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# The ‘Ossébo’ intervention for the prevention of injurious falls in elderly women: background and design

Patricia Dargent-Molina<sup>1,2</sup>, Fabienne El Khoury<sup>1,3</sup> and Bernard Cassou<sup>4</sup>

### Abstract:

This paper reviews the literature that contributed to the design of the ‘Ossébo’ intervention and describes the study that is underway.

**Background:** Falls and fall-related injuries are a major cause of morbidity and mortality among older people. Extensive research into falls prevention has established physical exercise as an efficient method to reduce falls, but the effect of exercise on serious injuries caused by falls remains unclear. Moreover, populations that would benefit most from these interventions, as well as factors that determine adherence to exercise remain underreported.

**The Ossébo intervention:** ‘Ossébo’ is an on-going multicenter randomized controlled trial, aiming to assess the effect of a two-year community-based group physical exercise program on the prevention of falls among women aged 75–85 years old. The primary outcome examined is the rate of falls and injurious falls: secondary outcomes include functional capacities, fear of falling and quality of life. This study will help determine the effectiveness of a large scale falls prevention program and the factors that can potentially assist its success. (Global Health Promotion, 2013; 20 Supp. 2: 88–93).

**Keywords:** physical activity, prevention, elderly

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## Background

Falls and fall-induced injuries are among the most serious and common medical problems facing elderly persons (1–4), and ageing of the population will further raise their burden and costs unless effective prevention measures are largely implemented. One in three people aged 65 years or older living in the community fall at least once a year: this proportion increases to one in two for those over 80 years (1). Falls can result in injuries, the most common of which are fractures, or loss of confidence which can progressively lead to decreased activity, functional deterioration, depression and social withdrawal (5). The reduction in mobility and independence are often serious enough to result in admission to a nursing home or even premature death (4,6).

Up until recently, research into fracture prevention has mainly focused on the prevention and treatment of osteoporosis. Several clinical scores have been proposed to identify subjects at high risk of low bone mineral density and fracture who should be treated (7–11). However, most fractures in the population occur in persons who are at moderate risk and do not have a very low bone mineral density for their age (12,13). This implies that, although a ‘high risk’ prevention strategy based on bone-acting pharmaceutical treatments is important, it will not be sufficient to significantly reduce the population burden of fractures. Additional effective preventive measures more widely applicable in the population are needed (4,14,15). In this respect, an intervention aimed at preventing falls may be particularly useful.

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Indeed, most fractures in the elderly are the consequence of a fall, and fall-related factors have been shown to be significant predictors of the risk of fractures in the elderly (13,16,17).

Researchers on falls prevention have been very active in the past two decades. Trials and systematic reviews (18–23) now provide clear evidence that falls in older people can be prevented with appropriately-designed intervention programs. The recently-updated Cochrane systematic review (18) concluded that exercise interventions reduce the rate of falls (i.e. number of falls per person-years) and risk of falling (i.e. number of people who fall) by up to 35–37%. Although many risk factors for falls have been identified (1,3), intervention trials have found that the size of falls prevention effects from exercise as a single intervention are comparable to those from multifaceted interventions (18,24). Therefore, widespread implementation of exercise as a single intervention seems to be the best approach to falls prevention at a population level.

However, not all types of exercise programs are effective. Current evidence indicates that for exercise programs to successfully prevent falls they should target balance and gait (18,19,22) and include progressively challenging balance exercises that are performed while standing and with minimal upper body support (19). The Cochrane review indicates that multiple component programs that include other activities (e.g. muscle strength/resistance, flexibility) in addition to balance/gait training are the most effective. Tai chi interventions have also been shown to be an effective exercise intervention when delivered to community-residing older adults. However, more general physical activities, such as walking, have not demonstrated any significant efficacy in reducing fall rates or risk (18,19).

Both home-based and group-based programs have been shown to prevent falls. Home exercises are most suitable for a frail and less mobile population without easy access to transport, such as people aged over 80. These exercises are safe if properly established by a trained therapist. For instance, the home-based Otago Exercise Programme has been shown to reduce rates of falls by 35% in older women aged 80 years or older (25). It involves five home visits from a physiotherapist or trained nurse to teach exercises to be undertaken at home and monthly phone calls to encourage on-going adherence. Group-based training, on the other hand,

has several advantages, including social interaction, peer reinforcement and encouragement, and efficient use of the instructor's time.

