2007), improvements in test results appear relatively modest. It may be that even small improvements in measured physical performances may have significant beneficial effects in older and already somewhat fragile people. In support of this hypothesis, women in the intervention group were found to have a significantly better perception of their overall physical function than women in the control group by the end of the intervention (as measured by the SF36). These findings suggest that improvements in physical performances have translated into improvements in global daily life functions.

Moreover, while fear of falling increased significantly in both groups over the 2-year study period, this increase was less pronounced in the intervention group, which suggests that the programme is effective in minimising the age-related decrease in older people's confidence in their ability to perform activities of daily living without falling. These findings are similar to few other published results in the literature. A literature review had shown that out of 19 RCT to prevent falls among community-dwelling older adults, 11 had shown a decrease of fear of falling in intervention group (Zijlstra et al. 2007). But among the individual interventions that managed to reduce fear of falling, only 2 were non Tai-Chi group exercise. Whereas 3 exercise interventions included in the review were not successful in reducing fear of falling. Another exercise intervention in that review had different results depending on the test used to measure fear of falling. Another more recent meta-analysis had concluded that exercise can have a low significant effect on fear of falling (Rand et al. 2011).

There was no significant difference in mean physical activity and sedentarity indicators between the two groups, which may be explained by the difficulty in making voluntary lifestyle changes at so old an age. Note that outcomes used to measure physical activity level in this analysis did not include participation in the Ossébo programme itself, which necessarily increased the overall activity level of the participant in the exercise group.

3.3.3.b. Limitations

One of the main limitations of this analysis is missing data at the follow-up examinations. At one year, 44 women in the control group and 53 women in the intervention were not examined. Moreover, more women were not examined in both groups at 2 years. This could potentially bias the results since some of these women did not show up for the examination probably because they had experienced deterioration in their health from the time the trial started. In fact women who did not get examined in the follow-up examinations were older (statistically speaking) than women who did get examined (1 year: 79.6 (SD=2.8) vs 79.2 (SD=2.9), $p=0.001$). However, there's no reason that the deterioration would happen in one group more than the other, especially that reason of drop-outs from the study were comparable between the two groups. Also, there was no difference in age or other risk factors for falling between women who were not re-examined in the two comparison groups. Nonetheless, the 14% rate of missing data means that these results should be interpreted with caution.

Another limitation is the subjective reporting of some items, such as the physical activity level. The use of accelerometers, which can objectively measure physical activity, in the design of future trials could be more informative and improve our ability to see a difference between the two groups. However that would mean facing another challenge; activity monitoring by accelerometry being a relatively new domain among older adults, there's no standardised protocols and normative data for that age group (Taraldsen et al. 2012).

Other limitations of this analysis are similar to the ones discussed above regarding the analysis of the effect of the programme on the reduction of falls and injuries. In particular, the less than optimum adherence to the intervention may have led to underestimate the effect of the exercise programme on the physical and psychological risk factors for falling. In particular, it may contribute to explain that differences between the 2 groups regarding fear of falling, vitality and casual walking that were significant at 1 year (in favour of the intervention group), were less apparent at 2 years.

3.3.3.c. Strength

One of the strength of this study is that it employed well standardised and validated measures of physical function, fear of falling and health-related quality of life among older women. This allows better interpretability and comparability with other studies. Another strong point of this analysis is that investigators performing the tests were blinded to group allocation therefore minimising bias.

Also, Ossébo is one the few fall prevention exercise trials that examined the effect of the intervention on a comprehensive set of other fall-related and health-factors including perceived physical function and psychological wellbeing, which helps to better evaluate the overall benefit of the intervention.

3.3.3.d. Conclusion

The Ossébo exercise programme has proved effective in improving balance and gait capacities, which probably partly explain the beneficial effect of the programme on the reduction of falls and fall-related injuries. The analysis further show that the programme also improves perceived physical function, even for this group of very old adults.

3.4. Characteristics associated with participation in the Ossébo trial

In this analysis we sought to identify socio-demographic, functional, health-related, and programme implementation factors associated with participation in the ‘Ossébo’ trial. The identification of factors linked with uptake to this kind of trial can potentially help future conception of fall prevention programmes and increase the rate of participation of older subgroup of community-dwellers.

3.4.1. Methodology

3.4.1.a. Individual characteristics

The individual variables were measured at the baseline examination and were described above. They include the functional tests of balance and motor function, the physical activity level, sedentary behaviour indicator, fear of falling, and health indicators. Socio-demographic characteristics, health-related behaviour, and programme implementation-related factors used in this analysis are detailed below.

Socio-demographic

These variables included age (<80 / ≥80), marital status (single/married/in a civil partnership/widowed/ separated-divorced), education level (up to secondary school /high school diploma or more), living arrangement (living alone (y/n)), and professional activity (executives and clerks/ blue-collar/ agriculture or craftswomen/not specified).

Prevention-related behaviour

Prevention-related behaviours were examined by asking women whether in the past 5 years they undertook a colposcopy, a mammography, a pap smear, a bone densitometry test, or a flu vaccine.

3.4.1.b. Programme-implementation factors

Implementation-related variables concern the design and execution of the intervention. These variables include the distance from a participant house to the exercise location, the setting of the exercise location, and the period of the year (season) when the baseline examination took place.

Distance from a woman's house to the intervention location

The geodetic (shortest path between two points on a curved surface) distance from a woman's house to the intervention location was calculated. In order to do so, the first step was to geocode both addresses. Geocoding is the process of converting addresses (for example "Sir Matt Busby Way, Manchester M16 0RA, United Kingdom") into geographic coordinates (for example latitude: 53.4630556, longitude: -2.2913889). This was accomplished via a free website ('batchgeocodeur.mapjnz.com'), which in turn uses the 'The Google Geocoding API' application ('The Google Geocoding API - Google Maps API Web Services — Google Developers' 2015). Geographic coordinates could then be employed to create a map, and to calculate the geodetic distance between the 2 coordinates (for each woman the distance from her house to the intervention location) with the SAS procedure 'Proc Geodist'. The SAS procedure uses the 'Vincenty distance formula' that models the earth in an accurate ellipsoidal structure (Vincenty 1975).

Intervention setting

An associative or municipal ('mairie') location for the intervention to take place was not available in all study centres. Therefore in some cities, study investigators in association with SIEL Bleu reserved halls in hospitals, geriatric centres or in residential care depending on availability. Therefore, for this analysis, study centres were classified depending on the setting where the group sessions occurred; distinguishing between 3 different settings: 'hospital or geriatric centre', 'nursing facility for older adults', and 'associative or municipal'.

3.4.1.c. Analysis

Individual and implementation-related characteristics of eligible women who accepted to participate in the exercise intervention were compared with those of eligible women who did not accept to participate. Individual characteristics (first level variables) were grouped into 5 domains: socio-demographic, functional capacities, health-related measures, activity level, and prevention-related behaviour. Chi-square test of association for categorical data and independent sample t-tests for continuous variables were used for the bivariate analysis. Bivariate logistic regressions were also run in order to estimate unadjusted Odds Ratio (OR) for each independent variable. Independent variables showing association with participation ($p < 0.15$) in the bivariate analysis were considered for the multivariate analysis.

Methodology

Due to the hierarchical structure of the data (participants nested within centres), multivariate analysis was carried out with a multilevel mixed effects logistic regression in order to identify factors independently associated with participation (Dai, Li, and Rocke 2006). Two ‘levels’ of characteristics were considered for this analysis; individual characteristics (first level) and characteristics relevant to the centre (2nd level) or ‘implementation’ factors (Figure 25).

The underlying hypothesis is that women from the same centre are more similar than those between centres, and this would result in clustering of the data. Multi-Level Modelling is a statistical technique that controls for the effects of clustering, as well as allowing the examination of explanatory variables at the two levels. As a result, individual and centre level variables can be considered in tandem when developing a model, adding considerably to the statistical robustness of the model (Dai, Li, and Rocke 2006).

Odds ratios with 95% confidence intervals are presented. A value of $p < 0.05$ was accepted as being statistically significant. Analyses were performed with SAS V9.4., with the ‘Proc Glimmix’ procedure, with the link function ‘logit’. All independent variables were entered as fixed factors, additionally; the random intercept was added at the centre (2nd) level.

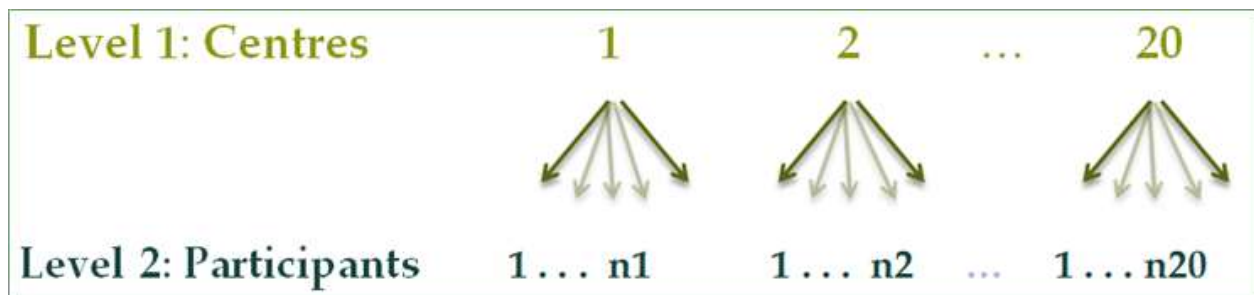


Figure 25: Multi-level structure of the data

3.4.2. Results

Table 17 presents the bivariate comparison of individual characteristics between eligible women according to participation.

Women participating in the trial, on average, weighed more and were younger than their counterparts. They were also more likely to be living alone and belonging to the 'Executive, and intermediate' social professional category. Participants were also more likely to practice leisure physical activity at least once a week, and perform casual activities more than once per week. Moreover, they tended to take part in health prevention behaviour such as undertaking a colposcopy in the 5 years before baseline examination more than their counterparts.

Concerning implementation-related factors; participants lived on average closer to the intervention centre than non-participants. Also, intervention's location setting seem to impact participation, participation rates were the lowest in centres where the intervention took place in nursing facilities for older adults. Recruitment also seems to be more successful in the winter months compared to other seasons. Among the psychological scores, only an increase in the mental health score was slightly associated with an increased likelihood to participate in the trial (though not statistically significant).

Table 18 presents results of the multivariate logistic regression. Multi-level logistic regression analysis indicated that intervention setting, living alone, weight, age, living alone, and having undertaken a colposcopy in the past 5 years were independently associated with participation to the trial.

