

## NEWS

### Multifactorial Interventions to Prevent Falls: Is There Reason to Doubt Their Effectiveness?

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Multifactorial falls intervention programs, in which the risk factors for falling are first assessed and then targeted with specific interventions to reduce those risk factors, seem like an eminently reasonable approach to preventing falls among elderly individuals living in the community. Indeed, because there are multiple risk factors for falling, it makes sense to identify as many risk factors as possible and then to implement preventive programs to improve the risk factor profile. For the osteoporosis field, a tantalizing goal of a falls prevention program would be to prevent fractures, a worthy aim since the overwhelming majority of hip fractures, for instance – more than 90% of them, in fact – result from falls.

What seems straightforward in theory, however, has sometimes been a bit more difficult to demonstrate in practice. For example, one of the more recent systematic reviews and meta-analyses of multifactorial intervention programs, published earlier this year in the *British Medical Journal* (1), found that these programs were less effective in reducing the number of fallers than previous reviews had found. In fact, the authors of the paper even wrote that their analysis “found little evidence to support the effectiveness of multifactorial interventions to prevent falls and injuries in older people in community and emergency care settings.”

Falls prevention experts, however, do not appear overly concerned by such recent findings and actually remain confident in the evidence that falls can in fact be prevented through multifactorial interventions. “Although there has been a lot of debate recently about the effectiveness of multifactorial interventions in preventing falls, it's really important to remember that

the weight of the evidence is almost as good as that for statins and anti-hypertensives for the prevention of heart disease,” says Mary Tinetti, a professor of medicine at Yale University School of Medicine. First author of a landmark clinical trial published in the *New England Journal of Medicine* in 1994 that demonstrated for the first time that a multifactorial falls intervention program could reduce the risk of falling in elderly individuals living in the community, Dr. Tinetti estimates falls risk reductions from multifactorial interventions of about 25-30%, a good result for prevention studies, she says.

In fact, the majority of the falls prevention experts who spoke to *BoneKEy* believe that the findings from the meta-analysis more likely reflect problems inherent to meta-analyses themselves, rather than problems in the rationale or effectiveness of the multifactorial intervention programs. “In general, these multifactorial falls prevention studies have had many between-studies differences and limitations to be fairly and reasonably included in one meta-analysis,” wrote Pekka Kannus in an email interview with *BoneKEy*. “A meta-analysis may therefore easily sink one or two good trials and their promising results into a mesh of insignificant results from several poor trials,” according to Dr. Kannus, a professor at Tampere University Hospital in Finland who along with colleagues argued recently in the *BMJ* that the osteoporosis field, in its focus on treating low bone mineral density, has neglected falls prevention to the field's great detriment (2).

But what distinguishes an effective multifactorial falls intervention from an ineffective one? And how should clinical trials be designed to test how well these

programs work? In their discussion of these issues, falls prevention experts reveal the complexities, challenges and opportunities facing their field.

### **Assessment and Intervention Quality, and the Strength of the Evidence**

One of the factors most often cited by experts that separates well-conducted falls interventions from poorly run ones is that in the former, not only are risk factors thoroughly and accurately assessed, but interventions are then matched appropriately to the risk factors. "If you do a fairly quick review of risk factors, and if you don't link the findings of that risk factor assessment to intensive interventions, it's not surprising that you don't find much of an effect," says Robert Cumming, a professor of epidemiology and geriatric medicine at Concord Hospital at the University of Sydney and a co-author of the last Cochrane Review on interventions for preventing falls in the elderly. As Dr. Cumming explains, what this means is that for an individual who has problems with vision, the intervention should be one that works to improve vision; for someone who has lower limb muscle weakness, working to improve balance and muscle strength through exercise makes more sense than sending the person to the eye doctor.

Fall experts also emphasize, however, that a successful linking of the intervention to the risk factor must go beyond simple referral. For instance, Dr. Cumming notes that referring the person with poor vision to a local optometrist is less likely to be effective than ensuring that the person see an optometrist in an adjacent office, and immediately. "The evidence is very weak for just the referral," Dr. Tinetti agrees, emphasizing that the most effective interventions are ones where the researchers who are evaluating the risk factors also themselves implement the interventions.