The frequency and intensity of the exercise program are also important to consider. A recent meta-analysis of 44 randomized controlled trials (19) showed a greater effect for programs that included a higher dose of exercise, i.e. more than 50 hours of exercise over the trial period which would equate to training classes twice weekly for six months or once weekly for one year. This finding has important implications for service delivery, because many 'balance/fall prevention' group-based programs are offered for shorter periods than this, typically for 10 weeks.

Further research is needed to determine which subgroups of the elderly population will benefit most from a fall exercise intervention (21,26). Is it the older adult who is at higher or lower level of fall risk? In the case of exercise interventions that include multiple categories of exercise, the Cochrane review indicates that fall rates can be lowered whether the older adults are at higher or lower risk for falls at baseline (18). To our knowledge, only one research group examined the effect of the same exercise intervention, the Otago home-based program, in different subgroups with different falling risk levels (27). The authors reported that the program was significantly more effective in those aged 80 and older than in younger trial participants (aged 65–79 years). The program was equally effective in reducing fall rates in those with and without a previous fall. However, since participants reporting a fall in previous year had a higher fall rate, the program resulted in a higher absolute reduction of falls and injuries when offered to those with a history of a previous fall. In a community-based public health approach, the selection of the target population must be based on simple criteria (age, sex, a history of fall or decreased performances as measured by simple functional tests easily usable by GPs) and allow the program to be offered to a large number of the 'at risk' population (26,28).

The mechanisms by which physical exercise prevents falls need to be understood better so that we can define the most effective programs. Programs that have been successful in decreasing fall risk generally showed improvement in some components of physical fitness, in particular balance and reaction time. However, physical exercise could also act by

restoring self-confidence (decreasing fear of falling), by improving mental health status and feeling of well-being or by increasing general activity level. The effect of successful interventions on these potential 'intermediate' variables has rarely been reported. Furthermore, the impact of a fall exercise intervention in terms of quality of life has been questioned (29).

For long-term benefit, it is important that subjects continue to practice regularly because the benefit wears off rapidly when exercise is discontinued. Low compliance rates may explain, at least partly, the absence of effect in some trials. There are limited data to understand what factors promote or check initial uptake of exercise as well as long-term compliance. It is evident that programs that place emphasis on pleasure, conviviality and social interaction and that foster a climate of confidence are more attractive and more likely to maintain subjects' motivation over time. Easy access to the exercise center is certainly another important factor for the elderly. A study aimed at determining the socio-demographic and health profile of those subjects who continue to exercise over the long run would also be useful not only to help design optimum programs but also to identify subgroups that deserve particular attention and efforts (26).

Yet, the essential question that remains today concerns the effectiveness of exercise in protecting against the most serious falls such as those accompanied by fractures (4,26,30). Some observational data suggest that while the highest functioning and more active older people have the lowest fall risk, they are more likely to sustain serious injuries when they do fall (31,32), maybe because they engage in higher-risk activities and fall with a higher energy. Hence, the effect of exercise on injury prevention may be less than expected. On the other hand, it is likely that regular practice with structured exercises aimed at improving strength, reaction time and coordination in addition to balance, will improve the efficacy of a person's protective responses during a fall (such as extending the arm to break the impact of the fall) as well as the thickness of local shock absorbers (like muscles), two key determinants of fracture risk, particularly for hip fracture. Furthermore, adequately designed programs may help people become more conscious of their capacities and limits, and help them develop strategies to effectively compensate while avoiding

dangerous situations, which should also contribute to decrease the risk of fall-related injury. Most randomized controlled trials are underpowered to detect a significant reduction in injurious fall rates owing to the relative infrequency of injurious fall events (22,26,33). Some studies suggest a reduction of falls causing injuries parallel to the reduction of overall falls (26,27,34,35). However, definitions of injuries varied a lot from one study to another, and often included relatively mild injuries such as bruises or scratches.

### The 'Ossébo' intervention trial

With the above issues in mind, we have set up a large-scale multicenter randomized controlled trial, the 'Ossébo' study, to assess the effect of a group-based physical exercise program targeting balance, gait, strength and coordination on the prevention of injurious falls. Additional objectives of the study are to improve our understanding of the mechanisms by which physical training helps to reduce falls and injuries, and to identify the socio-demographic and health-related individual factors that are associated with uptake and long-term adherence to the program. The target population were women, aged 75–85 years old, who lived at home but had diminished balance and gait capacities, i.e. a subgroup of the elderly population at higher risk of fractures and other fall-related injuries.