The adjusted OR associated with centres where the intervention took place in a nursing facility setting was 0.58 (0.38 – 0.88) compared to associative and municipal setting. Older age (≥ 80 years) was associated with a decreased probability of participation (0.64 (0.50 – 0.83)). Women living alone had an adjusted OR=1.57 (1.20 - 2.05) compared to their counterparts, while the OR associated with having a colposcopy in the past 5 years was 1.36(1.04 - 1.78). Also, the adjusted OR for women recruited in winter was 1.38 (1.0 - 1.88) compared to women examined in spring. The adjusted OR associated with an increase of 10kg was = 1.14 (1.01 - 1.28).

Table 17: Results from the bivariate analysis

Characteristics	Crude OR	p value
Socio-demographic characteristics		
Age (<80 vs ≥80)*	0.60 (0.47 - 0.77)	<0.0001
Professional category*		
Non manual vs Manual ‡	1.33 (1.02 - 1.74)	0.02
Agriculture, craftswomen vs Manuel	0.74 (0.45 - 1.22)	
Not defined vs Manual	0.87 (0.59 - 1.28)	
Education level: High school or more vs secondary school or less	1.07 (0.84 - 1.38)	0.58
Living alone (yes vs no)*	1.43 (1.11 - 1.83)	0.005
physical activities indicators		
Leisure physical activity ^{⊛*}		
Once or twice per week vs none	1.24 (0.88 - 1.74)	0.05
Three or more times per week vs none	1.4 (1.07 - 1.82)	
Frequency of casual activities ^{⊠*}		
2 to 6 times per week vs up to once per week	1.65 (1.14 - 2.39)	0.02
Every day vs up to once per week	1.64 (1.11 - 2.42)	
Frequency of social activities ^{⊠*}		
One time per week vs none	1.04 (0.77 - 1.42)	0.91
Twice or more per week vs none	0.97 (0.74 - 1.28)	
Time spent sitting (h/week)	0.98 (0.90 - 1.07)	0.69
Balance and mobility tests		
Time to walk 6m*	0.95 (0.88 - 1.01)	0.11
Time for 5 chair stands (s)	1.02 (0.99 - 1.05)	0.13
‘Timed Get Up and Go’ (s)	1.01 (0.97 - 1.05)	0.56
Time spent in single leg stance (s)	1.0 (0.99 - 1.02)	0.64
Fall and health-related characteristics		
Fear of falling Scoring (FES-I)	1.0 (0.99 - 1.02)	0.62
At least one fall in the last year vs no fall	1.05 (0.82 - 1.34)	0.69
Weight (kg)*	1.01(1.0 - 1.02)	0.02
SF36 mental health*	1.01(0.99 - 1.01)	0.11
SF-36 General health score	1.0 (0.99 - 1.01)	0.4
SF-36 Vitality score	1.0 (0.99 - 1.01)	0.24
SF-36 Physical function	1.0 (0.99 - 1.01)	0.18
Number of treatments in the last 6 months	1.0 (0.96 - 1.04)	0.99
Urinary incontinency (average per week)	1.06 (0.98 - 1.15)	0.16

Results

Prevention-related behaviour		
Dietary supplements in the past 5 years (yes vs no)*	1.28(0.96 - 1.7)	0.09
A pap smear in the past 5 years (yes vs no)	1.05 (0.82 - 1.36)	0.7
A mammography in the past 5 years (yes vs no)	1.18 (0.91 - 1.52)	0.2
A colposcopy in the past 5 years (yes vs no)*	1.33(1.04 - 1.71)	0.02
A bone densitometry test in the past 5 years (yes vs no)	1.0 (0.79 - 1.28)	0.98
A Flu shot in the past 5 years (yes vs no)*	0.92 (0.69 - 1.24)	0.59
Implementation-related factors		
Season*		
Autumn vs Spring	0.96 (0.7 - 1.31)	0.008
Summer vs Spring	1.3 (0.81 - 2.09)	
winter vs Spring	1.57 (1.17 - 2.1)	
Distance to intervention site (k)*	0.84 (0.75 - 0.94)	0.002
Intervention setting*		
Hospital vs associative- municipal	1.34 (0.94 - 1.9)	0.0003
Nursing facility vs associative- municipal	0.51 (0.35 - 0.75)	

*: Selected for the multivariate analysis

⌘: Non-manual workers: executives and clerks. Manual: blue-collar workers

◊: Activities such as walking to general practitioner, pharmacy or store.

☀: leisure activities include: walking, swimming, dancing, gym classes, gardening, biking, and yoga.

Table 18: Results from the multivariate analysis

Variable	Adjusted OR [‡]
Age (<80 vs ≥80)*	0.64 (0.49 - 0.83)
Intervention setting*	
Hospital vs associative- municipal	1.40 (0.98 - 1.96)
Nursing facility vs associative- municipal	0.58 (0.38 - 0.88)
Living alone (yes vs no)*	1.57 (1.2 - 2.05)
A colposcopy in the past 5 years (yes vs no)*	1.36 (1.04 - 1.78)
Weight (kg)*	1.01 (1.00 - 1.08)
Season*	
Autumn vs Spring	1.04 (0.74 - 1.46)
Summer vs Spring	1.61 (0.97 - 2.69)
winter vs Spring	1.38 (1.00 - 1.88)
Professional category	
Non manual vs Manual	1.28 (0.96 - 1.70)
Agriculture, craftswomen vs Manuel	0.71 (0.42 - 1.90)
Not defined vs Manual	1.02 (0.68 - 1.54)
Leisure physical activity	
Once or twice per week vs none	1.18 (0.82 - 1.70)
Three or more times per week vs none	1.29 (0.96 - 1.71)
Time to walk 6m	0.99 (0.93 - 1.08)
Dietary supplements in the past 5 years (yes vs no)	1.29 (0.95 - 1.74)
SF36 mental health	1.00 (1.00 - 1.01)
Frequency of casual activities	
2 to 6 times per week vs up to once per week	1.46 (0.99 - 2.16)
Every day vs up to once per week	1.49 (0.98 - 2.25)
Distance to intervention site (k)	0.93 (0.81 - 1.05)

*: independently associated with participation to the trial after adjustment to other variables

‡: estimated from a multilevel mixed effects logistic regression

3.4.3. Discussion

This analysis compared characteristics between participants and non-participants in the Ossébo trial. Only 61 % of the eligible participants agreed to enrol, these women were younger, weighted on average more, lived more often alone.

Most notably, centres where the intervention was set in a hospital setting had significantly more important recruitment rates compared to centres where the intervention was done in nursing facility for older adults. It's possible that nursing facilities are associated with negative aging stereotypes such as dependency and functional decline which in turn decreased enrolment. In contrast, an intervention taking place in a hospital could reflect more trustworthiness, similarly to the 'white-coat effect' (Brase and Richmond 2004). Indeed it seem that participants are more health-conscious than non-participants as shown in a more tendency to undertake prevention-related behaviour such as performing a colposcopy.

After adjustment to other variables, no association was found between participation and different balance and mobility-related factors such as: balance and gait tests, physical activity, fear of falling and having fallen in the past year, after adjusting for other variables. Although in the unadjusted analysis, participants were found to have a slightly faster gait than non-participants. This may be because eligible women were already rather homogenous concerning these factors, since having diminished functional capacities was an eligibility criteria.

In the bivariate analysis, the distance to the intervention location tends to be inversely associated with participation. This is not surprising, transportation and easy physical access to research centres has also been previously associated with better participation rates in physical activities studies among older adults (Witham and McMurdo 2007). This association, however, was not independently associated with participation after adjusting to other variables. This could be explained by the trial's design; only women living near (<5k) the eventual intervention sites were invited for the baseline examinations. It could also be because of the approximate method by which the distance was calculated.

The season of recruitment was associated with participation to the trial, with recruitment rate peaking in the winter months. Despite the absence of any previous studies examining the period of the year's effect on participation in trial, this finding was not expected. In fact, studies had shown that older adults tend to practice less physical activities in the winter months (Tucker and Gilliland 2007). One of the reason older people tend to avoid physical activities in winter is the increased risk of injuries; falls and injurious fall also tend to peak in the winter season (Bulajic-

Kopjar 2000; Gao, Holmér, and Abeysekera 2008). However, this perception of an increased risk of falls and injurious falls could've contributed to an increased participation in a fall prevention trial. Notably, the fear of falling score in the summer months (23.7 (SD=5)) was significantly lower than in other months (25.7 (SD=7)).

3.4.3.a. Limitations

Our results should be interpreted with caution because the study has limitations. One of the main limitations of our results is the approximate nature of the dependent outcome; participation in an exercise fall prevention trial was considered as a proxy for partaking in an exercise programme. However, the findings, such as the association of the intervention setting and living alone to participation, are valuable information that could be used in optimising participation in trials among older adults, as well as exercise programmes. Another limitation is the large number of non-eligible examined women; more than half of examined women were deemed as having good functional capacities and therefore were excluded from the trial. Therefore these findings on the characteristics associated with participation could only be valid for women with diminished physical function. Nevertheless, this is still very useful in a public health perspective, especially one that aims to target women at higher risk of falling; who could potentially benefit most from exercise programmes.

Additionally, the estimation of a geodetic distance between the women's houses and the intervention, instead of better indicators such as calculating the time it takes to go there by the mean of transport of choice. The latter indicator would've been more precise.

3.4.3.b. Strength

Ossébo is the first study to study individual and programme-implementation related factors associated with participation in a fall prevention trial among older (>75 years) women with diminished functional capacities.

Also, Ossébo's pragmatic design allowed the identification of intervention implementation factors, the intervention setting, and the period of the year of recruitment, as potentially easily modifiable factors that could increase recruitment rates of older adults not only in fall prevention trials but in other health promotion studies as well.

The findings could be used to better design and implement intervention trials as well as community-based programmes. For example, we found that living alone was independently associated with participation in the Ossébo trial, whereas risk factors for falls were not associated

Discussion

with participation. Which suggests that the convivial/social aspect of a fall prevention exercise programme is an important message to communicate that could potentially increase participation in trials and also, in exercise programmes. It's been previously documented that older people dislike engaging with services labelled as 'fall prevention' and hence a focus on positive health messages rather than negative messages (avoiding falls) was recommended (Yardley et al. 2006). However, adding and highlighting the convivial component could also help motivate older people to participate in fall prevention exercise programme and also decrease loneliness in older adults.

