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## Summary

To fall (verb): I. To descend freely (primarily by 'weight' or gravity): opposed to 'rise'. II. To sink to a lower level: opposed to 'rise'. III. To lose the erect position (primarily with suddenness): opposed to 'stand'. IV. To move precipitately or with violence; to rush. Obs. exc. combined with preps., as in to fall upon, to assault (see branch X). to fall about (a person's) ears: to assail suddenly with blows. V. To be determined to a specified position or object; to have a certain incidence. VI. To come casually, or without design or effort, into a certain position. VII. To pass suddenly, accidentally, or in the course of events, into a certain condition. VIII. To occur, come to pass, befall, result.

Bron: Oxford English Dictionary

[http://dictionary.oed.com/cgi/entry/50081894?query\\_type=word&queryword=falling&first=1&max\\_to\\_show=10&sort\\_type=alpha&search\\_id=6Rr0-HekOAY-557&result\\_place=1](http://dictionary.oed.com/cgi/entry/50081894?query_type=word&queryword=falling&first=1&max_to_show=10&sort_type=alpha&search_id=6Rr0-HekOAY-557&result_place=1)

## Prevention of falling in older persons with a high risk of recurrent falling

Falling is a major health problem in old age. About one in three persons of 65 years and older falls once per year and 15 % fall at least twice per year. The consequences of falling vary from minor injuries such as bruises and lacerations to serious injuries such as wrist or hip fractures. Also, falls may lead to fear of falling. Both the physical and mental consequences of falling may lead to decreased mobility, dependency in daily activities, an increased need for care, and finally nursing home admittance. Furthermore, previous falls is an important predictor for future falls.

Many physical, cognitive, behavioural, and environmental factors have been associated with falling and recurrent falling. Two important fall risk factors are muscle weakness and poor physical performance. Muscle weakness is seen in patients with hypercortisolism. Using data from the Longitudinal Aging Study Amsterdam (LASA), it was examined whether variations of cortisol within the normal range were associated with physical performance and changes in muscle parameters. LASA is an ongoing cohort study in a population-based sample of healthy older persons in the Netherlands. Data from the second (1995/1996) and fourth (2001/2002) cycle were used containing 1172 (65-88 years) and 884 (65-94 years) men and women, respectively. In the second cycle serum total and free cortisol were assessed; in the fourth cycle morning and evening salivary cortisol were assessed. Physical performance was measured by summing the scores on the chair stands, tandem stand, and walk tests. Appendicular skeletal muscle mass (ASMM) was measured using Dual-energy X-ray Absorptiometry (DXA) in the second cycle and three years later (third cycle). Grip strength was assessed using a handgrip dynamometer in the second, third, fourth, and fifth cycle. Regression analysis revealed that women with higher cortisol levels scored poorer on physical performance, which was mainly explained by poorer performance on the tandem stand (*Chapter 2*). Men with higher salivary cortisol scored poorer on physical performance, which was mainly explained by poorer performance on the chair stands and walk test. In addition, both morning and evening salivary cortisol were associated with loss of grip strength. Participants in the highest cortisol quartiles had a two-fold higher risk of loss of grip strength than participants in the lowest quartiles (*Chapter 3*). No relationships were found between serum cortisol, (loss of) ASMM, and (loss of) grip strength. In conclusion, high levels of cortisol were associated with poorer physical performance and a higher risk of loss of grip strength in older persons.

The effects of glucocorticoids on target tissues are mediated by the glucocorticoid receptor (GR). The ER22/23EK, N363S, 9beta, and *BclI* polymorphisms appear to be associated with altered sensitivity to glucocorticoids. We studied whether these polymorphisms mediated the associations between cortisol, muscle mass, and muscle strength. The ER22/23EK and

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N363S polymorphisms modified the relationships between serum cortisol and ASMM, and between serum cortisol and grip strength, respectively (*Chapter 3*). After stratification for the polymorphisms, the sample sizes in some of the cortisol categories were too small to detect a statistically significant association.

A third risk factor for falls is chronic diseases. High cortisol levels have been associated with several chronic diseases such as osteoporosis, diabetes mellitus, and depression. We studied the associations between both serum and salivary cortisol, mortality risk, and chronic diseases. The results varied for different cortisol measures and between men and women (*Chapter 4*). Men with high salivary morning cortisol had higher mortality risks. In addition, men with high serum cortisol had lower risks of chronic non-specific lung disease (CNSLD) and higher risks of hypertension and diabetes mellitus. In women, high salivary evening cortisol levels were associated with higher mortality risks and an increased risk of diabetes mellitus. No independent association between cortisol and the number of chronic diseases was found.

Another important risk factor for falling is physical activity. Previous studies suggest that the relationship between physical activity and fall risk may be U-shaped. We tested this hypothesis and examined whether the relationship was modified by level of physical functioning. We used data of 1337 community-dwelling persons of 65 years and older, again from the Longitudinal Aging Study Amsterdam. They reported falls for three years after baseline assessment in 1995/96. The time to first fall and time to recurrent falling (i.e. time to second fall within a 6-month period) were calculated. Physical activity was calculated in minutes per day weighted for intensity (range 0-2000). The Cox Proportional Hazards model yielded no evidence for a non-linear U-shaped association (*Chapter 5*). No association was found between physical activity and falling, but an increase in activity of 100 units led to a 4 % decrease in risk of recurrent falling. No interaction was found between physical activity and physical functioning. The hypothesized U-shaped relationship was not confirmed: the risk of recurrent falling seemed to decrease with higher levels of physical activity.