A total of 706 participants were recruited between December 2007 and April 2011 in 20 study centers located in medium to large cities throughout France. Voter registration lists were used to invite all women aged 75–85 years who lived near study centers to a 'balance health examination' that included a battery of well-standardized tests of balance and motor capacities. Selection for the intervention trial was then based on gait speed and ability to do four steps with feet in tandem position (tandem walk). These two tests have been chosen because they have been validated with regard to the prediction of hip fracture (one of the most serious fall-induced injury) in the EPIDOS (*Epidemiologie de l'Ostéoporose*) French cohort of 7500 women aged 75 years or older that had been recruited from voter registration listings like the Ossébo cohort (13). However, in case the benefit of the intervention is demonstrated, we will be able to assess whether the same effect is observed in different subgroups defined using other

tests and criteria recommended in clinical practice to identify older people at risk of falling (for example: previous fall, get-up-and-go test, one-leg stance, aged 80 or more).

Frailer women, i.e. women who had a particularly slow gait speed (below the 95<sup>th</sup> percentile in the EPIDOS cohort) or who were unable to stand for 10 sec with feet together, were excluded from the trial because they are at high risk of falling and would probably require individualized exercises. In other words, we included into the trial women who were 'not too fit and not too frail'.

Women with a substantial alteration in cognitive function (as assessed with the Pfeiffer test), a degenerative condition such as Parkinson's disease, or a medical conditions involving the neuromuscular, skeletal or cardiovascular system that generally precludes exercising, and women who were already taking exercise classes have also been excluded from the trial.

Eligible women who agreed to participate into the trial were randomized into one of two groups: a group that received the intervention and a control group without intervention.

Women from both groups received a summary of their test results and general advice regarding the prevention of falls and fractures based on recommendations from *Institut national de prévention et d'éducation pour la santé* (Inpes, French National institute for prevention and health education) and *Groupe de Recherche et d'Information sur les Ostéoporoses* (GRIO).

Women allocated to the intervention group were invited to attend exercise sessions in small groups of 10–15 persons, supervised by an instructor specialized in physical training for the elderly and specifically trained for the study. The participants take one class a week, an hour per class, for two years.

After a 5–10-min warm-up period including stretching of the major muscle groups, the participants are given various types of exercises such as:

- Exercises that help them become aware of the importance of the eye position, and of foot-eye coordination for balance and gait.
- Exercises designed to relax the trunk and arms with the aim to become conscious of the importance of axial tonicity and of the arms role in maintaining balance.

- Exercises involving variations of the base of support under static and dynamic balance conditions.
- Exercises designed to sharpen plantar sensations, and acquire a good foot unfolding movement on the ground.
- Going through a circuit while dealing with interfering elements.
- Movements of transfer in various directions (front-back, lateral) as well as in rotation.
- Muscle strength training exercises and improvement of muscle tonicity; use of repeated movements of short duration ensuring loading of major fracture sites (femur, spine, wrist, etc).
- Posture verticalization through lowering of the center of gravity, 'grounding', and straightening of the vertebral column.

Throughout the class, the instructor gives advice relevant to situations in everyday life (such as sitting or rising from a chair or bed, picking up an object on the floor, etc). The last phase of the class consists of a 10 min cool-down period involving gentle stretches, relaxation and controlled breathing. At the end of the class, an informal discussion time allows participants to talk about the problems they encountered during the session.

Implementation of the program is progressive to avoid discomfort and pain, with priority given to long-term activity maintenance rather than intensity. Although following a core theme, the exercise classes are adapted to the functional capabilities of the participants (for instance, by adapting the number of movement repetitions).

To complete the group sessions, the participants are encouraged to practice regularly at home, with a simple routine based on the class exercises and adapted by the instructor to each participant's physical ability.

The intervention is implemented in partnership with the association Siel Bleu ([www.sielbleu.org](http://www.sielbleu.org)) that is specialized in training of older adults and is largely present in most regions of France. The content of the exercise program has been developed based on the extensive experience of the two managers of Siel Bleu in training older adults in diverse settings and populations, on the published description of successful programs and

after direct contacts with some of the leader investigators in the field (25,28,35).