4. General discussion

4.1. Summary of findings

Exercise programmes emphasising balance training have been shown to be effective in reducing falls in older (> 65 years) community-dwelling adults (Sherrington et al. 2008; Gillespie et al. 2012). Nonetheless, trials have generally lacked the power to show an effect on injurious falls, few of them reported data on fall-related injuries and the definitions of injurious falls varied between studies. Moreover, these trials rarely presented the effect of exercise simultaneously on falls and other risk factors for falls such as functional capacities and therefore clarifying the mechanisms by which the exercise might work. Furthermore, individual and programme-related factors associated with participation of older adults in fall prevention trials have been scarcely reported.

To address all these voids in the literature, first, I carried out a systematic review of the evidence about the effect of fall prevention exercise programmes among community-dwelling older adults on different outcomes of injurious falls, based on physical damage and medical care. The results of the ensuing meta-analysis showed that exercise programmes designed to improve balance and prevent falls in older adults also seem to prevent injuries caused by falls, including the most severe ones. However, the methodological quality for several criteria (randomisation method, blinding of fall ascertainment, incomplete outcome data) of a number of included studies could not be judged with any certainty, few studies used a predefined standardised classification of the consequences of falls, and some pooled analyses showed significant heterogeneity between studies. Only a small proportion of fall prevention exercise trials reported data on fall related injuries and, although included trials were not all positive for a reduction in falls, the possibility of publication bias cannot be ruled out. Hence, the results of the meta-analysis must be interpreted with some caution.

The review also highlighted the lack of comprehensive information about the programmes' impact on other important outcomes, especially psychological factors (e.g., fear of falling), health-related quality of life, and potential adverse effects, although this knowledge is important in assessing the programmes overall benefit (Lamb, Jørstad-Stein, et al. 2005). Another limitation of the included studies is the lack of detailed descriptions of implementation procedures, whether planned or unplanned, so that readers can judge the applicability of the programme in different settings or on a large scale.

Furthermore, many of the interventions lasted only a few months, and their long-term benefit was unclear. Few studies targeted the subgroups of the home-living older adults at highest risk of falls and injuries, for whom the absolute benefit of the intervention should be greatest, such as older adults aged over 75 years and with risk factors for falls and injuries. Thus, designing and implementing interventions that are both effective against injurious falls and acceptable over the long term remains a challenge, especially for the oldest and more fragile subgroups.

The second part of my thesis consisted in analysing the results of the Ossébo trial. Ossébo is a community-based multi-centre randomised controlled trial that assesses the effectiveness of a long-term (2-year) exercise programme on the reduction of falls and fall-related injuries among community-dwelling women aged over 75 at risk of injurious falls. The trial was conducted in 20 sites located in 16 medium to large cities throughout France and applied a pragmatic approach intended to inform the design and implementation of future community-based intervention programmes. The 2-year progressive balance retraining exercise programme was conceived and implemented in partnership with SIEL Bleu, a non-profit associative group of professional physical activity therapists for the elderly. It involved supervised group sessions delivered in practice settings representative of ultimate target settings, complemented by individually prescribed home exercises. The criteria used to select the target population were simple (age, female sex, simple functional tests of balance and gait) and can be easily used by family physicians as well as health or physical activity practitioners providing care for older people. The study also provides comprehensive information on physical as well as psychosocial outcomes (fear of falling and health-related quality of life), and data on adverse outcomes. A well-defined classification of injurious falls, selected before data collection was used to classify injurious falls in the Ossébo trial. Subsequently, we showed that it is feasible to put into place a large-scale, long-term exercise fall-prevention programme that is safe and effective in reducing injurious falls, even among very old (>75 years) at-risk women. Furthermore, the results show that the programme improves balance and gait capacities but also perceived quality of life related to physical function for this group of very old adults.

Lastly, the analysis of factors associated with participation to the trial indicated that intervention setting, age, living alone, and prevention-related behaviour are all factors

independently associated with participation into the trial. On the other hand, a history of fall and other risk factors for falling are not associated with participation.

4.2. Common strengths

The strength of this work lies in its evidence-based approach, and the use of recommended justifiable methodological and statistical procedures. Randomised controlled trials represent the gold standard in evaluating health care interventions, and systematic reviews of randomised trials are the recommended method to identify and evaluate the existing evidence on health-related subjects (Khan et al. 2011). Furthermore, we used the recommended methods of reporting findings. The ‘PRISMA’ (Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Liberati et al. 2009)), an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses was used for the first part of thesis. And the ‘CONSORT’ (Consolidated Standards of Reporting Trials (Calvert et al. 2011)) recommendations for reporting randomised trials were followed for the second part. The ‘TIDieR’ (Template for Intervention Description and Replication (Hoffmann et al. 2014)) checklist and guide were also adopted. These checklists have been developed to improve the reporting of studies and make it easier for authors to structure accounts of their work, and readers to judge, replicate, and use the information.

For this work, we used a well-defined classification of injurious falls in both the systematic review and the Ossébo’s analysis. This classification could be replicated, allows comparability between different trials and pooling of data, and is based on clinically-relevant outcomes.

In fact, all reported outcomes in this thesis are clinically-relevant and patient-centred. This reflects the pragmatic nature of the research, for which the hypothesis and study design are formulated based on information needed to make a clinical and/or public health decision (Schwartz and Lellouch 1967).

4.3. Implications for public health

Our findings are important for health care professionals and public health decision makers and can assist them in developing fall injury prevention programmes for at-risk older adults. It also strengthens evidence for allocating resources toward these programmes in order to decrease disability and improve the quality of life among older adults. Especially at a time where active ageing is central to political agendas in the industrialised world (Walker and Maltby 2012).

The results of our systematic review were cited in a recent umbrella review of meta-analyses of randomised controlled trials assessing various fall prevention interventions, and that presented exercise as the most consistently effective and robust intervention to prevent falls among older adults (Stubbs, Brefka, and Denkingen 2015).

Additionally, knowledge on the mechanisms by which the intervention work, and information on the profile of older people who participate in interventions trials and of programme's characteristics that are associated with greater participation in intervention trials could be used in the design and implementation of fall prevention trial, in order to optimise effectiveness, and for a smoother transition from research to practice.

Findings from our study could be used to optimise the conception of future exercise trials and community-based programmes among older adults. For example, hospital settings and associative/municipal locations should be preferred to residential care homes in the future design of programmes.

4.4. Recommendations and perspectives

Systematic reporting of falls and injuries should be implemented in future fall prevention randomised controlled trials, where the different levels of severity of the injury should be standardised and defined in advance, to improve the comparison between studies and subsequently the accuracy of pooled estimates for each category of falls.

Moreover, future published study should use a standardised taxonomy that describes and classifies exercise intervention such as the one developed by the PROFANE group (Lamb et al. 2011). This could improve the understanding and replication of exercise interventions reported in literature, especially since different types of exercise can improve different

parameters (isometric strength, muscle power, balance, etc.) that are independently associated with the risk of falls among older adults (Muehlbauer et al. 2012).

Future trials should also provide data on other important outcomes such as physical and cognitive functional capacities, psychological outcomes, and quality of life and a thorough description of the implementation process, in order to improve comparability between studies, and better understanding of underlying mechanisms.

Strength and balance training is effective in preventing falls and fall outcomes, but it is challenging to implement community-based programmes of this type; take-up rates are suboptimal, with high discontinuation rates (Bunn et al. 2008). This low uptake and high drop-out rate may be caused by several factors, including a mismatch between programme requirements and participants' capabilities, or between the programme's format and participants' preferences. The good news is that different formats and types of exercise have been proven to be effective (home-based, group based, combined group and home-based exercise like the Ossébo programme, Tai Chi, individualised, etc.), and other formats are probably waiting to be developed, optimised or repackaged (web-based, exergames, etc.). Studies comparing the characteristics of older people who participate to different exercise programmes or activities with those who don't participate may help finding the best arguments to motivate people to participate and also to better target specific interventions.

Additionally, more studies should examine how to increase the implementation of exercise programmes into clinical practice, and health policies. Fall prevention awareness campaigns and training for health care professionals and community health workers could be effective in changing practice. Also, research accompanying the implementation of fall prevention programmes and the evaluation of their methods and effectiveness at the practice and policy levels is needed.

5. References

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Appendix

Appendix 1- Extraction form used in the data collection process of the systematic review

Participants	
Setting of recruitment and assessment	
Inclusion criteria (including assessment tools ; at higher fall risk versus unselected)	
Exclusion criteria	
Number of randomised subjects (Intervention)	
Number of randomised subjects (Control)	
% women	
Mean age (age range /SD)	
Intervention	
Type of exercise	
Moderate to high challenging balance component	
Mode of delivery (group / home / combination)	
Sessions frequency/duration	
Total programme duration	
Comparison group	
Adherence data	
Falls and injurious falls outcomes	
Definition of falls	
Rate ratio of (all) falls	
Rate of falls in control group	
Follow up period (for falls recording)	
Definitions of injurious falls (corresponding category classification)	
data on injurious falls for each category (Rate/risk ratio, number of injurious falls/fallers in each group, person-time in each group)	

Bias assessment	
Random sequence generation	
Allocation concealment	
Blinding of falls and injurious falls ascertainment	
Attrition data	
Method of falls recording	
Method used to verify severe injurious falls	
Adverse events	

Appendix 2: Published Article: The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials

BMJ



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The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials

OPEN ACCESS

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Abstract

Objective To determine whether, and to what extent, fall prevention exercise interventions for older community dwelling people are effective in preventing different types of fall related injuries.

Data sources Electronic databases (PubMed, the Cochrane Library, Embase, and CINAHL) and reference lists of included studies and relevant reviews from inception to July 2013.

Study selection Randomised controlled trials of fall prevention exercise interventions, targeting older (>60 years) community dwelling people and providing quantitative data on injurious falls, serious falls, or fall related fractures.

Data synthesis Based on a systematic review of the case definitions used in the selected studies, we grouped the definitions of injurious falls into more homogeneous categories to allow comparisons of results across studies and the pooling of data. For each study we extracted or calculated the rate ratio of injurious falls. Depending on the available data, a given study could contribute data relevant to one or more categories of injurious falls. A pooled rate ratio was estimated for each category of injurious falls based on random effects models.

Results 17 trials involving 4305 participants were eligible for meta-analysis. Four categories of falls were identified: all injurious falls, falls resulting in medical care, severe injurious falls, and falls resulting in fractures. Exercise had a significant effect in all categories, with pooled estimates of the rate ratios of 0.63 (95% confidence interval 0.51 to 0.77, 10 trials) for all injurious falls, 0.70 (0.54 to 0.92, 8 trials) for falls resulting

in medical care, 0.57 (0.36 to 0.90, 7 trials) for severe injurious falls, and 0.39 (0.22 to 0.66, 6 trials) for falls resulting in fractures, but significant heterogeneity was observed between studies of all injurious falls ($I^2=50\%$, $P=0.04$).