Given the high prevalence and the severe consequences of falling, preventive measures are needed. Many trials have studied the effectiveness of fall prevention strategies, but results are conflicting. The effectiveness may be higher in persons with a high risk of falling. We evaluated the cost-effectiveness of multidisciplinary assessment and treatment of fall risk factors in older persons with a high risk of falling. The study was designed as a randomised controlled trial (RCT) with an economic evaluation (*Chapter 6*). Community-dwelling persons of 65 years and older with a recent fall were screened for risk of recurrent falling using the LASA fall risk profile. Persons who had a high risk of recurrent falling were randomised into an intervention or usual care group. The intervention consisted of a multidisciplinary assessment and treatment

of multifactorial fall risk factors. The transmural multidisciplinary approach entailed close collaboration between geriatrician, family physician, physical therapist, and occupational therapist and was extended to other specialists if relevant. Participants recorded falls on a fall calendar during one year. Primary outcomes were time to first and second fall. Three, six, and twelve months after the home visit, questionnaires for the economic evaluation were completed. After one year, the secondary outcome measures were reassessed and the adherence to the interventions was evaluated. Data were analysed according to the intention-to-treat principle and compared with a per protocol analyses.

The data from this trial were also used to study the predictive validity of the LASA fall risk profile in a sample of older persons who consulted the Emergency department or family physician after a fall. For this purpose, we used the data from the participants in the low risk and usual care groups. The results show that 65 % of the recurrent fallers and non-recurrent fallers were correctly classified as high and low risk of recurrent falling (*Chapter 7*). The optimal cut-off value was 8, however, for use in clinical practice, a lower cut-off value may be more appropriate to minimize misclassification of recurrent fallers. It was concluded that in a group of older persons seeking care after a fall, the LASA fall risk profile only moderately discriminates occasional fallers from recurrent fallers.

To evaluate the effectiveness of the multidisciplinary and transmural care in older persons with the highest risk of recurrent falling, we compared the proportions of fallers and time to first and second fall in the intervention (n=106) and usual care (n=111) groups. During one year, 55 (52 %) persons in the intervention group and 62 (56 %) persons in the usual care group fell at least once, and 37 (35 %) and 35 (32 %) persons fell at least twice, respectively (*Chapter 8*). The time to first or second fall did not differ significantly between the two groups. When the participants who adhered to at least 75 % of the recommendations were compared to the participants who received usual care, again no differences in time to first or second fall were found. We concluded that multidisciplinary evaluation and treatment of fall risk factors did not lower the fall risk in persons with a high risk of recurrent falling.

Participants also reported how often they had consulted family physicians, other physicians, physical and occupational therapists, or other formal and informal caregivers, and whether they purchased aids or adaptations in the year after the presenting fall. Based on this information, costs made to prevent a new fall were estimated. We compared the costs in the intervention and usual care groups and concluded that the multidisciplinary evaluation and treatment of fall risk factors was not cost-effective in the high-risk group (*Chapter 9*). The treatment did not result in lowering the fall rate or the costs. The extra costs made to lower the percentage of fallers by 1 % were € 226 per person. If policy makers were willing to invest € 10,000, the probability that the

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treatment would be cost-effective is 80 %. At an investment of € 300,000, the probability is 30 % that the treatment will improve the quality of life.

In the General Discussion (*Chapter 10*) implications for further research and clinical practice were given. Before we can conclude that there is a relationship between cortisol, muscle mass and muscle strength, further research is necessary to confirm these associations in other studies. In the General Discussion, recommendations were given for the design of these studies.

Recently, the effectiveness of multifactorial strategies to prevent falls has been put forward for discussion. Should researchers and clinicians continue to improve these multifactorial strategies, or should we put this concept aside and focus on proven effective single factorial trials? Since only four out of ten trials on the effectiveness of multifactorial evaluation and treatment of fall risk factors in high-risk groups showed any effect on fall rate, this strategy does not seem to be effective in high-risk groups, especially in the Netherlands. In unselected groups, however, the multifactorial approach appears to be effective in programs of higher intensity. The effectiveness may be improved further by offering more supervision in the adherence to the recommendations and by expanding the multidisciplinary team. However, this will also increase the costs of the intervention. The cost-effectiveness of multifactorial strategies in unselected populations needs further investigation. Furthermore, the effectiveness of multifactorial measures in unselected populations has not been studied yet in the Netherlands.

The current evidence suggests that multifactorial interventions do not reduce the fall risk among high-risk persons. Although the burden of falling is the highest in this group, evidence for effective strategies is lacking and new preventive strategies are needed. Since the most important predictor for recurrent falling is a history of falling, primary prevention of falling is important. If the multifactorial approach can be optimized in unselected populations, the overall fall risk may be reduced and fewer persons may develop a high risk of recurrent falling. However, given the rise in number of older persons, it does not seem feasible to treat every older person and therefore the question remains: who should we treat?