Fall occurrence among all trial participants is monitored during two years by asking women to return monthly pre-paid pre-addressed calendar cards where they can mark the date of any falls. In case a fall is reported, a telephone interview is carried out to confirm the fall and to gather information on its circumstances and consequences (follow-up rates close to 90%). Falls are defined as 'unintentionally coming to rest on the ground, floor, or other lower level' (36). There is currently no consensus on the definition of an injurious fall to be used as an outcome in randomized controlled fall prevention trials. We intend to use various falls classification schemes, in particular the one of Campbell (which has been used most frequently in past exercise trials) and the one recently proposed by Swenk and colleagues from the PROFANE (Prevention of Falls Network Europe) group (33). Using the Campbell's definition, for instance, fall events are classified as resulting in (i) serious injury if the fall resulted in a fracture or admission to hospital with an injury or required stitches (sutures); (ii) 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; and (iii) no injury. For our sample size calculation, we had used a slightly modified version of the Campbell classification where bruises, sprains, cuts and abrasion that did not lead to medical care or any functional limitation were classified in the 'minor or no injury' category. Using this classification, we have calculated that we will have a statistical power of 80% (risk alpha 5%) to detect a 25% reduction in serious and moderate injuries assuming a 30 per 100 incidence rate in the control group (13,27) and a 10% drop out rate.

The investigator classifying fall events will be blind to group allocation. Serious injuries are confirmed from hospital and general practice records.

The main results regarding the effect of the intervention on serious falls are expected in 2013 (after all participants would have been followed for two years). To better understand how the intervention 'works', participants are reviewed at one and two years to assess changes in physical motor capacities, fear of falling, physical and social activity level,

perceived health and well-being. As of today, 580 women have been reviewed at one year, and 379 at two years (response rates around 85%).

## Expected results

The group intervention that we propose to assess is relatively simple to implement. It relies on a network of participants already established across France. In the case of a demonstrated benefit it could therefore be easily generalized as part of a population-based public health program of falls and fractures prevention in the elderly. Results of the Ossébo study should also contribute to better understand the determinants of compliance and to better define subjects who would benefit most from the intervention and, therefore, who should be targeted in priority. The intervention should enable elderly women to preserve two elements essential to their quality of life as they age, that is, their functional capacity and their independence. It may also lead to a global improvement in their health status since physical exercise can have beneficial effects on other aspects of health.

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## Conflict of interest

None declared.

## References

1. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med*. 1988; 319: 1701–1707.
2. Sattin RW. Falls among older persons: a public health perspective. *Annu Rev Public Health*. 1992; 13: 489–508.
3. Dargent-Molina P, Bréart G. [Epidemiology of falls and fall-related injuries in the aged]. *Rev Epidemiol Sante Publique*. 1995; 43: 72–83.
4. Kannus P, Sievänen H, Palvanen M, Järvinen T, Parkkari J. Prevention of falls and consequent injuries in elderly people. *Lancet*. 2005; 366: 1885–1893.
5. Vellas BJ, Wayne SJ, Romero LJ, Baumgartner RN, Garry PJ. Fear of falling and restriction of mobility in elderly fallers. *Age Ageing*. 1997; 26: 189–193.