Conclusions Exercise programmes designed to prevent falls in older adults also seem to prevent injuries caused by falls, including the most severe ones. Such programmes also reduce the rate of falls leading to medical care.

Introduction

Fall related injuries are common,¹⁻³ result in considerable healthcare utilisation, and are a major cause of long term pain and functional impairment among older adults.⁴ They also increase considerably the risk of discharge to a nursing home⁵ and have a high economic cost.⁶

It has been established that well designed exercise programmes can prevent falls in older adults living at home.⁷⁻⁹ However, evidence that these programmes can also prevent injuries caused by falls is poor. This void is partly because most previous trials were underpowered to examine the effect of exercise on injurious falls, in particular the most severe falls. In a supplementary analysis, the recently updated Cochrane review of interventions for preventing falls in older adults living at home examined the effect of exercise on fractures specifically.⁷ This analysis, which was based on six trials, showed that fall

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prevention exercise programmes are associated with a significantly lower risk of fractures.

To our knowledge, no review or meta-analysis has examined the effect of fall prevention exercise programmes on other injurious falls outcomes that are common and that can also have important medical, psychological, and economic consequences. Besides causing fractures or other serious injuries, falls leading to medical care ought to be considered since their cost to society is high and their burden on the healthcare system heavy.^{4,5} Even falls causing relatively minor injuries are important to consider, as they too may have serious consequences, such as diminished self confidence, social isolation, and restriction on activity, which in turn will accelerate functional decline and increase the risk of placement in a nursing home.⁴

Using a meta-analytical approach, we reviewed the current evidence about the effect of exercise interventions designed for community dwelling older adults on different outcomes of injurious falls, based on severity or medical care. There is no consensus about the outcomes of fall related injuries that should be evaluated in controlled trials, and published trials reporting injurious falls use quite different definitions.¹⁰

Methods

An essential first step of our work was to group definitions of injurious falls found in the studies selected for this review into more homogeneous categories to allow pooling of data. This systematic review was conducted in accordance with the PRISMA guidelines.¹¹

Search strategy and study selection

We searched the Cochrane Library, PubMed, Embase, and CINAHL to identify relevant studies published in peer reviewed journals from inception to July 2013. In the Cochrane Library the search terms were: (fall) and (exercise or tai chi or training or physical activity) excluding (Alzheimer or Parkinson's or dementia or nursing home or protocol or athletes) in the title or abstract of trials, with the word "prevention" in the text and the word variations option enabled. We also selected references in relevant reviews for screening.¹²⁻¹⁴ Two investigators (FEK, PDM) independently screened the titles, abstracts, and full text of identified papers to determine their eligibility for inclusion (see supplementary file). Discrepancies were resolved by discussion.

Inclusion criteria were randomised controlled trials of fall prevention exercise interventions, published in English or French, targeting community dwelling adults aged over 60 years, and providing quantitative data on injurious falls, serious falls, fall related injuries, or fall induced fractures. We included studies where exercise was compared with no intervention (usual activity or usual care) or a placebo control intervention (for example, general health education classes, social visits, or a low intensity exercise programme not designed to modify the risk of falling). We excluded studies in which exercise was part of a multifactorial programme such that participants received other interventions (for example, home management, visual treatment) in addition to exercise, and when participants were selected for a specific neurodegenerative disease or any other characteristic that greatly affected the risk of falling but was not correctable by exercise (such as severe visual impairment).

Data extraction and quality assessment

We used a form designed for this review to extract data on study and intervention characteristics, quality assessment, and

outcomes (see supplementary file). The taxonomy for fall prevention interventions developed by the Prevention of Falls Network Europe (ProFaNE)¹² was used to describe the characteristics of the interventions provided (for example, participants' selection criteria, type of exercises, and intervention procedures). This tool uses internationally agreed criteria to evaluate systematically the content and format of fall prevention interventions. We also extracted the definitions and methods used to collect falls and to classify fall related injuries, as well as the number, rate, or risk ratio of injurious falls and any available data on the nature of the injuries. We contacted authors of included articles to obtain more detailed data on the outcomes of injurious falls (for example, if authors reported the number of participants with an injurious fall but not the total number of injurious falls, or data on falls resulting in fractures but not data on other injurious falls).

After reviewing the case definitions used in the selected studies, we sought to group definitions of injurious falls into more homogeneous categories to allow results to be compared across studies and the data to be pooled. The ProFaNE group recently proposed a standardised classification of injurious falls to be used in future randomised controlled trials.¹³ As a foundation for developing a retrospective classification of the definitions of injurious falls found in the studies selected for this review, we used the ProFaNE classification along with the standardised classification of Campbell and Robertson,¹³ which is the classification most often used in published trials of these interventions.¹⁴ We also recorded any reports of adverse effects associated with interventions.

We followed the recommendations of the Cochrane Collaboration¹⁵ to assess risk of bias in the following domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of the assessment of falls and injurious falls (detection bias), and incomplete outcome data (attrition bias). We also assessed bias in the recall of falls owing to unreliable methods of ascertainment,¹⁶ using the criteria developed for the Cochrane review of fall prevention trials.⁷ The methods used to confirm serious injurious falls were also examined: we judged self reports from participants to be at a high risk of bias, whereas we considered the use of medical records or radiography reports (for fractures) to be at low risk. Two authors (FEK, PDM) independently assessed the risks of bias and extracted data. Disagreement was resolved by consensus or adjudication by a third party.

Statistical analysis

The rate ratio of injurious falls was the outcome of interest. If the rate ratio was not presented in the article, we calculated it from the ratio of the total number of injurious falls divided by the total length of time falls were monitored (person years) in the two comparison groups. In cases where data were available only for people who had completed the study, or where the trial authors had stated there were no losses to follow-up, we assumed that these participants had been followed up for the maximum possible period. We estimated the standard error of the rate ratio by using the formula given in the Cochrane handbook.¹⁷

We used the generic inverse variance method in Review Manager (RevMan 5.1) to group the trial results and we compiled forest plots for each category of injurious falls. To allow for variability among the participants, type of exercise intervention, and outcome definitions we used a random effect model. We report the pooled rate ratios for each injurious fall outcome, along with 95% confidence intervals. We assessed heterogeneity with the Q test and the I² statistic.¹⁸

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We conducted a prespecified subgroup analysis based on fall risk at enrolment (a priori); that is, trials with participants selected for inclusion based on fall history or other specific risk factors for falling (at higher risk) compared with non-selected participants. We also explored the possible impact of risk of bias on statistically significant pooled estimates of exercise effect by removing studies of poorer quality—that is, those for which the risk of bias was unclear for at least three of the quality components considered, or the risk was at least unclear for one category and high for another. To explore the possibility of publication bias we constructed funnel plots of effect estimates against their standard errors for analyses that contained at least 10 data points.

Results

The search strategy produced 1011 potentially eligible papers. Based on titles and abstracts we sought the full text articles of 199 selected references. Ultimately this systematic review included 17 trials (fig 1).

Characteristics of included studies and interventions

The 17 studies in the meta-analysis included a total of 2195 participants randomised in the exercise groups and 2110 randomised in the control groups, with sample sizes in individual studies ranging from 53 to 486 participants. The mean age of the overall population was 76.7 years, and around 77% were women. Seven studies selected participants based on a higher risk of falls—that is, history of falling, age over 80 years, or physical limitations (as measured by simple functional tests).^{17 19 24} Fourteen trials delivered the exercise intervention in a group setting, and six of those supplemented the group sessions with home exercise. In the other three trials, the intervention consisted of individualised exercises delivered at home.^{13 22 29} Tai Chi was the exclusive exercise intervention in two of the studies^{24 27}; the rest of the interventions included a gait, balance, and functional training component. Most also included strength/resistance training exercises. One study compared two similar multiple component exercise interventions, one with added endurance training, with the control group.²¹ In the analysis, the two exercise groups were combined to create a single pairwise comparison (intervention versus control). Table 1 summarises the characteristics of the included studies.

Classification of injurious falls

The definition and classification of injurious falls varied substantially and most trials did not provide a reference for their definition. Injurious falls usually included diverse consequences, ranging from relatively minor injuries such as bruises or abrasions to fractures or other serious injuries requiring hospital admission.^{19 27 28 29} Most often the definition referred to either the presence of symptoms or the use of medical care.^{13 19 23 24 28} In other cases, injurious falls meant simply any self reported physical consequence of a fall, without any details.^{20 21 24 28 30} Some definitions specifically required the use of medical care,^{23 25 26 28 31 32} by using non-specific terms such as “fall for which medical care was sought,” “falls requiring medical care/medical attention,” or “medical consultations/visits.” When serious injuries were distinguished or specifically reported, their definition was more homogeneous across studies. Such injuries usually included fractures, severe soft tissue injuries requiring suturing, or other injuries leading to hospital admission.^{22 24 26 27 31} Some studies reported only fractures.^{33 34}

Based on our review of case definitions used in the 17 studies, we distinguished four categories of injurious falls: those resulting in any reported consequences, including specific symptoms (ranging from bruises and cuts to more serious injuries such as fractures) or medical care; those resulting in medical care; those resulting in serious injuries such as fractures, head trauma, soft tissue injury requiring suturing, or any other injury requiring admission to hospital; and those resulting in fractures.

These categories represent increasingly specific subgroups of all injurious falls, which can also be considered to correspond to increasing levels of severity (except for those resulting in fracture, which is simply a specific type of serious injury).

Depending on the available data, a given study could contribute data relevant to one or more categories of injurious falls. Table 2 gives the definitions of injurious falls reported in each selected article (as a direct quotation), the category or categories of injurious falls in which it was classified for this review, and the rate ratio used in the corresponding analysis. For two studies, the rate ratio could not be calculated because the authors provided only the number of participants who had an injurious fall (rather than the number of such falls). In these cases, we used the ratio of the risk of at least one injurious fall in both groups instead. Of note, the outcomes of injurious fall in those studies were severe injuries²⁹ and fractures,²⁴ two outcomes that are relatively rare, so that the risk ratio was likely to be close to the rate ratio.

Methodological quality

Table 3 shows the results of the analysis of risk of bias. Although few studies were judged at high risk in any one domain, the quality of some studies could not be judged with any certainty in several domains. Prospective daily calendars returned monthly are the preferred method for recording falls,⁴⁵ and most of the trials used this method. However, only six of the 11 trials that reported data on serious injuries used medical records to confirm the injury.