If the falls risk factor assessments and interventions are carried out appropriately, do multifactorial interventions actually prevent falls? The consensus answer from

falls prevention experts is a confident yes, at least for interventions targeted towards individuals living in the community (the evidence for the effectiveness of interventions in hospitals and nursing homes is not as convincing, according to Dr. Cumming). The study cited most often as providing the strongest evidence is Dr. Tinetti's 1994 study. In that trial, risk factors for falling, including use of medications such as sedatives, the presence of environmental hazards in the home, impairments in gait, balance and muscle strength, deficiencies in transfer skills (e.g., difficulty in moving from a bed to a chair) and postural hypotension were assessed by a nurse and physical therapist, and interventions including medication review and education, removing hazards from the home, gait training and exercise, training in transfer skills, and other behavioral recommendations were then implemented. Results from the 300 HMO subjects followed in the study revealed statistically significant reductions in the proportion of subjects who fell (35% vs. 47%) and in the incidence of falls (adjusted incidence-rate ratio of 0.69, 95% CI 0.52 to 0.90) in the intervention group compared to the control group. In a second widely-cited study by Jacqueline Close and colleagues, published in the *Lancet* in 1999, statistically significant reductions in the risk of falling and in the risk of recurrent falling were found in the approximately 400 subjects who completed the study. Subjects in the intervention group received medical assessment of vision, balance, cognition, affect and prescribing practice, as well occupational therapy assessment of home environmental hazards, with interventions aimed at modifying those risk factors.

The studies by Dr. Tinetti and Dr. Close, as well as a clinical trial by Edward Wagner published in 1994, are cited as the 3 key pieces of research that jumpstarted the falls prevention field. While there remains uncertainty about which components, or combination of components, of multifactorial interventions reduce falls risk, the single interventions that have been included within multifactorial intervention studies that are now viewed as being the most effective include exercise that improves strength and

balance; cataract removal surgery; home safety assessment by an occupational therapist and then interventions to make homes safer in very frail elderly people; and a reduction in the use of psychotropic drugs.

While the clinical picture appears reasonably clear to most experts, the view from a more research-oriented angle is a bit fuzzier, according to Sallie Lamb, a co-author of the *BMJ* meta-analysis and of the Cochrane Review who has experience on both the research and clinical sides of falls prevention. Like other falls experts, when asked about the best clinical approach to preventing falls, Lamb, a professor of rehabilitation at the University of Warwick in England, points to the earlier work done in the 1990s. "If I'm thinking, as a clinician, about what is the best thing to do, the Tinetti study is the best piece of evidence from a single, well-conducted trial that exists," says Professor Lamb. However, from her perspective as a researcher, she is more cautious, noting that while there have been scores of falls intervention trials, many of them, particularly because of their small size, are not convincing to her, including some recent, very well-designed trials that have found little effect on preventing falls. "We don't have a huge evidence base of large, well-conducted studies, so there is uncertainty that exists," she says. "This uncertainty isn't saying that multifactorial fall prevention programs do or don't work, but rather we're not certain how well they work."

One factor cited by some experts to explain why more recent trials may not have found an effect of multifactorial interventions is that the usual standard of care for elderly people at risk of falling has improved, thus making it more difficult to demonstrate effects of interventions. Geographic variation in health care systems that determines how interventions are delivered could also explain variability in study findings. Nevertheless, to Dr. Tinetti, the big picture remains quite clear. "We're quibbling about things that aren't as important as the fact that the overwhelming amount of evidence suggests that we can prevent falls."

### **Is Two (or Three, or Four) Really Better Than One?**

This is not to say that no other questions remain in the falls prevention field – quite the contrary. One of the questions that falls prevention experts John Campbell and Clare Robertson are hoping to open up for debate is whether a single intervention might actually be preferable to a multi-factorial intervention, at least for a public health approach targeting community populations at risk of falling. While multifactorial interventions are effective and necessary for individual patients, they may be more expensive than single interventions and therefore less appropriate from a public health perspective, where the goal is to reach as many people at risk as possible.

One of their hypotheses is that multifactorial interventions may be too complicated to follow, with an overload of potentially conflicting information coming from too many sources. "There's always a danger that the person is either going to be confused by the amount of advice they are getting or to opt for the intervention that looks most simple and easiest to institute," says Professor Campbell, a professor of geriatric medicine at the Dunedin School of Medicine at the University of Otago in New Zealand. Professor Campbell and Professor Robertson have in fact found some evidence to support this view. In a clinical trial they published in the *BMJ* in 2005, two interventions were implemented for individuals who had visual impairments: a home safety program delivered by an occupational therapist, and an exercise program delivered by a physical therapist. They found that the home safety program was less effective in preventing falls when used together with the exercise program.

They suspect that contradictory messages may explain this unexpected finding. According to Professor Campbell and Professor Robertson, on the one hand, by advocating exercise, the physical therapist is encouraging individuals to take on a bit of risk by increasing their physical activity. On the other hand, by advocating safety in the home, the occupational therapist is

encouraging people to be more cautious by decreasing their activity. "These conflicting messages may explain why we observed an interaction between the two interventions in this particular trial," says Professor Robertson, an associate professor also at the Dunedin School of Medicine. Professor Campbell and Professor Robertson have also performed a meta-regression of falls prevention interventions and found that single interventions were as effective as multiple interventions in reducing falls (3).