6. Tinetti ME, Williams CS. Falls, injuries due to falls, and the risk of admission to a nursing home. *N Engl J Med.* 1997; 337: 1279–1284.
7. Black DM, Steinbuch M, Palermo L, et al. An assessment tool for predicting fracture risk in postmenopausal women. *Osteoporos Int.* 2001; 12: 519–528.
8. Dargent-Molina P, Piauxt S, Bréart G. A comparison of different screening strategies to identify elderly women at high risk of hip fracture: results from the EPIDOS prospective study. *Osteoporos Int.* 2003; 14: 969–977.
9. Dargent-Molina P, Piauxt S, Bréart G. A triage strategy based on clinical risk factors for selecting elderly women for treatment or bone densitometry: the EPIDOS prospective study. *Osteoporos Int.* 2005; 16: 898–906.
10. Kanis JA, Oden A, Johnell O, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int.* 2007; 18(8): 1033–1046.
11. Trémollières FA, Pouillès J-M, Drewniak N, Laparra J, Ribot CA, Dargent-Molina P. Fracture risk prediction using BMD and clinical risk factors in early postmenopausal women: sensitivity of the WHO FRAX tool. *J Bone Miner Res.* 2010; 25: 1002–1009.
12. Stone KL, Sealey DG, Lui LY, et al. BMD at multiple sites and risk of fracture of multiple types: long-term results from the Study of Osteoporotic Fractures. *J Bone Miner Res.* 2003; 18: 1947–1954.
13. Dargent-Molina P, Favier F, Grandjean H, et al. Fall-related factors and risk of hip fracture: the EPIDOS prospective study. *Lancet.* 1996; 348: 145–149.
14. Järvinen TLN, Sievänen H, Khan KM, Heinonen A, Kannus P. Shifting the focus in fracture prevention from osteoporosis to falls. *Brit Med J.* 2008; 336: 124–126.
15. Martin FC. Next steps for falls and fracture reduction. *Age Ageing.* 2009; 38: 640–643.
16. Nguyen T, Sambrook P, Kelly P, Jones G, Lord S, Freund J, et al. Prediction of osteoporotic fractures by postural instability and bone density. *Brit Med J.* 1993; 307: 1111–1115.
17. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. *N Engl J Med.* 1995; 332: 767–773.
18. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev.* 2009; CD007146.
19. Sherrington C, Whitney JC, Lord SR, Herbert RD, Cumming RG, Close JCT. Effective exercise for the prevention of falls: a systematic review and meta-analysis. *J Am Geriatr Soc.* 2008; 56: 2234–2243.
20. Chang JT, Morton SC, Rubenstein LZ, et al. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ.* 2004; 328(7441): 680.
21. Rose DJ, Hernandez D. The role of exercise in fall prevention for older adults. *Clin Geriatr Med.* 2010; 26: 607–631.
22. Province MA, Hadley EC, Hornbrook MC, et al. The effects of exercise on falls in elderly patients. A preplanned meta-analysis of the FICSIT Trials. Frailty and injuries: cooperative studies of intervention techniques. *JAMA.* 1995; 273: 1341–1347.
23. Campbell AJ, Robertson MC. Comprehensive approach to fall prevention on a national level: New Zealand. *Clin Geriatr Med.* 2010; 26: 719–731.
24. Campbell AJ, Robertson MC. Rethinking individual and community fall prevention strategies: a meta-regression comparing single and multifactorial interventions. *Age Ageing.* 2007; 36: 656–662.
25. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Tilyard MW, Buchner DM. Randomised controlled trial of a general practice programme of home based exercise to prevent falls in elderly women. *BMJ.* 1997; 315: 1065–1069.
26. Gardner MM, Robertson MC, Campbell AJ. Exercise in preventing falls and fall related injuries in older people: a review of randomised controlled trials. *Br J Sports Med.* 2000; 34: 7–17.
27. Robertson MC, Campbell AJ, Gardner MM, Devlin N. Preventing injuries in older people by preventing falls: a meta-analysis of individual-level data. *J Am Geriatr Soc.* 2002; 50: 905–911.
28. Skelton DA, Beyer N. Exercise and injury prevention in older people. *Scand J Med Sci Sports.* 2003; 13: 77–85.
29. Laybourne AH, Biggs S, Martin FC. Falls exercise interventions and reduced falls rate: always in the patient's interest? *Age Ageing.* 2008; 37: 10–13.
30. Karlsson M. Does exercise reduce the burden of fractures? A review. *Acta Orthop Scand.* 2002; 73: 691–705.
31. Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: a review of the epidemiologic evidence. *J Am Geriatr Soc.* 2000; 48: 883–893.
32. Speechley M, Tinetti M. Falls and injuries in frail and vigorous community elderly persons. *J Am Geriatr Soc.* 1991; 39: 46–52.
33. Schwenk M, Lauenroth A, Stock C, et al. Definitions and methods of measuring and reporting on injurious falls in randomised controlled fall prevention trials: a systematic review. *BMC Med Res Methodol.* 2012; 12(1): 50.
34. Lin MR, Hwang HF, Wang YW, Chang SH, Wolf SL. Community-based tai chi and its effect on injurious falls, balance, gait, and fear of falling in older people. *Phys Ther.* 2006; 86: 1189–1201.
35. Barnet A, Smith B, Lord S, Williams M, Baumand A. Community-based group exercise improves balance and reduces falls in at-risk older people: a randomised controlled trial. *Age Ageing.* 2003; 32: 407–414.
36. Buchner DM, Hornbrook MC, Kutner NG, et al. Development of the common data base for the FICSIT trials. *J Am Geriatr Soc.* 1993; 41: 297–308.

# Erratum

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Owing to errors made at SAGE, the article ‘The ‘Ossébo’ intervention for the prevention of injurious falls in elderly women: background and design’ by Patricia Dargent-Molina, Fabienne El Khoury and Bernard Cassou, *Global Health Promotion*, Volume 20, Supp. 2, June 2013, pp. 88–93, DOI: 10.1177/1757975913483341, appeared with incorrect author affiliations.

SAGE apologizes to the authors and readers for any inconvenience or embarrassment caused. The correct author details and affiliations should have appeared as follows:

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