Effect of exercise on injurious falls

Figure 2 shows the forest plots of the exercise effect estimate by category of injurious fall. Most of the exercise interventions tended to reduce injurious falls in all categories. Ten trials provided figures for all injurious falls; the pooled estimated rate ratio was 0.63 (0.51 to 0.77, $P=50\%$, $P=0.04$). The pooled estimate for falls resulting in medical care was 0.70 (0.54 to 0.92, $P=20\%$, $P=0.27$, eight trials) and for falls resulting in serious injuries was 0.57 (0.36 to 0.90, $P=46\%$, $P=0.09$, seven trials). Exercise seemed to significantly decrease the rate of falls resulting in fractures as well, with a pooled effect of 0.39 (0.23 to 0.66, $P=0\%$, $P=0.96$, six trials).

Sensitivity and subgroup analyses

To explore the possible impact of risk of bias on the exercise effect, we removed from the analyses studies for which the risk of bias was unclear for at least three of the quality components considered,^{19 27 30 34} or for which the risk was at least unclear for one component and high for another.^{22 24 30 32} This barely changed the pooled estimate of the effect of exercise in any of the four injurious fall categories, but it greatly reduced the heterogeneity between studies included in the analysis of all injurious falls (rate ratio 0.69, 95% confidence interval 0.58 to 0.82, $I^2=26\%$, $P=0.22$, eight trials).

In the subgroup analysis of the effect of exercise in reducing injurious falls based on risk of falls at enrolment, no significant

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difference was found in pooled estimates between trials with participants selected for their higher risk of falling^{11 19 21 24} and trials with unselected participants,^{22 25 26 30} in any of the four categories.

Publication bias

The funnel plot constructed from the 10 trials included in the analysis of all injurious falls shows a barely asymmetrical scatter (fig 3||).

Adverse reactions

A total of eight participants in two studies reported brief temporary musculoskeletal discomfort related to exercise.^{28 31} No other adverse events, in particular no fall related injuries occurring during the exercise sessions, were reported in any of the included studies. Only six trials specifically reported the absence of adverse reactions.

Discussion

This systematic review provides evidence that fall prevention exercise programmes for older people not only reduce the rates of falls but also prevent injuries resulting from falls in older community dwelling people. The protective effect seems most pronounced for the most severe fall related injuries: the estimated reduction is 37% for all injurious falls, 43% for severe injurious falls, and 61% for falls resulting in fractures.

Many of the risk factors for falls and fall induced injuries are similar.³² These factors are correctable by well designed exercise programmes, even in the very old and frail.^{26 34 35} All exercise programmes that have proved to be effective for fall prevention (and all trials included in this review) emphasise balance training, and there is now ample evidence that this type of programme improves balance ability.^{17 36} However, most programmes are multicomponent—that is, also include other types of exercise such as gait and functional training, strengthening exercises, flexibility, and endurance. There is evidence that these types of interventions can improve reaction time, gait, muscle strength, coordination, and overall physical functioning as well as cognitive functions, especially executive function.^{15 28 37} It is therefore thought that exercise prevents injurious falls not only by improving balance and decreasing the risk of falling, but also by improving cognitive functioning,⁴¹ and the speed and effectiveness of protective reflexes (such as quickly extending an arm or grabbing nearby objects) or the energy absorbing capacity of soft tissues (such as muscles), thereby diminishing the force of impact on the body.^{48 49} Hence, for any given initial energy of a fall, improved protective responses should decrease the severity of the resulting trauma, which may explain why the estimated protective effect of exercise is stronger for severe injurious falls than for all injurious falls, the latter including severe but also minor and moderate injuries.

Although exercise reduces the severity of injury, the pooled effect of exercise on reducing all injurious falls (37%) was larger than the effect of exercise on falls resulting in medical care (30%) (which are presumably more severe). However, medical care seeking behaviour is influenced by the type and availability of care and sociodemographic characteristics as well as by other personal factors such as personality, pain tolerance, and anxiety.^{42 43} Accordingly, the mere fact that medical care was sought does not necessarily imply that an injury was more severe, although this is probably less true when different categories of injurious falls are examined within the same

population. Of the 10 studies included in the analysis of all injurious falls, five also contributed to the analysis of falls resulting in medical care,^{11 21 29 36 38} and three also contributed to the analysis of severe injurious falls.^{12 24 36} Within these studies, the point estimate of the effect of exercise decreased from all injurious falls to falls resulting in medical care for all studies but one, and from falls resulting in medical care to severe injurious falls for all studies. These results support the argument that exercise reduces the severity of the injuries caused by falls.

Other risk factors are specific to the risk of trauma during a fall, and correction of these factors by exercise may also help explain the larger protective effect of exercise on serious injuries such as fractures. In particular, low bone mass is a major determinant of the risk of fracture once a fall begins. In three of the five trials included in the analysis of fall related fractures,^{29 33 38} the intervention was specifically designed to improve bone mass and hence included high intensity impact exercise in addition to balance, gait, and functional exercises. It resulted in a significant positive effect on bone mass at bone sites that varied with the study. However, these interventions were tested in women who were on average less than 75 years of age and did not have specific risk factors for falling. Hence, they may not be appropriate for older people aged more than 75 years, who are at the highest risk of falls and fractures, especially hip fractures.

The large estimated pooled effect of more moderate intensity exercise training on serious injuries found in this meta-analysis suggests that reducing the risk of falling and improving protective responses during a fall are important and feasible means of preventing fractures and other serious injuries in elderly people, as others have emphasised.^{44 45} This finding is especially important because large epidemiological studies have shown that most fractures in the population occur in people at moderate “bone risk” for their age.^{46 50} Hence, while prescription of antioestrogenic drug treatments is currently recommended for older people with low bone mass, who are at the highest risk of fracture, additional effective strategies that can be proposed to larger segments of the elderly population will be necessary to significantly reduce the burden of fractures in this population.⁵¹ Fall prevention exercise training seems to be one such strategy.

Comparisons with other reviews

One group of researchers conducted an individual level data meta-analysis of the results of four trials conducted by their fall prevention research group to estimate the overall effect of the Otago individualised strength and balance exercise programme on falls and injuries.¹⁴ The study demonstrated a 35% reduction in the risk of an injurious fall (moderate or serious), a result similar to that presented here, but it failed to show a significant reduction in serious fall related injuries. A more recent review including three additional trials of the Otago exercise programme,³⁷ failed to support the previous finding that the programme significantly reduced the risk of injurious falls, possibly because of a lack of access to individual level data or because of differences in the implementation and supervision of the programme (as suggested by the significantly lower compliance rates reported in the three additional trials than in the first four).

The recent Cochrane review of fall prevention interventions conducted a specific analysis to examine the effect of exercise interventions on the risk of fall related fractures and obtained similar results (pooled relative risk 0.34, 95% confidence interval 0.18 to 0.63).⁷ Of the six trials included in the Cochrane

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analysis, five are also included in our analysis. We excluded the one study because participants were recruited in the hospital while in the acute phase of an injury (hip fracture) so that the results of this trial may not be comparable to those not recruiting on the basis of an injury.³³ Inversely, we included one study³⁹ that compared an exercise intervention including balance, gait, and strengthening and flexibility exercises to a “wellness” exercise programme designed not to affect the risk of falling, whereas this study was not considered in the Cochrane analysis of fracture risk.

Strengths and limitations of this review

Heterogeneity was notable among studies included in the analysis of all injurious falls ($P=50\%$, $P=0.04$). Although no significant heterogeneity was detected in the analysis of severe injurious falls, the inconsistency was also moderately large ($P=46\%$, $P=0.09$). Pooled data from studies with significant heterogeneity require cautious interpretation because this indicates the possibility of meaningful differences between these studies. Although this review focused on interventions based solely on exercise and targeting specifically community dwelling elderly people, the selected interventions are still quite diverse, in particular in terms of intervention components (type of exercises, intensity, frequency, mode of delivery, and total duration) and inclusion criteria for participants. Similar or even larger measures of heterogeneity have also been reported in other meta-analyses of fall prevention exercise interventions.^{7 34}

To explore possible reasons for heterogeneity, we carried out pre-planned subgroup analyses based on fall risk at enrolment and found no difference in pooled estimates between trials with participants selected for their higher risk of falling versus lower risk (unselected), for any of the four categories of injurious falls. Among intervention components, the type of exercise seems to be a key factor that influences effectiveness against falls: interventions including a balance training component seem to be more effective.^{7 34 35} One study found that the intensity of the balance training component was also important: interventions that include moderate to high challenging exercises (that is, standing exercises in which people sought to stand with their feet closer together or on one leg, to minimise use of their hands to assist, and to practice controlled movements of the centre of mass) are more effective in reducing falls than interventions that include less challenging balance exercises.⁹ All interventions included in this review include a balance training component, hence we performed an additional subgroup analysis by comparing trials where the exercise programme provided a moderate or high challenge to balance (based on Sherrington's definition),^{13 19 21 23 27 31 33} versus a low challenge.^{22 28 36 32 34} No significant difference in exercise effect was found between the two subgroups with regard to the reduction in all injurious falls or falls resulting in medical care. For severe injurious falls and falls resulting in fractures, there were not enough studies to perform subgroup analyses by intensity of balance training. The relatively small number of studies included in this review did not allow us to perform additional subgroup analyses exploring the effect of other components within interventions or other factors related to the way interventions were implemented that might have affected results.

Although we tried to reduce heterogeneity in the definitions of injurious falls as much as possible by grouping them in more homogeneous categories, remaining inconsistency in definitions may also help explain the heterogeneity observed between studies. In the category of all injurious falls, in particular, several studies used imprecise definitions of injurious falls^{20 22 34 39 36} but were nevertheless included in the analysis since this category

is the largest and refers to any types of physical consequences of a fall. We performed a sensitivity analysis excluding from the analysis of this category studies that used imprecise definitions: the resulting pooled rate ratio was similar to that obtained in the main overall analysis (0.69, 0.53 to 0.90, $I^2=49\%$, $P=0.10$) and indicated that our results are robust to differences in outcome definitions between studies. Results of the sensitivity analysis excluding trials judged to be at higher risk of bias in all four categories of injurious falls barely changed the pooled effect estimates and indicates that our results are also robust to key risks of bias.

The funnel plot of the 10 trials contributing to the analysis of all injurious falls showed a barely asymmetrical scatter.