### Outcomes

Another topic on the minds of falls prevention experts when asked about the *BMJ* meta-analysis concerns the most appropriate outcome measure that clinical trials of multifactorial interventions should report. Traditionally, falls prevention studies have compared numbers of fallers between intervention and control groups. However, experts now advocate comparing not numbers of fallers but rather numbers of falls between the two groups. "There's a reasonable consensus now that that's the superior way," says Stephen Lord, an expert on randomized clinical trials of falls prevention and a professor at the Prince of Wales Medical Research Institute in Sydney, Australia.

There are several reasons to prefer this approach. One that Professor Lord mentions is that in a clinical trial, some people might only fall once, while others might fall numerous times, important information that will be lost when only considering numbers of fallers. Research has also shown that people who fall more than once are most likely to benefit from interventions. According to Professor Campbell, another reason to focus on falls is that it is the falls themselves that actually cause the damage. In addition, measuring falls rather than fallers has the advantage that the number of the former will be greater than that of the latter, which will make it more likely for studies to detect significant effects of interventions. Unlike the *BMJ* meta-analysis, which reported numbers of fallers, Professor Campbell notes that the recent meta-analysis he performed with Professor

Robertson used the number of falls as the outcome measure and in doing so did in fact reveal the effectiveness of falls intervention programs (3).

While there is widespread agreement that measuring numbers of falls is the best tactic, there is also unanimity that the most pressing issue in the falls prevention field concerns another outcome that will be of great interest to osteoporosis experts: does preventing falls actually prevent fractures? The primary hindrance to answering this question is that very large studies are needed to detect an impact on fractures; most studies of falls interventions have been too small to detect an effect. For instance, the largest study in the *BMJ* meta-analysis included just 1,242 participants, while many other studies have included only 200 or 300 participants. Professor Lamb notes that one tactic to overcome this limitation is to measure effects of falls intervention programs on soft tissue injuries, but because definitions of these injuries vary from study to study, results are hard to interpret.

A second obstacle that has hampered efforts to understand whether multifactorial interventions prevent fractures is the difficulty in finding funding for the necessary studies. Unable to secure pharmaceutical company support for falls prevention trials, falls experts are left to rely on public funding for their research, making larger, more expensive studies, of the sort that will have sufficient power to detect an impact on fractures, less likely to happen. Nonetheless, it remains the goal. "If we want to make steps forward to joining up the falls prevention and bone health agendas, we have to start using peripheral fractures as an endpoint," Professor Lamb stresses.

### Two Different Worlds

Historically, those agendas have been quite separate: geriatricians have focused on falls, while endocrinologists have focused on bones. While this situation has started to improve over the past 5 years or so, with examples of interaction between falls authorities and bone health specialists,

experts in both areas say that the fields are often still far apart, with not enough cooperation between the two.

However, the increasing interest by the osteoporosis field in clinical risk factors that go beyond BMD *per se*, stimulated by the advent of the FRAX™ fracture algorithm, may make bone experts more likely to be interested in falls, which are in fact an independent risk factor (and actually the strongest risk factor) for fracture. While not all fracture risk prediction tools have excluded falls as a risk factor, thus far FRAX™ has.

"We excluded falls risk in FRAX™ because we weren't quite sure whether patients who had falls risk as part of their risk for fracture would be equally responsive to a bisphosphonate," explains Eugene McCloskey, a senior lecturer in metabolic bone disease at the University of Sheffield in England. In an abstract presented at the recent ECTS meeting in Barcelona, Dr. McCloskey and colleagues found that the bisphosphonate clodronate was equally effective in subjects who had difficulty in rising from a chair (which is a surrogate marker of falls risk), and concluded that, if these findings can be replicated with other agents, falls risk factors could be incorporated into risk assessment tools like FRAX™.

What might this mean from a clinical perspective, for physicians who treat osteoporosis? Dr. McCloskey says that a patient who is at high risk of fracture according to a FRAX™ calculation will have an even higher risk of fracture than indicated by FRAX™ if he or she is also a faller. In this situation, if further studies, examining other bisphosphonates, can replicate Dr. McCloskey's findings with clodronate, doctors could feel confident that a bisphosphonate will still be effective, but should also, at the same time, work to reduce the patient's falls risk, by sending the patient to a falls clinic, for instance; a focus on both bone health and falls is appropriate and necessary.

If the advent of FRAX™ might help bring the bone and falls fields closer together, another opportunity for collaboration may lie further in the future, with studies designed to look at the combined effects of falls intervention programs and bone health agents. But first things first: experts in both areas are still awaiting definitive word on whether multifactorial falls intervention programs prevent fractures.

## References

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