Asymmetrical funnel plots may indicate publication bias or may be due to exaggeration of treatment effects in small studies of low quality.¹⁵ However, the funnel plot in this analysis showed no clear evidence of “small study effects.” Note that almost all the trials included in this review were designed to prove that exercise has an effect on the fall rate and not on the rate of injurious falls. Among the 17 studies considered in this review, eight did not demonstrate that exercise had a significant effect on falls. Moreover, the pooled effect of exercise on the rate ratio of falls was 0.68 (95% confidence interval 0.61 to 0.77), which is similar to the effect of exercise reported in the Cochrane review.⁷ These points suggest that the trials included in this review, because they presented data on fall related injuries, do not represent a special selection of fall prevention exercise trials biased towards “positive” trials for all falls. None the less, we cannot exclude the possibility that trials are more likely to report injurious falls when there tend to be a positive effect on injurious falls. It is also possible that some trials did not report data on injurious falls simply because these data were not collected.

Only minor adverse reactions were reported in two of the 17 included studies. However, close to half of the selected studies did not even mention intervention adverse effects. It has also been suggested that exercise fall-prevention programmes may have adverse psychological effects that may affect the quality of life (for example, through self imposed activity restriction).^{36 37} Some studies have reported the effect of the intervention on fear of falling, physical activity levels, or other dimensions of quality of life.^{39 21 24 26 27} Their results show either no effect or a tendency towards a beneficial effect of the intervention on these outcomes, in particular a reduction in fear of falling. More complete data on adverse physical reactions as well as on psychological and quality of life outcomes would improve our ability to judge the overall benefit of exercise fall prevention interventions. Another limitation of the included studies is that they often lack information on “intermediate” outcomes such as gait, balance, and other physical or cognitive functions, which would help us to understand how exercise “works” and design optimum programmes. Future trials should also provide more detailed descriptions of implementation procedures, whether planned or unplanned, so that readers can judge the applicability of the programme in different settings or on a larger scale.

Conclusion and recommendations

The results presented in this paper show a positive effect of exercise on injurious falls, including the most severe falls and those that result in medical care—that is, those with the greatest consequences for people's health and use of resources. These results should provide useful additional evidence for healthcare providers to encourage participation in exercise fall prevention programmes, and further justification for decision makers to provide funding for those programmes.

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Systematic reporting of falls and injuries should be implemented in future randomised controlled trials, where the different levels of severity of the injury should be standardised and defined in advance, to improve the comparison between studies and subsequently the accuracy of pooled estimates for each category of falls. Future trials should also aim to deal with some of the limitations of published studies, in particular by providing data on other important outcomes (physical and cognitive functional capacities, psychological outcomes, and quality of life) and a thorough description of the implementation process.

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Ethical approval: Not required.

Data sharing: No additional data available.

Transparency: The lead author affirms that the manuscript is an honest, accurate, and transparent account of the review being reported; that no important aspects of the review have been omitted; and that any discrepancies from the review as planned have been explained.

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What is already known on this topic

Falls and the resulting injuries are among the most serious and common medical problems experienced by older adults
Well designed exercise programmes can prevent falls in older adults living at home
But there is no clear evidence that these programmes can also prevent severe or more moderate injuries caused by falls.

What this study adds

Exercise programmes designed to prevent falls in older community dwelling people seem to reduce injuries caused by falls, including the most severe injuries
Such programmes also seem to reduce falls resulting in medical care

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Tables

Table 1 | Study characteristics

Trial	No randomised (% women)	Mean age (years)	Participant selection criteria	Type of exercise*	Moderate to high challenge to balance†	Mode of delivery	Exercise sessions frequency	Programme duration	Follow-up period (for recording fall data) (months)	Comparison group	Rate ratio for all falls (fall rate in controls (person/year))
Barnett 2003 ²⁶	163 (67)	74.9	≥65, ≥1 risk factors for falling	Gait, balance, and functional training; strengthening exercises; flexibility	Yes	Home exercise+group exercise	1 hour/week plus home exercise	1 year	12	No intervention	0.60 (0.36 to 1.00) (0.95)
Campbell 1997 ¹¹	233 (100)	84.1	≥80	Gait, balance, and functional training; strengthening exercises; flexibility; general physical activity	Yes	Home exercise	30 minutes×3/week	1 year	12	Social visit by research nurse	0.68 (0.51 to 0.89) (1.34)
Cornillon 2002 ²¹	303 (83)	71	≥65, activities of daily living independent	Gait, balance, and functional training	Yes	Group exercise	1 session/week	8 weeks	12	No intervention	0.82 (0.58 to 1.17) (0.47)
Fitzharris 2010 ²⁸	1090 (59.8)	76.1	≥70	Gait, balance, and functional training; strengthening exercises; flexibility	No	Home exercise+group exercise	1 hour/week+daily home exercise	15 weeks	18	Factorial design; all groups that did not have exercise	0.79 (0.66 to 0.94) (1.14)
Freiburger 2012 ²⁷	207 (44)	75.1	≥70, fell in past 6 months or fear of falling	Gait, balance, and functional training; strengthening exercises; endurance	Yes	Group exercise	1 hour×2/week	16 weeks	24	No intervention	0.82 (0.62 to 1.08) (0.67)
Haines 2009 ¹	53 (60)	80.7	≥65, gait instability or use of mobility aid; discharged from hospital	Gait, balance, and functional training; strengthening exercises; 3D (modified Tai Chi exercises)	Yes	Home exercise	3 to 7/week	18 weeks	6	No intervention	0.72 (0.33 to 1.57) (1.09)
Kemmler 2010 ²⁹	246 (100)	69.1	≥65	Gait, balance, and functional training; strengthening exercises; flexibility	No	Home exercise+group exercise	60 minutes×2/week+home exercise (20 minutes×2/week)	18 month	18	Low to moderate intensity (low frequency) "Wellness programme"	0.60 (0.47 to 0.76) (0.28)
Korpelainen 2006 ²⁵	160 (100)	73	Low bone mineral density (hip T score <-2)	Gait, balance, and functional training; strengthening exercises; 3D (dancing)	Yes	Home exercise+group exercise	1 hour/week+home exercise (20 minutes daily)	18 month	30	Twice yearly seminars on health related topics	0.79 (0.59 to 1.06) (0.53)
Li 2006 ²⁴	256 (70)	77.5	≥70, walks independently	3D (Tai Chi)	Yes	Group exercise	1 hour×3/week	26 weeks	6	Low level stretching	0.45 (0.29 to 0.69) (0.53)
Luukinen 2007 ²²	486 (78)	88	≥85, ≥1 risk factor for falling, or ≥2 falls in past year	Gait, balance, and functional training; flexibility; general physical activity; other	No	Home exercise+group exercise	Individually prescribed, frequency depends on individuals	16 months	16	Asked to visit general practitioner without written intervention form	0.93 (0.80 to 1.09) (1.15)

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Table 1 (continued)

Trial	No randomised (% women)	Mean age (years)	Participant selection criteria	Type of exercise*	Moderate to high challenge to balance†	Mode of delivery	Exercise sessions frequency	Programme duration	Follow-up period (for recording fall data) (months)	Comparison group	Rate ratio‡ for all falls (fall rate in controls (person/year))
McRae 1994 ¹⁶	80 (100)	71.1	≥60	Gait, balance, and functional training	No	Group exercise	1 hour×3/week	1 year	12	Group discussions (health promotion, safety education)	1.28 (0.90 to 1.83) (—)
McMurdo 1997 ¹⁷	118 (100)	64.5	≥60, postmenopausal	Gait, balance, and functional training; strengthening exercises	No	Group exercise	45 minutes×3/week	30 weeks	24	1000 mg calcium carbonate daily (also in intervention group)	0.53 (0.28 to 1.00) (—)
Means 2005 ¹⁸	338 (57)	73.5	≥65, able to walk at least 30 feet without assistance	Gait, balance, and functional training; strengthening exercises; flexibility	No	Group exercise	90 minutes×3/week	5 weeks	6	Group seminars on non-health related topics	0.41 (0.27 to 0.62) (1.18)
Robertson 2001 ¹⁹	240 (68)	80.9	≥75	Gait, balance, and functional training; strengthening exercises; flexibility; general physical activity	Yes	Home exercise	Individually prescribed; at least 3 times a week (about 30 min/session×walking 2×/week)	1 year	12	Usual care	0.54 (0.3 to 0.90) (1.01)
Skelton 2005 ²⁰	100 (100)	72.8	≥65, ≥3 falls in past year	Gait, balance, and functional training; strengthening exercises; flexibility; endurance	Yes	Home exercise+group exercise	1 hour/week+home exercise (30 minutes×2/week)	36 weeks	9	Home based seated exercises not designed to improve fitness or balance	0.69 (0.50 to 0.96) (3.12)
Smulders 2010 ²¹	96 (94)	71	≥65, osteoporosis, ≥1 falls in past year; able to walk 15 minutes without device	Gait, balance, and functional training; general physical activity; endurance; other	Yes	Group exercise	11 exercise sessions	5.5 weeks	12	Usual care	0.61 (0.40 to 0.94) (1.18)
Wolf 1996 ²²	136 (81)	76.2	≥70, ambulatory	3D (Tai Chi)	Yes	Group exercise	45 minutes/week	15 weeks	8	Group discussions on topics of interest to older people	0.67 (0.41 to 1.09) (1.82)

*ProFaNe classification of exercise intervention.²³†Moderately challenging—two of the following criteria, or highly challenging—all three criteria: movement of the centre of mass, narrowing of the base of support, and minimising limb support.²⁴

‡Ratio of risk of being a faller in two comparison groups.

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Table 2| Injurious falls: extracted definitions and subsequent categorisation with estimates of intervention related fall reduction

Trial	Extracted definitions	Rate Ratio of injurious falls			
		A: all injurious falls	B: falls resulting in medical care	C: falls resulting in serious injuries	D: falls resulting in fractures
Barnett 2003 ¹¹	"Falls that resulted in bruises, strains, cuts and abrasions, back pain and fractures" (A)	0.73 (0.46 to 1.17)	—	—	—
Campbell 1997 ¹²	Falls were classified as resulting in "serious" injury if the fall resulted in a fracture, admission to hospital or stitches were required, "moderate" injury if bruising, sprains, cuts, abrasions or reduction in physical function for at least three days resulted, or if the participant sought medical help, (A=moderate+severe), (C=severe). "Falls for which medical care sought" (B)	0.45 (0.30 to 0.67)	0.97 (0.58 to 1.64)	0.82 (0.37 to 1.79)	—
Cornillon 2002 ¹³	"Cumulative number of medical consultations" (B). "Falls requiring hospitalization" (C)	—	1.16 (0.57 to 2.37)	0.15 (0.02 to 1.16)	—
Fitzharris 2010 ¹⁴	"Cut, scrape, gash, bruise or fracture; a head injury resulted or where the fall resulted in hospitalization" (A). "Falls requiring medical care" (B)	0.85 (0.70 to 1.04)	0.74 (0.50 to 1.10)	—	—
Freiberger 2012 ¹⁵	"Number of injurious falls" (A)	0.70 (0.46 to 1.08)	—	—	—
Haines 2009 ¹⁶	"Falls with self-reported physical injury" (A). "Falls resulting in medical review (general practitioner or hospital medical officer if fall took place in a hospital)" (B). "Falls resulting in fracture" (D)	0.82 (0.32 to 2.12)	0.34 (0.07 to 1.62)	—	0.88 (0.06 to 9.70)
Kemmler 2010 ¹⁸	"Subjects who experienced injurious falls" (A). "Fractures due to falls" (D)	0.65† (0.45 to 0.92)	—	—	0.49 (0.18 to 1.30)
Korpelainen 2006 ¹¹	"Fall-related fractures" (D)	—	—	—	0.36 (0.14 to 0.93)
Li 2005 ¹⁹	"If falls resulted in fractures, head injuries, sprains, bruises, scrapes, or other serious joint injuries or if the participant sought medical care" (A). "Medical care visits resulting from a fall" (B). "Severe falls requiring medical attention" (C)	0.40 (0.17 to 0.95)	0.31 (0.11 to 0.85)	0.28* (0.09 to 0.88)	—
MacRae 1994 ²⁰	"Fall related injury requiring medical attention" (B)	—	0.18 (0.02 to 1.77)	—	—
Lukkinen 2007 ²¹	"The injuries included fractures, dislocations and soft tissue injuries needing suturing and even more severe injuries" (C)	—	—	0.94 (0.60 to 1.49)	—
McMurdo 1997 ²²	Number of people with fractures (D)	—	—	—	0.22* (0.01 to 4.59)
Means 2005 ²³	"Any detectable residual adverse physical change persisting beyond 1 hr after the fall" (A)	0.35 (0.22 to 0.56)	—	—	—
Robertson 2001 ²⁴	"If bruising, sprains, cuts, abrasions, or reduction in physical function for at least three days resulted or if the participant sought medical help (moderate injuries). "Fall resulted in a fracture, admissions to hospital with an injury, or stitches were required" (severe injuries) (A=moderate+severe), (C=severe). "Falls for which medical care sought" (B)	0.80 (0.53 to 1.21)	0.64 (0.35 to 1.17)	0.22 (0.04 to 0.95)	0.28 (0.06 to 1.32)
Skelton 2005 ²⁵	"Falls requiring medical attention" (B)	—	0.60 (0.33 to 1.08)	—	—
Smulders 2010 ¹⁸	"Self-reported injuries" (A). Fractures, concussion and wounds that needed suturing (C). Fractures reported as a consequence of a fall (D)	0.55 (0.32 to 0.96)	—	0.19 (0.02 to 1.57)	0.31 (0.03 to 2.93)
Wolf 1996 ²⁷	"Fall that resulted either in fractures; head injuries requiring hospitalization; joint dislocations; sprains defined as injury to a ligament when joint carried through range of motion greater than normal; other non-specified serious joint injuries; and lacerations required sutures" (C)	—	—	0.69 (0.42 to 1.12)	—
Pooled rate ratio		0.63 (0.52 to 0.77)	0.70 (0.53 to 0.92)	0.57 (0.37 to 0.90)	0.39 (0.23 to 0.66)

*Risk ratio of at least one injurious fall (rate ratio unavailable).

†Unpublished data on total number of injurious falls provided by authors.

RESEARCH

Table 3| Assessment of risk of bias in included studies

Trial	Random sequence generation	Allocation concealment	Methods of ascertaining falls	Blinding of falls and injurious fall assessment	Incomplete outcome data	Methods of ascertaining serious injuries
Barnett 2003 ¹⁵	Unclear	Low	Unclear	Unclear	Low	NA
Campbell 1997 ¹²	Low	Low	Low	Unclear	Low	Low
Cornillon 2002 ¹⁴	Low	Unclear	Low	Unclear	Low	Unclear
Fitzharris 2010 ²⁸	Low	Low	Low	Low	Unclear	NA
Freiberger 2012 ²⁵	Low	Low	Low	Low	Unclear	NA
Haines 2009 ¹⁶	Low	Low	Low	Low	Low	High
Kemmler 2010 ²	Low	Low	Low	Low	Low	High
Korpelainen 2006 ²³	Low	Low	High	Low	Low	Low
Li 2006 ¹⁸	Low	Unclear	Low	Low	Low	Low
Luukinen 2007 ²⁶	Low	Unclear	High	Low	Low	Low
MacRae 1994 ¹⁷	Unclear	High	Low	Unclear	High	NA
McMurdo 1997 ²⁴	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Means 2005 ²²	Low	Unclear	Low	Low	High	NA
Robertson 2001 ¹³	Low	Low	Low	Low	Low	Low
Skelton 2005 ²¹	Unclear	Unclear	Low	Low	Low	NA
Smulders 2010 ¹⁹	Unclear	Unclear	Low	Low	Low	High
Wolf 1996 ²⁷	Low	Unclear	Low	Unclear	Unclear	Low

Figures

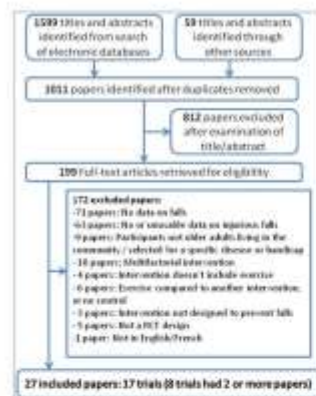


Fig 1 Flow chart of study identification process

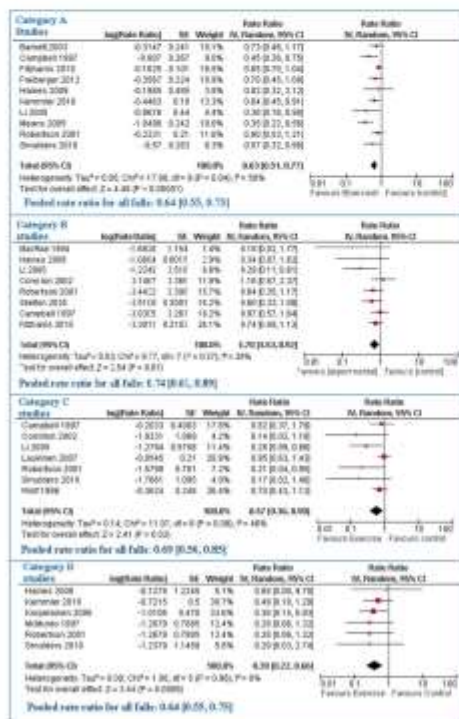


Fig 2 Forest plots of studies for four injurious fall categories: A, all injurious falls; B, falls resulting in medical care; C, falls resulting in serious injuries; and D, falls resulting in fractures

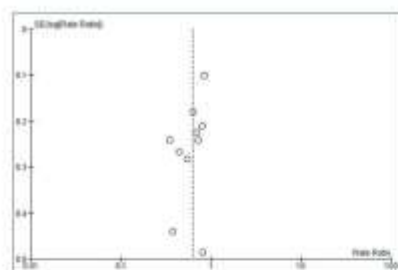


Fig 3 Funnel plot of studies included in analysis of all injurious falls

Appendix 3: Reporting checklists used



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed.1000097

For more information, visit: www.prisma-statement.org

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
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.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
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.	
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.	
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.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
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).	
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.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
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.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
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.	

Page 1 of 2



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	_____
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	_____
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	_____
	2b	Specific objectives or hypotheses	_____
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	_____
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	_____
Participants	4a	Eligibility criteria for participants	_____
	4b	Settings and locations where the data were collected	_____
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	_____
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	_____
	6b	Any changes to trial outcomes after the trial commenced, with reasons	_____
Sample size	7a	How sample size was determined	_____
	7b	When applicable, explanation of any interim analyses and stopping guidelines	_____
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	_____
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	_____
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	_____
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	_____
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	_____
CONSORT 2010 checklist			
			Page 1
Statistical methods		assessing outcomes) and how	_____
	11b	If relevant, description of the similarity of interventions	_____
	12a	Statistical methods used to compare groups for primary and secondary outcomes	_____
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	_____
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	_____
	13b	For each group, losses and exclusions after randomisation, together with reasons	_____
Recruitment	14a	Dates defining the periods of recruitment and follow-up	_____
	14b	Why the trial ended or was stopped	_____
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	_____
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	_____
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	_____
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	_____
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	_____
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	_____
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	_____
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	_____
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	_____
Other information			
Registration	23	Registration number and name of trial registry	_____
Protocol	24	Where the full trial protocol can be accessed, if available	_____
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	_____

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming; for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	_____	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	_____	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	_____	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	_____	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	_____	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	_____	_____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	_____	_____

TIDieR checklist

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	_____	_____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	_____	_____
	MODIFICATIONS		
10.*	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____	_____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_____	_____
12.*	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	_____	_____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** - use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see [BMJ 2014;348:g1687](#)) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see [www.consort-statement.org](#)) as an extension of **Item 5 of the CONSORT 2010 Statement**. When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see [www.spirit-statement.org](#)). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see [www.equator-network.org](#)).

TIDieR checklist

Appendix 4: Description of the ‘Ossébo’ fall and injury prevention exercise programme

Overall description

Programme duration: 2 years/8 quarters

Weekly frequency: 1 group session (1hour) + 1 individual home session

Number of people/session: 15 max

Target population: women 75-85 years old with diminished balance and gait functional capacities (see specific study inclusion/exclusion criteria)

The Ossébo exercise programme was specifically conceived for the Ossébo randomised controlled trial and is based on a careful analysis of the literature (in particular, description of specific fall-prevention programmes that demonstrated their effectiveness (published or requested from the authors); various published and on-line guidelines and reference articles on exercise for fall management) and on the long (> 15 years) field experience of the SIEL BLEU group in the design and implementation of fall-prevention programmes among older adults in the community (www.sielbleu.org).

The programme’s technical content has been described in detail in a reference document written by D. Lutz (Product Director) and C. Hénon (Scientific programmes coordinator) for the SIEL BLEU group and intended for the SIEL BLEU instructors involved in the Ossébo trial (French version available upon request to P. Dargent-Molina). The programme description that follows has been extracted from this document.

The programme was designed to ensure a progression in the difficulty and intensity of the exercises over the 2-year intervention period. It is standardised so that instructors in each study centre deliver the same intervention to all exercise groups. However, instructors were allowed to make some adaptations to the programme in order to take into account differences in progression between exercise groups.

General objectives

The Ossébo exercise programme has three general objectives:

1/ to improve physical factors that affect balance and contribute to a higher risk of falls and fall-induced injuries,

2/ to raise consciousness about behavioural factors that increase the risk of falling and bring awareness of “positive” behavioural changes,

3/ to foster long term balance training and physical activity maintenance

Improvement of physical factors involved in posture and balance control occurs through exercises aimed at:

- strengthening the hip-stabilising muscles, quadriceps, foot flexor/extensor muscles in an analytical as well as comprehensive way, and any muscle chain involved in a movement or posture for which balance is a key factor for its performance,
- mobilising target joints involved in actions specific to locomotion and in general skeletal strengthening,
- sharpening the perception of plantar sensations.

Raising awareness of the risk of falling and fall prevention through behavioural changes, accomplished through exercises aimed at helping women:

- to move better (e.g., standing movements, cross-steps, position changes, floor work)
- to be more attentive (e.g., perform all movements mindfully, training of peripheral vision)
- to become aware of one’s body in space (e.g., sharpen the reflexes, manage body weight).
- to analyse risk factors (e.g., understand balance mechanisms, lift an object safely, distribute loads)

Education for the long term preservation of balance aims at integrating some exercises and behaviours into the routines of daily living for a healthier lifestyle. A series of home exercises initially designed for group sessions are selected for individual self-directed home-based sessions. The aims are that the participants:

- memorise the exercises,
- become able to perform the exercises alone correctly,
- and practise regularly.

Technical contents

General framework:

The programme is divided in 8 terms, each corresponding to 12 sessions (one trimester). The framework of each term is shown in Table 1 (see next page). Reading the table vertically shows the sequence of exercises included in a session of a given term. Reading the table horizontally shows the use of a given exercise according to the terms. All exercises are individually described in the reference document. The general objectives of each term are shown in Table 2.

Progression of programme:

Two elements, considered below, combine to increase the programme's intensity over time:

- The increase in the number of repetitions and/or sets for a given exercise:

An increase in the number of times a person can perform a strength training exercise corresponds to an adaptive response to effort and can therefore be considered a sign of progress. However, the number of repetitions cannot increase indefinitely and adjustment will reach a ceiling level. Priority must be given to the preservation of the level of adjustment achieved, especially considering the possible breaks due to absences, vacations, and public holidays. The number of repetitions that is indicated for each exercise is a reference. It should be adapted depending on the general fitness level of the group and, for the home exercises, of the participant.

- The progression towards the acquisition of more global motor skills:

The first term will be devoted to learning the techniques to perform exercises correctly, and will allow the acquisition of isolated motor skills. Once acquired, these isolated skills will be combined into global exercises integrating several different skills during the following terms. Exercises will become more and more global with time (i.e., involve an increasing number of skills in combination).


Table 1: General framework of programme

Reading the table:

Vertically: exercise flow of a typical session in a given term

Horizontally: use of exercises according to the terms

	Stance	Domain	Description	Terms							
				1	2	3	4	5	6	7	8
↓	SITTING/ STANDING	Proprioception	Stimulate the soles of the feet with massage disks and massage balls	x	x	x	x	x	x	X	x
	SITTING	Joint mobilisation	Dorsiflexion, plantar flexion, Leg extensions , ‘bicycle movements’	x	x	x	x	x	x	x	x
	STANDING	Movement/ joint movement	Movements interspersed with joint movements in standing position				x	x	x	x	x
	STANDING	Moving/ muscle strengthening	Moves interspersed with muscle-strengthening exercises in standing position				x	x	x	x	x
	SITTING	Muscle strengthening	Squats onto chair	x	x	x	x	x	x	x	x
	STANDING	Muscle strengthening	Lunges/ chair		x	x	x				
	STANDING	Muscle strengthening	Lateral leg raises/ chair				x	x	x	x	x
	STANDING	Muscle strengthening	Calf raises			x	x	x	x	x	
	STANDING	Balance	Stand on one foot with or without hand support	x	x	x	x	x	x	x	x
	STANDING	Movement	Variety of movements, of foot / ground contact zones	x	x	x	x	x	x	x	x
	STANDING	Gait movements	Tandem walking, on lines, etc.	x	x	x	x	x	x	x	x
	STANDING	Cross steps	Various heights and lengths	x	x	x	x	x	x	x	x

	SITTING/ STANDING	Joint mobilisation	All joints of the upper limbs				x	x	x	x	x
	STANDING	Muscle strengthening	Upper limbs: deltoids, back, triceps				x	x	x	x	x
	STANDING/ ON THE FLOOR	High- kneeling lunge	From the standing position to all fours		x	x	x	x	x	x	x
	STANDING/ ON THE FLOOR	Low- kneeling lunge	Stand – on all fours – lie on back - stand			x	x	x	x	x	x
	STANDING/ ON THE FLOOR	<i>On all fours</i>	Cat/cow poses (arch back like a cat upwards and then arch spine downwards)				x	x	x	x	X
	ON THE FLOOR	Ground locomotion	Move a short distance: on all fours, forward, backward, to the side, repeat on buttocks				x	x	x	x	
	ON THE FLOOR	Transfers	On all fours to sitting, sitting to lying on stomach, lying on stomach to lying on back, back to stomach, stomach to sitting, sitting to all fours					x	x	x	x
	ON THE FLOOR	Joint mobilisation/ muscle strengthening	hip extensions					x	x	x	x
	ON THE FLOOR	Joint mobilisation/ muscle strengthening	Lateral leg raises while lying on back					x	x	x	x
	ON THE FLOOR	Stretching the quadriceps	Lying on the side					x	x	x	x
	ON THE FLOOR	Stretching the hamstring	Seated					x	x	x	x
	ON THE FLOOR	Stretching the	Lying on back					x	x	x	x

		glutes maximus										
	STANDING	Calf stretch	against a wall	X	X	X	X	X	X	X	X	X
	SITTING	Breathing exercises		x	x	x	x	x	x	x	x	x
		Games		As desired, in the end of the session or during recuperation								
		Technical explanations	balance, carrying loads, exercises	As desired, in the end of the session or during recuperation								

Table 2: General objectives of each term

Term	Objectives	Comments
1	<ul style="list-style-type: none"> - Create adherence to the study overall - Memorise exercises on chair destined to be home-based support exercises) - Design individual home-based support exercises 	<ul style="list-style-type: none"> - Start the intervention while taking into count the gradual arrival of some participants
2	<ul style="list-style-type: none"> - Maintain and consolidate the motor and technical skills acquired during the first cycle - Lunges/ chair - Moving to the floor: kneeling on one knee 	<ul style="list-style-type: none"> - The exercises seen in the first cycle are considered as acquired - Warm-up is done while sitting, in a more automatic manner (participants have memorised the exercises), and the instructor asks a participant to lead the warm-up phase at each session - Constraints (balls, glass of water, closed eye, etc.) are systematically introduced in the standing movement exercises.
3	<ul style="list-style-type: none"> - Maintain and consolidate skills and techniques acquired during the first 2 cycles - “Globalise” the exercises: from isolated acts (analytic individual exercises) towards the global motor act, while respecting the framework - Maintain participants’ adherence 	The third term is less strictly framed. Instructors can use their creativity and teaching skill in choosing the combinations of techniques and exercises, while respecting the general framework, as described.
4	<ul style="list-style-type: none"> - Maintain and consolidate skills and techniques acquired during the 3 previous terms - Strengthen the full musculature (in response to the possibility of a fall); add upper body work - Develop floor exercises (short moves) 	<ul style="list-style-type: none"> - Introduce upper limb gymnastics
5	<ul style="list-style-type: none"> - Develop the capacity to exercise longer - Transfers on floor 	Move from an activity purely dedicated to fall prevention towards a more general gymnastics and maintenance (although long term fall prevention remains the main objective)
6		
7		
8	Prepare the ‘post-Ossébo’	

Tailoring (adaption and changes to the programme content):

Instructors can change/adapt the following elements:

- The number of repetitions of a given exercise
- The presentation of an exercise (some exercises can be done with or without equipment)
- The total number of exercises, by adding games at the end of the session.

Instructors cannot change (without the consent of D Lutz, programme developer and supervisor) the following:

- The nature of an exercise
- The overall framework (combination and sequence of exercises) and objectives of any exercise cycle.

General instructions:

- Most of the exercises are performed barefoot or with women wearing only socks (without shoes or slippers). However, shoes are needed for certain exercises.
 - Allow short breaks for the women to drink in order to prevent dehydration; participants may also drink at will.
 - If possible, and if the weather conditions allow it, replace the activity into context, for instance by going out in a park or in town for practice
 - Plan thematic sessions: reminder of techniques for performing exercises, use of new materials, in-depth explanation of a new exercise (objectives, names of the muscles involved, etc)
 - Have some sessions with music
 - Allow time at the end of each session for sharing experience and enjoyment
 - When going from isolated motor acts to global acts, link with activities of daily living to foster integration of exercise into routine lifestyle
- for instance: “picking a travel bag from the floor to put it on top of the wardrobe” combines two exercises: knee bends (standard squat) and overhead shoulder press

Individualised home-based exercises:

Home sessions support the group sessions and are part of a comprehensive message aimed at reducing sedentary behaviour (for example, they can be complemented by encouraging participants to walk 30 min a day)

Objectives:

- Promote the intrinsic adherence to a global ‘management’ project
 - Optimise subject’s adherence to methods used in the group training
 - Do not reduce the intervention to a once-weekly appointment, but develop the idea of a constant engagement in the project
 - Prevent sedentary behaviour
- The home sessions should provide support for the group session exercises based on the above objectives.

Frequency:

One full session per week should be recommended throughout the duration of the intervention.

Implementation:

The introduction of individual support sessions occurs in 3 steps:

1. Learning the exercises in the group sessions:

In the first cycle, the first fifteen minutes of each session is devoted to the explanation, execution and repetitions of the exercises with the group. After 2-3 weeks of familiarising participants with the exercises supervised by an instructor, the participants will be asked to start individually executing some of them at their home.

A fact sheet of the exercises, also used to record their execution, is given to each participant individually.

2. Progression (increase in intensity): variety of techniques, number of repetitions and sets; as prescribed individually

3. Identifying the techniques as ‘individualised support exercises’, and instilling them in the participants’ lifestyle. The aim is to create an effective session that is not perceived as a constraint. For this reason, exercises are presented in a particular timeline that promotes memorisation as well as adherence.

Appendix 4b: Selected pictures of live exercise sessions



